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POST-EXPOSURE PROPHYLAXIS (PEP) TO PREVENT HIV INFECTION

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[video transcript]

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Today's speaker Dr. Antonio E. Urbina. Dr. Urbina completed his residency in internal medicine at St. Vincent Catholic Medical Center in Manhattan. He has pioneered innovative educational programming for community based clinics, hospitals and public health departments. Dr. Urbina has directed more than 10 HIV clinical trial research protocols and serves on the New York State Department of Health AIDS Institute clinical guidelines committee from 2007 to 2009. Dr. Urbina served on the Presidential Advisory Council on HIV AIDS, and from 2014 to 2015, served on the governor's task force to end AIDS the AIDS epidemic in New York State. Dr. Urbina is currently the medical director for the Mount Sinai Institute for Advanced medicine downtown clinic in New York City, a professor of medicine at the Icahn School of Medicine at Mount Sinai, and also serves as medical director here at CI for the HIV Primary Care and Prevention Center of Excellence, part of the New York State Department of Health AIDS Institute. So without further ado, thanks, Dr. Antonio, for being here and presenting your expertise. And I'll turn it over to you.

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Tara, thank you so much for that introduction. And, you know, I'm going to talk about post exposure prophylaxis really in the context of really the ending the AIDS Initiative here in New York state. So we know one of the pillars is to provide prevention services, primarily PrEP, but also pet in the event of a high risk exposure to someone with HIV. So I'm just going to talk about some of the kind of implementation and some of the data to support that. So these are my disclosures. As Tara said, these disclosures have been mitigated. So our learning objectives are going to be to discuss how to evaluate exposures where post exposure prophylaxis may be indicated. Describe the the recommended PEP regimens, the dose initiation and baseline and also follow up laboratory testing, counseling and some of the best care practices.

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Okay, so what is post exposure prophylaxis so, it's the prevention of an infectious disease after and exposures, it's flu, meningitis, Hepatitis Coronavirus, and our focus is really going to be on HIV and also Hepatitis, so Hepatitis B and C and other sexually transmitted infections. And PEP is a form of emergency HIV prevention, as contrasted with PrEP. So PEP is really kind of like the gunshot wound. It's someone coming to an to an emergency situation where they think they may have been exposed to HIV. And we really have to put in all of our efforts to abort the infection. So it's time limited. So we have a window in which we can intervene. And it treats an exposed individual as soon as possible after a known or potential exposure. And it can really be effective in occupational exposure. I think that's what we're most used to in healthcare settings, needlestick exposures, but it's also very effective in non occupational exposures, consensual sex, but also for sexual assaults and also pediatric exposures to HIV. So just talking a little bit about occupational PEP, so healthcare workers are the most likely to seek occupational pet for HIV after a needle stick or eye exposure and that's mucosal exposure. And other candidates include police, firefighters or other emergency personnel and prison guards. So remember, for

health care workers, it's mainly going to be either needlestick or some type of blood exposure to a mucous membrane. So the mucous membranes are the eyes, the lining inside the nose, or the lining inside the mouth are the most typical mucosal exposures. Now non occupational pet is typically sought by individuals who have engaged in condomless sex, in particular if their partner is known to be ah, IV and also if their partner is known to be HIV, but not on antiretroviral treatment, where if they have a partner of unknown status, but also needle sharing with an individual of unknown or who is HIV positive. So again, non occupational, it's for sexual or for needle stick exposures in a non occupational setting. And then for sexual exposure to PEP those are assault by an individual who has been sexually assaulted and experienced mucosal to mucosal contact or mucosal contact with bodily fluids. So that's blood, semen, vaginal fluids, and really, with or without physical injury, tissue damage or presence of blood. Again, with sexual exposure, the bar for initiating PEP is quite low. Again, lots of trauma, there may not be physical evidence of injury, although it can be present because of the trauma associated with that exposure and event. So those are mainly the scenarios for where post exposure prophylaxis can be offered. So how are we doing with new HIV infections, so the estimated number of new HIV infections continues to go down. In fact, we're seeing an overall decrease in new HIV infections over time. So that's good news. And if we looked at the prevalence of HIV by region across New York state, not surprisingly, it is concentrated more around urban centers.

