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Literature Reviews

National HIV Curriculum Podcast

Occupational PEP Guidelines: 2025 Update

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National HIV Curriculum Podcast Editors Dr. Jehan Budak and Dr. Aley Kalapila discuss an occupational needlestick exposure as they highlight key updates to recommended medications regimens and laboratory monitoring included in the “2025 US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Post-exposure Prophylaxis in Healthcare Settings.”

Topics:

- needlestick
- postexposure
- PEP
- oPEP
- HIV

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Disclosures

Disclosures for Jehan Z. Budak, MD
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Disclosures

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Transcript

Read along with the audio or jump to a particular chapter.

In this episode:

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introduction--background**[00:00] Introduction & Background**

Hello everyone. I'm Dr. Jehan Budak from the University of Washington in Seattle, and welcome to the National HIV Curriculum Podcast. This podcast is intended for health care professionals who are interested in learning more about the diagnosis, management, and prevention of HIV.

I'm back with my colleague, Aley Kalapila, an ID physician at Emory University in Atlanta. Hi, Aley.

Dr. Kalapila

Hi, Jehan. Hi, everyone. Excited to be back here to do another podcast episode.

Dr. Budak

Today, we are going to highlight the 2025 US Public Health Service Guidelines for Management of Occupational Exposure to HIV. Now, these are an update to the 2013 guidelines for occupational post-exposure prophylaxis (or oPEP). So, with that, I'd like to put these updates into a clinical context to make this more practical for the listeners. And the case starts with a 31-year-old woman who we will call Jane, who is a medical student who sustained a needlestick while drawing blood on a patient in the emergency room. The source patient was obtunded, and there was no information available about the patient's HIV status.

Dr. Kalapila

So, as a reminder to our listeners, post-exposure prophylaxis (or PEP) is the use of therapeutic agents to prevent infection following an exposure, and that can be a sexual exposure, a needlestick, splash, bite, et cetera. And the exposure is typically to a bloodborne pathogen. Now, in this case, we are discussing oPEP as compared to nonoccupational post-exposure prophylaxis (or nPEP). And typically, we worry about multiple bloodborne pathogens, including HIV, but also hepatitis B and C. But of course, this is the National HIV Curriculum, and the primary focus of our discussion today is going to be occupational post-exposure prophylaxis, specifically in the context of preventing HIV transmission.

Dr. Budak

And Aley, to your point about other bloodborne pathogens, I'd like to highlight a few other resources. There are the 2018 CDC MMWR Hepatitis B PEP guidelines, which combine guidance for both hep B, oPEP, and nPEP. And then for hepatitis C, there are the 2020 hepatitis C oPEP guidelines. So, back to the case of Jane and the 2025 HIV oPEP update, what do they suggest regarding determining eligibility for occupational PEP?

hiv-opep-eligibility**[02:16] HIV oPEP Eligibility**

HIV Dr. Kalapila

So that's the first step, right, is to determine whether or not Jane is eligible for occupational post-exposure

prophylaxis. So, in order to do that, you have to first assess the risk of the exposure. Now, the factors to consider here are the timing of the exposure, the type of exposure, the HIV status of the exposed person, so that's Jane, and the HIV status of the source person or the source patient. And of course, if the source patient is HIV positive or has HIV infection, then we would ideally want to know their HIV treatment history as well. Now, breaking that down for the timing of the exposure, as with nPEP, the recommendation is to initiate HIV oPEP within 72 hours of the exposure, but ideally it should be done as soon as possible and preferably within the first 24 hours of the exposure.

Dr. Budak

And this is a good moment to discuss the principle of HIV PEP and the reason why that timing matters. A lot of the scientific principles behind HIV PEP are extrapolated from studies in non-human primates. And we know that in studies from these animals, giving ART [antiretroviral therapy] sooner after exposure is better because we are attempting to prevent cellular infection and local propagation of HIV. And these studies have shown that the efficacy of HIV PEP decreases after 72 hours. So, the sooner, the better. Now, the next criterion you mentioned daily was the type of exposure.

Dr. Kalapila

Yes. The exposure that carries the highest risk for transmission is a percutaneous needlestick. Other common exposures in a health care setting could be mucocutaneous or a cutaneous exposure. Now, if these exposures occur from a source person with HIV who is actively viremic, then the risk of acquisition for HIV for a percutaneous exposure is 0.23%, and the risk of HIV acquisition for a mucocutaneous or cutaneous exposure is 0.09%. Then it's also important to consider the type of body fluid involved. If the type of body fluid involved in the exposure is either blood or visibly bloody, then these are considered to be infectious sources. Potentially infectious body fluids could include things like semen, vaginal secretions, cerebrospinal fluid (or CSF), synovial fluid, pericardial fluid, pleural fluid, peritoneal fluid, and amniotic fluid. And then noninfectious fluids are nasal secretions, saliva, sputum, vomit, feces, urine, sweat, and tears.

