Expert Interviews

National STD Curriculum Podcast

Management of Patients on Doxy-PEP

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University of Washington Assistant Professor Dr. Chase Cannon answers National STD Curriculum Podcast Editor Host Dr. Meena Ramchandani questions about how to manage patients on Doxy-PEP including exposure to syphilis, STI testing frequency, and key counseling points for patients.

Topics:

- Doxy-PEP
- dPeP
- Syphilis
- sti testing

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Transcript

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In this episode:

introduction**[00:00] Introduction**

Hello everyone. My name is Meena Ramchandani. I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STD [sexually transmitted disease] review for health care professionals who are interested in remaining up-to-date on the diagnosis, management, and prevention of STDs.

For this episode, we welcome Dr. Chase Cannon to discuss Doxy-PEP. Dr. Cannon is an assistant professor at the University of Washington and the Medical Director of the Public Health - Seattle and King County Sexual Health Clinic. Welcome, Chase. I'm going to jump right in and ask you some questions on this important topic.

exposure-to-syphilis**[00:41] Exposure to Syphilis**

Dr. Ramchandani

Let's say you're seeing a patient and you have a discussion with them about Doxy-PEP, counseling is done, and your patient is taking Doxy-PEP as prescribed. The patient comes in a few weeks later, and they're informed that their partner was just diagnosed with syphilis. They last had sex with that partner two weeks ago. How would you recommend the exposure to syphilis be managed by this patient's health care provider or you in that setting?

Dr. Cannon

Yeah, that's a tough one. So, the challenge that we all have is that, in theory, if someone is taking intermittent Doxy-PEP that we could sort of sub-therapeutically be treating syphilis. And so, how Doxy-PEP impacts our ability to diagnose syphilis in terms of the RPR [rapid plasma reagin] kinetics, how those kind of change over time if someone's had an exposure or they have a new infection, we don't really know. So I think at this time, we are generally recommending that people be managed for syphilis exposures the way that they would be if they weren't taking Doxy-PEP, especially if we know that this person had a contact that was known. We would recommend that they get testing and then also go ahead and receive empiric treatment with something like benzathine penicillin just because we know that there can be a lag between someone's exposure and when syphilis serology might increase or the titer might increase. And so, the challenge is sort of around that. Make it that we just say, "go ahead and empirically treat." I wouldn't mess around with it or sort of wait around. I would recommend that they get it then.

Dr. Ramchandani

Yeah, we don't know if the Doxy-PEP that they took prevented the transmission of syphilis and sexual transmission of syphilis is so high, especially in the early stages, that it would be better to empirically treat contacts of syphilis rather than rely on the Doxy-PEP to have prevented that infection.

Dr. Cannon

Yeah, that's correct. And, it is something that's a little counterintuitive and can be a challenge to explain to patients because if they say, "Well, we saw in the trials that Doxy-PEP worked really well at preventing syphilis, so why would I need treatment?" It's a valid question and it's hard to actually explain. I think the simple kind of way to say it is that we don't have a good way to know if Doxy-PEP worked for that episode. So, we know that it was around 80% effective; if you were in that 20% of people who acquired syphilis, we

wouldn't have a good way to know that because your titers may not go up in the same way. So we would rather just go ahead and give you the treatment if we know that your other partner had syphilis, and we can just say that we're sort of done with that, move forward, continue taking your Doxy-PEP like normal.

impact-on-syphilis-rpr-titers**[03:29] Impact on Syphilis RPR Titers?**

Dr. Ramchandani

Now you just mentioned that their titers might not go up in the same way. Can you talk to us a little bit more about that? Because I've heard that concern from providers. Is there any evidence that taking Doxy-PEP would reduce someone's syphilis titers or alter the titers that it may not go up fourfold with a new diagnosis?