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But what the data still supports is that if we look at the breakout for the epidemiological risk, for persons newly diagnosed with HIV, predominantly, it's still male to male sexual contact. And overwhelmingly, it's disproportionately impacting black and Latino, and Latin X populations. In fact, if we look at the total number of all cysts and trans women, over 90%, of new infections are in black and Latina women. Similarly, if we look at men, close to 60%, are in men who have sex with men, and of those 78% are in either black or Latino populations. And not shown here in the diet data, but nationally across, you know, over half of new infections, also, you know, have occurred in those living in poverty. So, let's talk a little bit about pre versus post exposure prophylaxis. So again, post exposure prophylaxis is initiated soon after an exposure, and it reduces the chance of infection. Basically, from exposure to HIV getting into beyond a mucosal surface, getting into those immune cells being transported to a lymph node, and then replicating. You know, it takes about one to three days for that process to happen. So really, the way that PEP works is that we provide the same antivirals that we give to people living with HIV with those that have had an exposure. And then these drugs prevent these cycles of viral replication, prevent HIV from penetrating from lymph nodes into the blood system. And then it allows the body's own immune system to abort the infection. But again, it's time limited, time sensitive. So based on animal data, really, we have up to 72 hours, and a lot of patients not just for occupational but also for non occupational think, oh, I can wait up to 72 hours to make a decision. Really, the sooner you dispense PEP, the more effective it can be. pre exposure prophylaxis begins prior to any exposure. And again, it's antivirals as opposed to three. It's two that are given primarily daily to build up enough drug levels in the tissues and in the bloodstream, so that you build up these protective levels in the event of a future exposure. Typically, it's one week after daily dosing that you get these protective levels and it may be a little longer for vaginal cervical tissue exposure versus anal rectal, so again, maybe 21 days of daily dosing to reach those maximal protective levels in vaginal tissue versus a week for anal

rectal exposures. So what are some of the animal data to support post exposure prophylaxis. So in the Simian model, immunodeficiency infection prevented in macaques, who were treated 24 hours post exposure with antiretroviral therapy, half of the subjects that receive PEP at 48 and 72 hours developed infection. macaques that were exposed to HIV and for vaginally were initiated on PEP back 12 and 36 hours post exposure with antiretroviral which prevented infection. And there was some breakthrough infections that occurred when PEP was initiated beyond 72 hours. And that's how we really came to this threshold time of 72 hours beyond which PEP is unlikely to be effective. And a meta analysis of 16, animal studies of PEP

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reported that the risk of serial conversion was about 90%, lower among primates exposed to PEP than among controls. So again, that's where we get the most recent data for PEP is at least 90% effective. And really, I would say it's probably closer to 99% effective in averting HIV infection. So again, the earlier data just looked at monotherapy with Zai WD. But using a full cocktail, those rates of preventing HIV are close to 100%. So occupational post exposure prophylaxis. So from 1985 to 1999, there were 58 cases of suspected or confirmed occupational HIV exposure, mostly from needlestick. And since 1999, there's only been one case of occupational HIV infection documented in the in the US. And I think this is something that's very important that when we counsel patients about whether or not to take occupational exposure, and that it's highly affect. And if it's given within 72 hours when we haven't had a case of serial conversion since 1999. Importantly, these are medications that we give to patients living with HIV for decades. All we're talking about is either a one time dose or a dosing this for 28 days. Again, I think the cocktails of antivirals are safe, effective, lack drug drug interaction. So again, I think because a potential serial conversion can have such deleterious impacts. That again, I think, because of good safety and tolerability that we really need to stress that with patients in terms of buy in to starting PEP, and then to really stress retention and adherence. So not a lot of data with occupational exposure in 1997, there was this retrospective case control data in healthcare workers. And it really looked back to show those that were given and it was really monotherapy with Sadove eating versus no intervention. And that's where that data showed the 81% reduction in HIV infection with the use of AZT for for pet versus no pet. But again, that was with one antiviral, but with three antivirals, just like the previous slide has shown that efficacy rates are really closer to 90% and beyond. And in 2017, there were 266 healthcare workers with percutaneous or mucocutaneous exposures to HIV contaminated body fluids. And there was 00 conversions over 13 years at a US academic medical center. So again, just really attesting to that one, the risk of HIV infection from a needle stick is already low. When you add on that the protective effects of post exposure prophylaxis, it's really near perfect protection against HIV. So I think these concerns about the drugs being toxic. We're no longer using AZT that induced a lot of nausea, vomiting, anemia, drugs now are super well tolerated, lack really drug drug interactions, and really are only taken for a month. So where can I find guidance on post exposure prophylaxis. So really, we have the updated guidelines for antiretroviral post exposure prophylaxis, from the Centers for Disease Control that was recently updated 2016. But we also have guidelines from the New York State Department of Health AIDS Institute. And these can be accessed through the HIV guidelines.org. We also have the US Public Health Service guidelines that really review the guidelines for the management of occupational exposure to

HIV. But I really want to focus in on the guidelines from the New York State Department of Health AIDS Institute, they are very instructional, easy to use. It's almost like

