Projeto Praça Onze
Universidade Federal do Rio de Janeiro

Post-Sexual Exposure Prophylaxis (nPEP)

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Reducing HIV Infections

Antiretrovirals for Prevention

Uninfected Person

- PrEP
- PEP
- Treatment as prevention
- Drug use behavior change
- Condom use
- Sexual behavior change
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REDUCTION OF MATERNAL–INFANT TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS TYPE 1 WITH ZIDOVUDINE TREATMENT

Edward M. Connor, M.D., Rhoda S. Sperling, M.D., Richard Gelber, Ph.D., Pavel Kiselev, Ph.D., Gwendolyn Scott, M.D., Mary Jo O’Sullivan, M.D., Russell VanDyke, M.D., Mohammed Bey, M.D., William Shearer, M.D., Ph.D., Robert L. Jacobson, M.D., Eleanor Jimenez, M.D., Edward O’Neill, M.D., Brigitte Bazin, M.D., Jean-François Delfraissy, M.D., Mary Culnane, M.S., Robert Coombs, M.D., Ph.D., Mary Elkins, M.S., Jack Moya, M.D., Pamela Stratton, M.D., and James Balsley, M.D., Ph.D., for the Pediatric AIDS Clinical Trials Group Protocol 076 Study Group*
Reducing HIV Infections

PEP

PrEP

Treatment as prevention

Uninfected Person

Drug use Behavior Change

Sexual behavior change

Condom Use

Behavior Change for Prevention

Antiretrovirals for Prevention
Post-Exposure Prophylaxis

- Provision of medication or other immune products following an exposure to an infectious substance in the hope of preventing or stopping disease

- Equine serum first used in 1989 after bite by a rabid dog (13 failures reported)
## Estimated Per-Act Risk for Acquisition of HIV, by Exposure Route

<table>
<thead>
<tr>
<th>Exposure Route</th>
<th>Risk per 10,000 exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood transfusion</td>
<td>9,000</td>
</tr>
<tr>
<td>Needle-sharing injection drug use</td>
<td>67</td>
</tr>
<tr>
<td>Receptive anal intercourse</td>
<td>50</td>
</tr>
<tr>
<td>Percutaneous needle stick</td>
<td>30</td>
</tr>
<tr>
<td>Receptive penile-vaginal intercourse</td>
<td>10</td>
</tr>
<tr>
<td>Insertive anal intercourse</td>
<td>6.5</td>
</tr>
<tr>
<td>Insertive penile-vaginal intercourse</td>
<td>10</td>
</tr>
<tr>
<td>Receptive oral intercourse</td>
<td>1</td>
</tr>
<tr>
<td>Insertive oral intercourse</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Challenges for PEP research

- Premise of PEP is that it is a one-off event, necessitating prompt initiation of meds
- HIV transmission is relatively inefficient (i.e. <1% transmission rate), so not instituting PEP will not → HIV infection most of the time
- Given animal model data (Tsai et al), occupational case control (Cardo et al), observational MSM study (Schechter et al), it would not be ethical to randomize to placebo
- So, guidelines are based on review of case series
Pathogenesis

24 hours

48 – 72 hours

5 days

Mucosa

Regional nodes

Blood

CCR5

CD4

The New England Journal of Medicine

A CASE–CONTROL STUDY OF HIV SEROCONVERSION IN HEALTH CARE WORKERS AFTER PERCUTANEOUS EXPOSURE

Denise M. Cardo, M.D., David H. Culver, Ph.D., Carol A. Ciesielski, M.D., Pamela U. Srivastava, M.S., Ruthanne Marcus, M.P.H., Dominique Abiteboul, M.D., Julia Heptonstall, M.R.C.Path., Giuseppe Ippolito, M.D., Florence Lot, M.D., Penny S. McKibben, David M. Bell, M.D., and the Centers for Disease Control and Prevention Needlestick Surveillance Group
San Francisco PEP Study

- 401 participants
- 94% sexual risk (anal receptive in 40%)
- Median time from exposure to treatment: 33h
- Six months after the exposure, no participant had developed anti-HIV antibodies

Kahn, JID 2001; 183: 707-714
The São Paulo PEP Study

Sexual Assault

<72 Hours
Zidovudine
Indinavir
Lamivudine
* For 28 days

Group 1 (ARV)