Dr. Budak

And in this case, the student had a needlestick exposure. So, based on the above, we can assume that this is an infectious fluid. Stat labs were obtained on the source patient, including a point-of-care positive HIV antigen antibody test. And then on the source patient, an HIV RNA and confirmatory serum HIV antigen antibody is obtained and pending.

Dr. Kalapila

Okay. So based on all that information, since we have a positive HIV antigen/antibody test on the source patient, and we are unaware at this time of their viral load, this is an occupational exposure that may carry a very high risk of transmission, and that's because we have to assume that the source patient is viremic because we don't have access to their viral load data and we are unable to obtain a history from them. And so, in this case, as per the guidelines, our exposed person, which is Jane, would meet criteria to receive HIV oPEP because she is at risk for HIV acquisition and was exposed to someone with known HIV with possible viremia. Now, in the cases of a needlestick or other high-risk occupational exposures, we do tend to err on the side of caution. Typically, we do obtain labs on the source patient as soon as employee health is informed about the exposure, but we don't wait for those labs to result to determine the need for oPEP. We would start oPEP immediately.

Dr. Budak

And when it comes to PEP and specifically oPEP, as you just mentioned, we want to start ART as soon as possible, though we have up to 72 hours to do so. And again, I will reemphasize because this is such an important point that we should not wait for a lab result before initiation of oPEP, and that we can always

discontinue PEP once results on the source patient come back. So now that we've *really* emphasized that point, let's discuss the regimens.

hiv-opep-regimens**[06:36] HIV oPEP Regimens**

Dr. Kalapila

This is one of the areas where some of the biggest changes have been made in the 2025 oPEP guidelines. Now, they still recommend a three-drug antiretroviral therapy regimen, which includes two nucleoside reverse transcriptase inhibitors (or NRTIs or nukes) paired with an integrase inhibitor. Whereas previously, the recommended regimens were tenofovir disoproxil fumarate (or TDF) combined with emtricitabine and administered with raltegravir twice daily. Now, the latest recommendations are to use tenofovir, either TDF or tenofovir alafenamide (or TAF), paired with either emtricitabine or lamivudine, and given in combination with a newer generation of oral integrase inhibitors, specifically dolutegravir or bictegravir. Now, if bictegravir is used, you have to give it as part of the single-tablet regimen: bictegravir, emtricitabine, and TAF. There is an alternative regimen recommendation as well, which is to use a protease inhibitor-based regimen, and that's specifically boosted darunavir combined with any formulation of tenofovir as well as emtricitabine or lamivudine.

Dr. Budak

Exactly. The guidelines state that the two options you mentioned, dolutegravir- or bictegravir-based therapy, are listed in alphabetical order and not listed in order of preference. So, I think deciding between the two options depends on a variety of factors, whether it be patient or clinician preference, cost, and/or insurance coverage. And this 2025 updated change in regimen is advantageous because the once-daily PEP regimens with dolutegravir or bictegravir have much higher completion rates than the twice-daily raltegravir-based regimens.

Dr. Kalapila

Yes. I mean, these oPEP updated guidelines really sort of reflect the efficacy, the tolerability, and, really, the simplicity of taking once-daily regimens. We've talked a lot about the regimen that we would give, but also, we have to discuss quickly the duration. So oPEP has to be taken for 28 days, and this recommendation is also based on non-human primate studies.

baseline-follow-up-labs**[08:42] Baseline and Follow-Up Labs**

Dr. Budak

Now let me talk a bit about labs and monitoring. Another area in which there were some significant updates in the 2025 HIV oPEP guidelines. First, let me discuss baseline HIV testing. So a baseline HIV test on Jane is necessary, and this should ideally be an antigen/antibody HIV blood test. A new addition to the guidelines states that if a health care professional had received cabotegravir-based HIV PrEP within the prior 12 months should also have, in addition to the antigen/antibody test, an HIV-1 RNA (or viral load test). And that's because the antigen/antibody HIV test may be unreliable during and after cabotegravir use. And that's because cabotegravir has such a long elimination half-life, it can complicate interpretation of the HIV antigen/antibody tests, thus making HIV RNA testing essential for accurate detection in such a case.