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very short snippets of information that can that providers can easily access. And it's going to tell you exactly when is PrEP indicated, when is it not? What are gray areas? What are the baseline labs to get? What are the recommended regimens, and what is the best practice for management and follow up. And we also have these pet cards that can be provided to you. And they take you through the pet triage protocols. So that's on one side of these pet cards. And on the other side, it gives you the preferred regimens, along with some alternative regimens, and we rarely need to use the alternative regimens. We'll talk a little bit about what those scenarios may be a known allergic reaction and somebody that was previously on a PEP regimen or if there's been potential that the source person has maybe evidence of multidrug resistant HIV, or if there's some issues in the exposed person in terms of acute or chronic kidney or liver injury. But really what I want to direct everybody is to the CEI guideline here, if you call this number, you can get expert consultation regarding maybe a more complicated PEP exposure. But what I want to say is that the triage really and the protocol is if that is PEP is indicated, you can give that first dose, and you should give that first dose. And then you should bring that patient in if they're not on site, and you should perform that baseline testing. If there are some issues that come up in terms of kidney or liver or tolerability or even if their HIV test should return positive. Then again, you can call this line for expert advice on what are the best next steps and practices that should occur. But don't delay or withhold PEP based on concerns about either the source patients virus or the exposed patients kind of medical conditions. Again, if it's a significant exposure, that the benefits of dispensing PEP still outweigh any potential risks. So we're going to talk a little bit what's new in the guidelines and again, the HIV guidelines.org. So PEP, the initial dose ideally should be given within two hours and no later than 72 hours, the sooner the better. The provision of a full course of PEP whenever possible. So really that prescription should be for that full 28 dates, which I think is easier also for pharmacies to fills. Unless you're working at an institution or healthcare setting where you have these 10 packets. HIV testing of a source of a patient who is testing PrEP is also recommended if that source patient should be available and is amenable to HIV testing and then have an unexposed person when taking PrEP. So if a person is on PrEP, and if they should sustain a sexual exposure to HIV they do not need to die. Um, PEP on top of PrEP, as long as they've been adherent to their PrEP medications. And it's been really, I would say less than three days that they have been taking their medications or patients have been off of their PrEP medication for three days or longer, then you may want to consider re prepping. But in a patient that has been adherent, stable on PrEP, if they've had a sexual exposure to HIV, PrEP really should cover for that exposure, and additional PEP is not indicated. And then really, what's also important is transitioning from PEP to PrEP. And those should occur seamlessly. So a patient that starts on PEP, after they continue or complete their 28 day course, they get their four week HIV test. If negative, you should then

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seamlessly transition them to a form of pre exposure prophylaxis, ideally without any gap. And again, this is really if the patient will be an ongoing risks for HIV. If it's an isolated exposure, a

sexual assault, I think one can have a shared decision making with with the patient. But ideally, you want to transition then seamlessly from PEP to PrEP or turning your peppers to preppers. You really want to link patients to an HIV provider in case of an HIV sero conversion, which again is unlikely to happen. I think the scenarios that may happen is that if you're dispensing PEP, prior to getting that baseline HIV test, and then they come in for HIV testing, and they're found to be positive, or if they should not be adherent to their medication, and have a breakthrough infection, then again, that's why testing is important for weeks. And what you would want to do is then then refer or to manage that patient now that is living with HIV. And then we'll talk about some of the alternative PEP regimens that may be available including single tablet regimens. So you really want to have some consideration about the negligible risk of sexual transmission when undetectable equals on transmittable applies. So basically, in a person living with HIV, if they're on antiretroviral therapy, adherent and viral logically suppressed for at least six months, then they cannot sexually transmit HIV. But again, that's really only applicable in patients that are stably coupled, where the person living with HIV is on therapy is inherent and has, you know, documentation that their viral load is undetectable, and that the exposed person has trust in that person's information. You what goes new is not a exposed person saying I met somebody they told me they were undetectable. Again, I'm really you equals you really applies to stably coupled serial discordant couples. And then in that situation, it's a shared decision of whether the exposed wants additional HIV protection. Despite the data showing that really in this in a person living with HIV that's undetectable that they cannot sexually transmitted. Want to talk a little bit about some of the considerations regarding the use of W Tegra veer in the first trimester of pregnancy. What I want to say is that there were initial studies that showed an association of W Tegrity. Or with neural tube defects, the more data we receive the more exposures of persons of childbearing potential. And in the studies, it was really cisgendered women, what they found is that that association went away. So again, I think post exposure prophylaxis can be recommended to persons of childbearing potential. Understanding that the new data does not really confirm that there's now a statistically associated increased risk for neural tube defects. Again, it's a shared decision making saying that this data initially showed this association but with more data, more exposures that though your Tegrity or was found to be safe, including use in the first time stir or in the dairy consumption period. And then some of the changes in the requirements of laboratory testing, monitoring of renal and liver function. And I'll go over some of those. But it's basically, if the baseline testing for liver and kidney are normal, we don't need to repeat it again. So really, the only test that we need to repeat are HIV and STI testing. And then talk about some of the special considerations of PEP. So for Oh pepper, occupational really, it's about linking in with your

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occupation, occupational health program. within your institution, non occupational PEP, it's about having those systems in place at an urgent care health centers, emergency rooms and clinics, where patients have easy access to that first or a couple of doses of medication. And then for sexual assaults. I think that one we have to ensure that patients get forensic testing, if that's something that they want to pursue, but that we don't deny them access. And again, the threshold is a little bit lower. And then in even rare cases, pediatric exposures. And again, I encourage for pediatric exposures really, to call the CEI clinical consultation line, just to give