>72 Hours
Control

Group 2 (CTR)

Drezett, 2000
The São Paulo PEP Study

<table>
<thead>
<tr>
<th>GROUP 1 (PEP)</th>
<th>SEROCONVERSION</th>
<th>GROUP 2 (NO PEP)</th>
<th>SEROCONVERSION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES</td>
<td></td>
<td>NO</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>182</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>2.7</td>
<td>141</td>
</tr>
</tbody>
</table>

Fisher’s exact test:  \( p = 0.037771 \)
Post-Sexual Exposure Prophylaxis

Epidemiology and Social Science

Behavioral Impact, Acceptability, and HIV Incidence Among Homosexual Men With Access to Postexposure Chemoprophylaxis for HIV

Mauro Schechter, MD, PhD,* Regina F. do Lago, MPH,* Aaron B. Mendelsohn, PhD,† Ronaldo I. Moreira, PhD,* Lawrence H. Moulton, PhD,‡ and Lee H. Harrison, MD,§ for the Praça Onze Study Team

Background: Little is known about the behavioral impact, acceptability, and incidence of HIV infection in persons with easy access to post–sexual exposure prophylaxis (PEP) to prevent HIV.

Methods: Participants were recruited from a well-characterized, high-risk HIV seronegative homosexual male cohort in Rio de Janeiro, Brazil, given a 4-day supply of zidovudine and lamivudine, and instructed to begin PEP immediately after an eligible exposure. For eligible exposures, an additional 24-day supply was provided. Reported behavior, PEP utilization, adverse events, and incident HIV infection were the main study outcomes. The observed and expected incidences of HIV infection were compared.

Results: Two hundred subjects were enrolled and followed for a median of 24.2 months. The median age was 28 years. PEP was initiated 109 times by 68 participants (34.0%). In comparison to reported behavior at baseline, reported high-risk sexual activities on average declined over time for both PEP and non-PEP users. There were no serious drug-related adverse events. There were 11 HIV seroconversions, 10 among non-PEP users and 1 that was a PEP failure. The overall seroincidence was 2.9 per 100 person-years (95% CI = 1.4, 5.1). The expected number of new HIV infections and corresponding expected seroincidence based on the risk profile were 11.8 and 3.1, respectively (P > 0.97). The most commonly reported reasons for not initiating PEP among seroconverters were sex with a steady partner and not considering the exposure to be of sufficiently high risk to warrant PEP.

Conclusion: PEP was safe and did not appear to be associated with increases in reported high-risk behavior in our cohort. Ready access to PEP did not appear to substantially affect HIV transmission, suggesting a limited public health impact of this intervention.

Key Words: postexposure chemoprophylaxis, postexposure prophylaxis, HIV, HIV incidence, lamivudine, zidovudine

(J Acquir Immune Defic Syndr 2004;35:519–525)
PEP for HIV: Rio de Janeiro Prospective Cohort Study

- PEP may stimulate high-risk sexual behavior, which could theoretically negate any protective effect of the regimen
  - To identify behavior changes in a cohort of 200 seronegative MSM with ready access to PEP
  - To determine acceptability, tolerance and safety of PEP
  - To measure HIV seroincidence

Schechter, J AIDS 2004
• 4-day supply of combination ZDV+3TC at enrollment
• Instructed to begin PEP immediately after exposures that fulfill eligibility criteria
• Instructed to report for evaluation after exposures
• For exposures that fulfill criteria, additional 24 day supply given
• Behavior interview and blood drawn at every visit
• All participants were interviewed and serologies performed every 6 months

Schechter, J AIDS 2004
Reported Risk Behavior at Enrollment and at the 24 Month Visit

Schechter, J AIDS 2004
PEP for HIV: Rio de Janeiro Prospective Cohort Study

- PEP started 109 times
- 100 (92%) exposures considered eligible
89 (89%) completed full 28 day course

11 (11%) did not complete the full course

2 did not return for the 28 day-visit

8 due to side effects (nausea)

1 due to increase in pancreatic enzymes
Most common reasons for not starting PEP:

- Did not consider as high-risk practice
- Sex with a steady partner
- Worried about side effects
<table>
<thead>
<tr>
<th></th>
<th>Overall (n=197)</th>
<th>PEP + (n=66)</th>
<th>PEP - (n=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>11</td>
<td>1*</td>
<td>10</td>
</tr>
<tr>
<td>Incidence</td>
<td>2.9</td>
<td>0.6</td>
<td>4.2</td>
</tr>
</tbody>
</table>

* *M184V mutation present on day 28*
• Availability of PEP was not associated with increase in reported risk behavior

• Underestimating high risk behavior with a steady partner was the main reported reason for not starting PEP

• Although side effects were common most participants completed the full 28-day PEP course

• Only one PEP failure was observed

• Virus sequenced on last day of PEP showed the M184V mutation
Updated CDC nPEP Recommendations (2016)

• Last recommendations published by CDC in 2005

• Updated version released April 18, 2016

https://stacks.cdc.gov/view/cdc/38856
CDC nPEP Recommendations

• All persons considered for nPEP should undergo HIV testing, preferably with a combined rapid HIV antigen-antibody or antibody blood test.

• If a rapid HIV test is unavailable and nPEP is indicated
  • nPEP should be initiated without delay and
  • nPEP can be discontinued if the patient is later determined to be HIV-uninfected.

https://stacks.cdc.gov/view/cdc/38856
nPEP is **recommended** when
  - the source of the body fluid is known to be HIV-positive and
  - the reported exposure would present a substantial risk of transmission.

[https://stacks.cdc.gov/view/cdc/38856](https://stacks.cdc.gov/view/cdc/38856)
Substantial Risk for HIV Infection

Exposure of vagina, rectum, eye, mouth, or other mucous membrane, nonintact skin

Percutaneous (e.g., needlestick or cut through skin) contact with

- Blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood

When the source is known to be HIV positive

https://stacks.cdc.gov/view/cdc/38856
A case-by-case determination about nPEP use is recommended when the:

- HIV infection status of the source is unknown and
- exposure would present a substantial risk of transmission if the source was HIV-infected

https://stacks.cdc.gov/view/cdc/38856
nPEP is **not recommended** when

- the reported exposure presents **no substantial risk** of HIV transmission
- care is sought > **72 hours** after potential exposure.

[https://stacks.cdc.gov/view/cdc/38856](https://stacks.cdc.gov/view/cdc/38856)
CDC nPEP Recommendations

- All persons offered nPEP should be prescribed a 28-day course of a 3-drug antiretroviral regimen

https://stacks.cdc.gov/view/cdc/38856
No strong evidence exists, based on randomized clinical trials, that any specific combination of antiretroviral medication is optimal for nPEP use.

Although a limited number of studies have evaluated the penetration of antiretroviral medications into genital tract secretions and tissues, evidence is insufficient for recommending a specific antiretroviral medication as most effective for nPEP for sexual exposures.

Therefore, the recommended regimens for nPEP in these guidelines are based on expert opinion from the accumulated experience with antiretroviral combinations that effectively suppress viral replication among HIV-infected persons for the purpose of HIV treatment and mainly observational studies of the medication tolerance and adherence when these same drugs are taken for nPEP.

https://stacks.cdc.gov/view/cdc/38856
• Preferred regimen for otherwise healthy adults and adolescents
  • tenofovir DF (300 mg) with emtricitabine (200 mg) once daily plus
  • raltegravir 400 mg twice daily or dolutegravir 50 mg once daily

• Regimens are also provided for children, pregnant women, and persons with decreased renal function

https://stacks.cdc.gov/view/cdc/38856
CDC nPEP Recommendations

- As a part of evaluation for nPEP, should provide any indicated prevention, treatment, or supportive care for other exposure-associated health risks and conditions such as:
  - bacterial sexually transmitted infections
  - traumatic injuries
  - viral hepatitis B or C infections
  - pregnancy

https://stacks.cdc.gov/view/cdc/38856
• Provide risk-reduction counseling and intervention services to persons who report behaviors or situations that place them at risk for future HIV exposures such as
  • injection drug use
  • sex without condoms
  • receipt of one or more courses of nPEP

https://stacks.cdc.gov/view/cdc/38856
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