Dr. Kalapila

So, along those lines, we've talked a lot about HIV viral load testing, but it is also very important in the setting of occupational exposure to also evaluate for hepatitis B and hepatitis C. And of course, both of these are referenced in the hep B and hep C exposure guidelines, which you had discussed earlier on in this podcast, Jehan. Now, in addition to all of that, we also need a baseline assessment of our exposed person, that's Jane's

renal and liver function. And of course, if there are any issues with those labs, then we would need to consider adjusting our PEP regimen or using an alternative regimen. And of course, any additional testing can be decided on a case-by-case basis based on our health care professional's medical history. Last but not least, for women of childbearing age, it is very important to do a pregnancy test.

And just as an aside here, if it so happens that the exposed person is pregnant, the Health and Human Services (or HHS) perinatal guidelines were updated also conveniently for us in 2025. These reflect that the first-line regimens recommended in pregnancy or breastfeeding. For women who have never taken antiretroviral therapy before, the regimens that are recommended are tenofovir, either TDF or TAF, combined with emtricitabine and bictegravir or dolutegravir. And conveniently, all of those regimens match up perfectly with our HIV oPEP regimens.

shared-decision-making**[11:06] Shared Decision-Making**

Dr. Budak

And that wraps up the baseline evaluation. Now, follow-up evaluation, which is another area with important updates. If oPEP is started within 24 hours of exposure and there are no problems with medication adherence, a four to six-week laboratory evaluation is no longer required. However, if oPEP is initiated after 24 hours from the exposure, or if any doses are missed, then repeat testing at four to six weeks with both an antigen/antibody test and an HIV RNA test is recommended. All individuals who take oPEP should also have a final HIV antigen antibody and HIV RNA test at 12 weeks from the exposure. And then if Jane at any point were to develop symptoms consistent with acute HIV, both tests, antigen/antibody and viral load, should be performed immediately. And the guidelines further recommend checking renal and liver function at the four to six-week and 12-week visits only if baseline abnormalities were present or if drug toxicity is suspected. Again, highlighting the strong safety profile of the current antiretroviral regimens. Now, back to Jane, what if the viral load result on the source patient came back as undetectable? Is oPEP still recommended for her?

Dr. Kalapila

That is another major update in the 2025 oPEP guidelines because it really kind of focuses on shared decision-making when a source patient is found to have an undetectable viral load. Now, in nonoccupational settings, multiple studies have confirmed that people with an undetectable viral load do not transmit HIV sexually, but we don't have that equivalent data for occupational exposures. So historically, what that meant was that we generally recommend postexposure prophylaxis even when the source patient has an undetectable viral load. Now, the new guidelines shift towards a more nuanced case-by-case approach. So if the source patient had a recent undetectable HIV RNA level, then the actual risk of transmission from an occupational exposure is unknown, but probably very low, but it isn't zero. And so, unlike sexual exposures, of course, we have to keep in mind that needlesticks can introduce whole blood cells that may carry latent virus, even when a plasma viral load is undetectable. So, because of this uncertainty, the 2025 oPEP guidelines do recommend shared decision-making, looking closely at the type of exposure, individual circumstances, and, of course, patient preference to determine whether PEP should be offered.

summary**[13:37] Summary**

Dr. Budak

So that wraps up our oPEP discussion. In summary:

- Occupational exposures to blood or potentially infectious bodily fluids are urgent medical issues that require immediate evaluation.
- The US Public Health Service recommends three-drug oPEP regimens: tenofovir plus emtricitabine or lamivudine, combined with either dolutegravir or bictegravir, due to their high efficacy, good tolerability, and minimal drug interactions.

- The recommended duration of HIV occupational PEP is 28 days, and when indicated, it should be started as soon as possible and always within 72 hours.
- All exposed health care personnel should receive baseline testing, including an HIV antigen/antibody test, assessment of renal and liver function, and pregnancy testing when applicable.
- Follow-up and final HIV testing at 12 weeks should include both an HIV antigen/antibody test and an HIV RNA.
- Interim testing is recommended at four to six weeks only if oPEP was started more than 24 hours after exposure, or if any doses were missed, and should include an HIV antigen/antibody test plus an HIV-1 RNA.
- And then last, in complex cases, such as if there is suspected drug resistance and/or the exposed patient is pregnant or breastfeeding, or there has been a delay beyond 72 hours before seeking oPEP, we recommend seeking local expertise and/or calling the National Clinician Consultation Center.

So, Aley, with that, I'll say thank you.

Dr. Kalapila

Thanks.

credits**[15:04] Credits**

Transcripts and references for this podcast can be found on our website, the National HIV Curriculum at www.hiv.uw.edu. The Health Resources and Services Administration (HRSA), Department of Health and Human Services (HHS), provided financial support for this podcast. The award provided 100% of total costs and totaled $1,175,136. The contents are those of the author. They may not reflect the policies of HRSA, HHS, or the US government.

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