more accurate and up to date information about dosing in the pediatric population. All right, so really, for any percutaneous or mucosal exposure to HIV, again, remember, the virus replicates locally in these tissue and dendritic cells of the exposed individual starts to migrate to lymph nodes within the lymph node and starts to then replicate them. By day five, we get these little baryons that spill out, that's acute HIV infection, that infection cannot be reversed. So different lecture, but the signs and symptoms of acute HIV infection and typically persons will acquire HIV or have symptoms of acute HIV infection about 10 to 14 days after an exposure again, well beyond that 72 hours. And persons in acute HIV infection, I would also argue for immediate start of antiretroviral therapy, just to preserve that very early immune devastation that HIV confers on the immune system, in particular the gut associated lymphoid tissue. So again, PEP is administer within 72 hours works immediately stops these initial viral replication blocks, it contains the infection locally, HIV is then averted. PEP is not if PEP is not administered within 72 hours by replication is not blocked. And then viremia and acute HIV infection can happen. So again, what I would recommend if it's beyond 72 hours, really the the correct counseling to the patient is you're beyond the window where this intervention can be effective. What we can do is that we can monitor you for very early HIV infection by doing viral loads, maybe two weeks after an exposure, and even four weeks after an exposure really to detect very early HIV infection. So in the event, somebody has had an exposure, and it's beyond that 72 hour window, then it doesn't mean we don't continue to do baseline and monitoring, screening for HIV. It's just that we may want to also include more sensitive testing for early or acute HIV infection. So the first dose of PEP as soon as possible, really, it's these that golden two hours after an exposure, and really no later than 72 hours, I would say first dose stat, what we call gorilla triage. Was there a significant exposure? And was there a potentially infectious fluid? If both of those are yes, then I would say first dose and access to that first dose as soon as possible. There's not been a lot of updates in terms of what are the recommended doses, it's really tenofovir disoproxil fumarate, also called Truvada. And it's with emtricitabine or Lammi. View Dean. Again, those are with to nomophobia combined with emtricitabine. That's Truvada. Now there are some generic versions of to NOFA V or with Lam IV UD Same duo that are also recommended in the guidelines as well. And then you can either use route Tegra Veer,

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which is an integrase strand transfer inhibitor. And that's typically one tablet twice daily, we'll go over those dosing. There's also this HD formulation of it, which is two tablets one daily, so both of those can cannot be used. But really, I think the preferred regimen still continues to be to know fovea, plus either interested in being or laminating. And I would say most commonly Truvada, which is a co formulation of the Tenova Vir plus the emtricitabine with dou u Tegra. Vir and who your viewers dose one tablet daily, again, the consideration for route Tegrity are really was in the first trimester of pregnancy if it was a person of childbearing potential. But again, I think with data that has come out more recently, that I think that we can safely after shared decision also just dispense this in persons of childbearing potential. And this is the integrity of your data. So in a large observational clinical trial in Botswana, the rate of infant neural tube defects with maternal exposure to doggy Tegra veer based antiretroviral regimens, initially was point nine, then it went down to point three, and then more recent data showed point one and now really, that association has gone away. However, because of the historical nature of the dissociation, it's something that we do want to discuss with patients and have a shared decision

making. If a person of childbearing potential would feel more comfortable still, just with the alternative or WebTegrity here. So let's hone in again on the preferred post exposure regimens for patients who weigh at least 40 kilograms. So again, it's either to know for Vir emtricitabine, or Truvada once per day, or this generic now formulation of Genovia. With lamb maybe you need it's called sim duo. once daily, plus either route tag revere the 400 milligrams one tablet twice daily, or you can do two of the 600 milligram tablets of Route Tiger beer or round Tiger beer HD. But again, draw your Tiger beer is one tablet 150 milligram tablet once daily, given with either the Truvada or this and duo guidelines are being looked at and will be updated. But go your Tegra veer again even in persons of childbearing potential, I think the data reassuringly show safety. One thing that's important is that both DOJ Tigerair and REL tag revere should not be given with di Vaillant cat ion, so calcium magnesium supplements and also iron supplements should not be taken concurrently. So they should be dose separated to know for the year. There are indeed there are dose requirements where it does need to be really adjusted if the Creatinine clearance is less than 50 ML is obviously you're not going to have that information at your baseline encounter with the patient. So again, you're going to dispense that first regimen. Once those labs come up then then you can call that CEI line and get expert recommendations about how to move forward but again, it requires dose adjustment if the Creatinine clearance is less than 50 ml so some there are alternative post exposure regimens for patients who weigh at least 40 kilograms. So one of them is the single tablet regimen co formulation of albite Tegra. Vir boosted with Kobe emtricitabine. And to know for beer and that is called stripe bill and it's a fixed dose single tablet once daily regimen on it can be dose for patients with a creatine clearance of at least 70. And then other alternatives are to use Truvada plus a protease inhibitor so a right time of year boosted regimen of either darunavir

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Um, is the recommendation. You can also substitute the FTC as I explained earlier with lemon Dean, and the darunavir with the atazanavir, or the Folsom premiere, and you'll see the some of the notation there about baseline create knee clearance. But again, these are alternatives, I think you can, for the most part, prescribe the recommended regimen. And then if there's an issue or more information, more discovery comes about, then you can make a change. All right. So I'm not going to talk about this too much. But these are the post exposure prophylaxis for patients aged two to 12 years of age. So again, the preferred is that to NOFA beer plus the emtricitabine plus either though route Tiger beer as a fixed dose combination, but substitutions can be you substitute the emtricitabine for La midview. Dean, or do you check your beer. And then here are also some of the alternative regimens. But again, if you do have a pediatric patient, I think you can call up that that CEI line and get immediate consultative services.

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So

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we're going to shift a little bit about non occupational post exposure prophylaxis, and I think that's the one that has a little bit more of a gray area. So how risky was the source? Or is there anything known about that source patient? Is the source available for HIV testing? Does the source have any known risk factors for HIV? And then how risky was that exposure? And you

kind of need for both of these to be true. In order to say that, yes, PEP is indicated. So let's go over some of that. So one of the things with the source patient is you want to obtain verbal consent for HIV testing, you do not need written informed consent, just verbal consent. I'd like to perform HIV testing is that okay? And again, there are seven points that you want to review with the patient. HIV is a virus that causes AIDS, those, those can be kind of, you can wave your hand at those either in a poster or online information or a brochure, but again, just verbal consent for testing. And then you do want to obtain lab based or point of care, HIV antigen antibody testing. But if the source patient has had any exposure to HIV in the last four weeks, or if they're on PrEP, then you also want to get an HIV RNA of the source patient. And that's because what you really want to exclude is any earlier acute HIV infection, where the antigen or antibody tests may have not had enough time to turn. But don't delay PEP while waiting for the HIV results in the expose. PEP can be stopped later if the results indicate no me. But again, what you want to do is really the only time you would ever stop PEP in an exposed person is if that source patient, you know, agrees to testing, things like that they are HIV negative, but also RNA negative. And that's the really only time that you would consider stopping PEP in the expose other information. If the source patient is living with HIV, you would want to get their most viral load just to kind of estimate a little bit better risk, and then any antiretroviral or medication history that may just suggest that the patient may have some underlying drug resistance. And again, for exposures that are involving consensual sex, again, want to have that discussion about undetectable equals on transmittable. So if that patient living with HIV is on therapy suppressed as a known undetectable viral load recently, then, you know, PEP may not be indicated in the exposed and the New York State Department of Health really does support this concept that patients living with HIV there are on therapy adherent and have an undetectable viral load for at least six months cannot sexually transmit HIV to their partner. All right. So other information that you may want to gather or for discovery is for the available source with confirmed HIV, get their viral load resistance test their current regimen, previous regimen, contact information, but again, you're not going to delay PEP what's been shown To be true is that even in the presence of multidrug resistant virus, that antivirals still have a prophylactic effect. So let's make sure to do that. Okay, and then the available source with unknown HIV status is informed the source of the exposure incident perform HIV testing. Using a fourth generation antigen antibody tests, assess the source patient for risk of HIV infection within the past four weeks. And if the source is unknown or unavailable, assess the exposure to identify the exposed individuals risk of HIV infection and assume the source has HIV until proven otherwise. All right, sharps, so sharps really so if somebody should obtain a needle stick injury in the community. Yeah, PEP is indicated. And it just depends on the serial prevalence of HIV within your community. I think the air is if somebody should sustain a needle stick injury in the community is that you do offer them post exposure prophylaxis. needles with hollow bores and visible blood have a higher risk of transmission as opposed to solid bores, but other objects like condoms, sex toys are negligible risks for HIV.

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So let's take a

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talk a little bit now. After understanding your source risks, consider your type of exposure. Um, so blood transfusions carried a highest risk. So these are per 10,000 exposures, almost assuredly, HIV transmission, that person receives an HIV positive blood transfusion. Needle sharing is 63 out of 10,000 meal stick is only 23 or point three out of 10,000 and receptive penal or anal intercourse 138 Out of every 10,000 What we're noticing here is that the risk for some sexual exposures is actually higher than needlestick exposures, inserted anal intercourse less inserted vaginal, even lower, and then oral intercourse very low. And we're going to talk about when it may be indicated and then biting, spitting throwing body fluids or sharing of sex toys is also negligible. Again, only if in the events of biting where there's visible blood. So types of exposures for which en PEP should be recommended. So that's receptive and inserted vaginal sex. If the source is either HIV positive or unknown status, the same with needle share. And this is if the exposure to blood or other potentially effective fluids. Types of exposures that do not warrant are kissing oral to oral human bites not involving blood and exposure to solid bore needles or sharps that are not in recent contact with blood and then mutual masturbation without any skin breakdown or blood exposure. And then we have these gray areas and the gray areas are oral vaginal contact, oral anal contact, contact receptive penal oral contact and inserted penal oral contact with or without ejaculation and factors that may decide whether or not you do despite dispense PEP is if the source person has a high viral load. If there was a break in the oral mucosa, ginger, Gingivitis, oral lesions, and if there was a presence of a concomitant Ulcerative, genital Ulcerative disease, those may be indications where you may want to dispense back but again, sometimes if it's unclear, you got to do a little bit more digging. So, PEP side effects most are mild, non existent. nausea, headache, vomiting and fatigue. You can give antiemetics you can give anti nausea medications like on den, Citron, or the CLO provide patients who vomit physical tablets should repeat the dose. And again very few side effects and most of these go away. So there have been rare cases of allergic reactions, so rash hepatic toxicity, mildly mildly elevated levels of Truvada may occur if patients are also prescribed a a Cytochrome P 450. inhibitor to no phobia as described can be kind of some mild nephrotoxicity. It's rare and reversible, but again, it can induce a Fanconi syndrome. There are longer term effects of bone thinning, which NOFA we are but again in the short term, we're not really going to see these issues. So baseline testing, you want to get an HIV ideally fourth generation, antigen antibody test, pregnancy tests for persons of childbearing potential, potential STI testing, and then the rest his kind of primary care sexual health screening, syphilis, Hepatitis A, B, and C, and then also liver function test. So counseling and education so prior to initiating PEP providers should document the duration of PEP, let them know it's going to be for 28 days, the importance of adherence, no skip doses, how to take it, separation of the, the cat ions, and that the patients are going to need some monitoring visits to be aware about the potential signs and symptoms of acute HIV infection. And those are fever, fatigue, rash, headache, lymphadenopathy, pharyngitis, body aches, oral ulcer, so again, in this era of COVID, there are some also overlay of some of these symptoms. However, with acute HIV infection, there's typically an absence of sinal, pulmonary symptoms, no coughing, no sneezing.

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So you do want to offer risk reduction counseling. So for OPEP, you really want to let patients know that they need to follow their internal protocols for their HR and occupational medicine divisions. And again, really err on the side of really letting patients know that the risk of

seroconversion with with HRT is very low, and assess really for any emotion or psychological, or social factors that may impact on adherence. For patients that are on end PEP really try to make a seamless transition, transition to PrEP. So ideally, you want to reevaluate within 48 hours after an exposure that can be a phone call, check in with the patient really reevaluate with them in two weeks, that can also be via phone. And then at four weeks, you want HIV testing, and again at 12 weeks, and again, because they may have potentially been exposed to HIV, you want to really inform them about steps that they can take really to prevent any subsequent any transmission should they have a breakthrough infection. So obviously, using condoms, avoiding pregnancy, or breastfeeding, or veto sharing, and refrain from donating blood. So going over here a little bit, just some of the testing. So the baseline visit, you just want to follow up with them. And again, that 48, two week, those don't have to be done in person, you really just want to get your baseline fourth generation baseline at Week Four and 12. At baseline, also you want to get your comprehensive panel and your pregnancy test. You want to repeat that at four weeks, you want to get Hepatitis B surface Hepatitis C, I think also a is a good practice. And then syphilis testing you want to really do at baseline now the STI testing can be repeated again in two weeks, and or at four weeks. And four weeks is when you want to on review or obtain again, the HIV test. So for sexual assaults, what's important is that you give the patients a seven day starter pack, all right, and ideally the full 28 days and you want to empirically treat for sexually transmitted infections that they don't recommend on doing baseline STI testing on sexual assault victims because of a bias in court proceedings, if there's baseline STI infection, so they really just want to to empirically treat. And again, all of these services should be offered free of charge. And the empiric treatment for STIs are going to be gonorrhea. Chlamydia, trichomonas, and for Hepatitis B, you want to offer them vaccines. So administering the first emergency dose of PEP medications really, again, get as much information as you can about the source patient. But if you don't have information, just go ahead and dispense that first dose. For non occupational PEP, really, the determination is was there condomless anal or vaginal sex, yes or no? And is there potentially infectious fluids, then you're going to dispense it? If it's a gray area, then you're going to have to dig a little bit more to see was there concomitant blood? Was there evidence of a gender of a general Ulcerative disease, and then you want to initiate the regimen, perform the baseline testing, and then the following follow up testing as I just described, I arrived. And then for sexual assault patients, really, this is something that you want to make sure that you start them on medications. Regardless if there's visible trauma regimens are the same, baseline testing is different, you're not going to do the baseline STI testing. And you're going to make sure that they have really that full month, ideally, of the PEP medications. And again, we can either use route Tegra, Vir here, or W Tegra. Vir. All right. And then lastly, I'm just going to end up here with occupational exposure to Hepatitis B, just to know that the risk for a percutaneous exposure to HIV is 0.3. But if a person is not immune to hep B, and they have a potential exposure, it can be up to 50%, you really do need a little bit more

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information about the source patient, whether the exposed person is vaccinated whether the exposed person has immunity. The good thing about determining prophylaxis against hep B is that you have about a week to decide all of this information. And if in doubt, you can vaccinate the exposed person with hep B. So again, if the person let's say here, if they're if they're previously vaccinated, and they when they're a known responder, you don't have to do anything.

It's only if the person is unvaccinated. Or if they're not a known responder that you would want to initiate the vaccine or in the riskiest of cases also provide immunoglobulin, which is in kind of short supply. So again, you have about a week to determine it, you're going to get back to testing. And again, if in doubt, you can reinitiate the Hepatitis B series. And then for hep C, also, Hep C exposures are something that we also need to determine both in the source and the exposed patient if you can. And we're basically going to do this by getting the liver panel and HCV antibody testing and also RNA testing. If we have more information about the source patient. So really, we're gonna get baseline HCV testing, antibody testing, liver enzyme testing, if we do have information about the source and they are positive, what we're going to do is we're going to do more frequent testing in the exposed person, not just looking at liver enzymes, but also at Hep C viral loads at week 412. And then also 24 weeks exposure. But again, this is something that I also want you to consider by reviewing the guidelines, you can also call up the clinical consultation line, and just remind patients that Hep C is curable. So let's just start starter packs are important, at the very least for occupational exposure seven days, but I think the full 28 days is really the way that we want to go for sexual assault exposures, it's also really 28 days for those that are under the age of 18. And just to summarize, really PEP encounters due to workplace exposure really have to comply with OSHA standards. So employees really do have to have timely access to these medications and payments for these medications for that full 28 days. And there are medication assistance programs that can help in particular for non occupational exposures. And again, these are some of the antivirals that can be accessed through these pharmaceutical medication assistance programs. So I want to stress again, patients who require repeated courses of PEP or even that one off PEP, they're at risk for HIV, they may be at ongoing risk for HIV. So really start those conversations about PrEP very early on. And one of the things is that PrEP for you. So in New York State, they've established the legal capacity of minors to consent for treatment, and for preventive services, because HIV has now been delegated to a sexually transmitted infection. So minors can consent to PEP under this law and to HIV testing. So where are we where are we moving? Well, maybe TAF based regimens may may be included in future recommendations. We know that there's decreased vaginal, cervical and rectal concentrations in some healthy volunteers. We have small cohorts of patients that have been on Jin Jin Voya, and the CO formulation of tap with big temper gear, big tarbiyah. And to date they've been shown to be well tolerated with no serial conversions. And we also have these longer acting antivirals like this latch Revere, where potentially we may be able to dose one tablet after an exposure and that will provide pharmaceutical and pharmacokinetic coverage for the entire month. So PEP is an effective means of preventing HIV after a risky exposure to HIV, both for occupational, non occupational and sexual trauma, there's no need to provide PEP if the exposure was not significant. Or if u equals u applies. But again, when in doubt, I think it's better to err on the side of providing that first dose of medication because you stop the clock if it's beyond 72 hours that you monitor for acute HIV infection. So again, we do have the New York State pet hotline, this is a number this is for consumers, anybody out there with a

55:40

this is for New York City that's had a exposure to HIV can call this line and be provided with access to pet meds and also follow up visits. And I'm just going to end here to show that CEI, the new state provides live webinars for your workplace, you can request these at the at our

surveymonkey.com. And I'll have Taryn talk about this a little bit more now. But thank you so much.

Tara 56:12
Okay, great. So let's hop into our questions here. We have quite a few. So thanks for writing. So our first question here is How do you feel about using Victor Harvey for PEP?

56:23
Yeah, that's a great question. So I think the data shows that there was a data out of Fenway in Boston that it was, well tolerated, they couldn't show efficacy, just because it wasn't powered the study to do that. So it's not really part of the guidelines. However, if you don't have access to the Truvada rotogravure, or Truvada who we are, I do think it's a viable option. You do have to explain to the patient that it's off label. And again, we don't really have the data yet. Assuredly with Taff based regimens. But again, I think it's promising. And if you don't have alternatives, I think after you inform the patient, I think it's something that can be considered.

Tara 57:13
Great, thanks. Our next question is actually from one of our CI faculty, Josh Sawyer, so thank you for writing. And so he noted regarding pharmacies offering seven days of PEP in Western New York, there are pharmacies interested in helping but it's impossible to find prescribers who are interested in working with the pharmacies to do so how do you convince prescribers to partner with pharmacies to ensure rapid start with PEP when it's needed?

57:40
Yeah, that's a great question. And it really involves just like, it's more boots on the ground, reaching out to these pharmacies, letting them know that and building a relationship to let them know, pharmacies have their cost issues. It's not you know, these requests for peps are not going to happen often. But I think if you build a relationship with a pharmacy, and it's a, you know, a bi directional relationship, hey, can you have these weed starter packs? Or can we collaborate? And then also, once a patient does present on you know, and I send them? Can you also have linkages to where patients can follow up with their clinics? Or respective? So there's no easy answer to that. It's mainly calling up pharmacy directors and having a conversation, a water cooler conversation.

Tara 58:32
Okay, great. Thanks so much. Our next question here is kind of short. So is PEP covered by insurance?

58:38
Yes, is covered by insurance. And, again, if there's an issue, um, there are these assistance programs that can assist. Those may be a little timely sometimes. But yes, post exposure prophylaxis should be covered by any insurance. And again, one of the tricks, and this is something that was mandated now nationally is that if you bill our code, or put a modifier 33, all prevention services should be covered by a patient's insurance.

Tara 59:16
Okay, great. Thanks so much. Our next question, I'm going to try to get to everyone here. So sometimes patients using 211 PrEP are not perfect with the timing of their second and third doses, maybe 24 hours plus or minus, you know, to six hours or 48 hours plus or minus two to six hours. So how do you exact how exactly do patients need to be with timing of their 211 PrEP, versus give PEP to cover a late to one one dose?

59:45
Yeah, that's a great question. Yeah. So I would say that, um, what's important with the 211 is that they get at least those two tablets prior to their exposure and at least two hours before so that's like a big one. And, and then 124 hours after the exposure and then the second 148 hours after that exposure. I would say that if it's been more than seven days since their 48 hour dose that you should definitely consider pepping them. And I would say even after three days, potentially the levels may drop. So, I would say that if they've had an exposure, three days post there, 48, you know that, that last one dose that you may consider re prepping them, but definitely by seven days, if they haven't had any Truvada on board, then yes. The other thing is that if they haven't taken those two pills prior, and they've had an exposure, then yes, I would PEP them.

Tara 1:01:03
Okay. Our next question here is how often should one be tested after exposure and receive PEP? I understand it could sometimes take up two years before it shows is that correct?

1:01:13
Yeah, so that is not correct anymore. So I think what the data has been showing is that really, I think by three months, that an HIV antigen antibody test and fourth generation test should be able to pick up HIV. So again, you got to do a baseline for weeks and then at 12 weeks, and really by then you should assuredly pick up any potential HIV for that exposures. You don't need to go out to six months, and you certainly don't have to go out to a year.

Tara 1:01:48
We have one question here. Could you go over the indication for immunoglobulin A bit further?

1:01:54
Oh, sure. Yeah, yeah. So let me go back to this one. And, and, and then I'm just so the immunoglobulin here is if the patient is either unvaccinated or if they're previously vaccinated, but they're unknown rock non responder. And if the source patient you deem that they have surface antigen, that's when you want to give immunoglobulin plus initiate the Hepatitis B vaccine. Also, if they're undergoing vaccination at the time of the exposure, then you would also get immunoglobulin. You know, these are extremely rare cases. And again, immunoglobulin is in rare supply. And we often don't have information about the source patient. And I think data shows that if you give that if you start the first dose or re start the Hepatitis B vaccination, that that's also very highly effective. So again, it's if you have if you know that the source patient is surface antigen positive, and they expose either not vaccinated, non responder or just haven't finished their series, that's when you would administer immunoglobulin plus vaccine.

Tara 1:03:04
Thanks so much. This is a Spitfire speed question. So thanks. Our next question is, do you find some patients are familiar with PrEP 211, and want to just take PEP, for a couple of days after an exposure? How do you handle this?

1:03:19
Yeah, so I'll just quickly say that when so that's not really effective, really the PEP the data, because if the animal data show that, you know, after an exposure, the amount of virus is, you know, potentially greater, and that you kind of really you have to take it for a month. Otherwise, there's a greater likelihood of breakthrough through. So yeah, just taking it for a couple of days PEP after exposure, what seems to really make that 211 work is those two tablets prior to the exposure. So that's really the main driver of the effectiveness of 211. Are those two, not just one, but two tablets of Truvada prior to the exposure, and then those two followed. So really, it's a bit dangerous, just doing PEP for a couple of days after an exposure in that it may not be enough to avert an infection without that pre dos.

Tara 1:04:14
Okay, great. And just for time sake, I'm gonna just pick one more question. And other questions, we will save I can send those out to everyone so everyone can have their questions answered. But our last question here is, if you discuss that PEP has not yet sorry, if you've discussed that PEP has not been shown to be effective past 72 hours and the patient is insistent on waiting, wanting to try it anyway. What is the risk to the patient as far as resistance if the patient is in fact positive? The resistance they know that I know Rapid Start for HIV treatment is encouraged. So I'm just trying to figure out if there's any other risks that we need. Yeah, and thanks for a great presentation.

1:04:54
Yeah, that's a that's a very, very good question, you know, on and again, It's a judgment call. I mean, this data really shows that after 72 hours really just no effectiveness, or they're just kind of taking these medications with very low kind of efficacy, you know, and that's not really going to avert an infection. That's a case by case scenario, there was data that showed even a week after an exposure that PEP was indicated for this blood transfusion where it was known to be positive, and they weren't able to detect it about a week later, and they put them on PEP for a month and the patient did not see or convert. You know, the harms are few now with the rapid start, actually, because if they were to zero convert, then you're starting them on essentially Rapid Start. It's just that I think they feel that really, that just the cost and the kind of burden of of like having to take these medications when the benefit is so small that it just kind of changes that ratio. And just to really kind of like monitor for HIV. Remember that an HIV transmission event is low probability anyway. So that kind of when the horse is out of the barn, kind of exposing someone to these antivirals when they really probably shouldn't need them. I think just kind of places the guidelines in that maybe we can just watch and monitor and do a viral load in two weeks and four weeks, but you're absolutely right. Would there be great harm if they did in fact seal convert and we picked it up early? No.

Tara 1:06:31
Okay, great. So I would just like to thank you Dr. Urbina for presenting today.

[End Transcript]