Dr. Cannon

I think all of that right now is theoretical. As far as I'm aware, we don't have any sort of formal or systematic data to support that theory, but I think all of us, as infectious disease providers and people who do sexual health care, are aware that titers can already be kind of frustrating and don't always act the way that we want. And so, if people are taking doxycycline two to three times a week perhaps, it seems plausible to me that that might abort an early syphilis infection and maybe keep the immune response from being such that we would see a titer increase at two-, four-, eightfold. So we don't know for sure, but I think it's something that we just have to be aware of, and I don't actually know the best way to study this. So that's an open-ended question for somebody to look at as we are rolling this out across the country.

Dr. Ramchandani

Okay, good to know. So, more data to come, but for now, continue with the recommendation that a fourfold increase in RPR titers indicates a new diagnosis and a fourfold decrease in titers would indicate adequate response to treatment.

Dr. Cannon

Yeah, I think that's still a good rule. That's kind of based on the CDC guidelines, but [Dr.] Khalil Ghanem did a great talk about syphilis management at CROI [Conference on Retroviruses and Opportunistic Infections], and there's even some people saying, if you have a high suspicion and you know someone with a contact like the case that you just talked about and their titer only went up twofold, you might even think about whether that's a new infection because maybe it would've been fourfold if they weren't on Doxy-PEP. So, it just makes syphilis all the more challenging and confusing when it already was, but we'll kind of see how things shake out, hopefully, as more people are on it and we get a better understanding of what happens.

Dr. Ramchandani

That's helpful. So continue empiric treatment for contact with syphilis, continue the titer recommendations per the CDC STI Treatment Guidelines, and then a close follow-up of patients, especially for clinical signs and symptoms of syphilis, to monitor patients in case they need treatment.

Dr. Cannon

That's correct. And always, always ask about neurosymptoms, just because that's another thing that people are concerned about that Doxy-PEP may suppress and make neurologic manifestations sort of less subtle, so where people may have less symptomatic neurosyphilis, so we should always be screening for that as well.

Dr. Ramchandani

That's a really great point, thank you.

sti-testing-frequency**[06:32] STI Testing Frequency**

Dr. Ramchandani

Now for patients taking Doxy-PEP, what is the optimal frequency of STI testing?

Dr. Cannon

We don't really know. I think most people are recommending that people on Doxy-PEP continue on a similar schedule as they would if they were taking HIV PrEP. So, every three months they should get routine testing. And I've even heard some people recommend that we might want to do syphilis screening even more frequently, so maybe doing that on an every two-month schedule and then doing gonorrhea and chlamydia less frequently, so like every four months, so people might come in every two months, but maybe not get gonorrhea, chlamydia every time. There's no standard schedule or recommendation for that right now. So, I think every clinic is sort of doing their own thing. So, maybe if the CDC guidelines later this year come out, they will have a stance and some guidance for us on that. But for right now, it seems like it's just similar to what people are doing for PrEP monitoring.

Dr. Ramchandani

That's helpful. So, for clinical providers, probably doing the every three to six months STI testing would be appropriate. Only every three months, right, if they're on Doxy-PEP and HIV PrEP?

Dr. Cannon

I think so, because really, for HIV PrEP, you want them to have the HIV screens every three months. And so if they're on both, I think that one kind of trumps the Doxy-PEP schedule.

Dr. Ramchandani

I like that.

doses-refills--timing**[08:02] Doses, Refills, & Timing**

Dr. Ramchandani

Let's go to another patient scenario. You see a patient in your clinic and, after shared decision-making, decide to prescribe Doxy-PEP. How many pills would you prescribe at one time, and how many refills?

Dr. Cannon

So again, there's no consensus on this. I think every clinic or jurisdiction that's making their guidelines have sort of decided what they want to do. But here in Seattle, King County, what we've suggested to people would be reasonable is something like prescribing 30 pills with one refill, so that would be a total of 60 pills that someone would get, and that would cover them for 30 sex acts. So, if they happen to go through those within six weeks and they need more, then it's a good time to check in with them and say, "Hey, how's this going? How are you using it? Do you find that you don't have enough? And then we can maybe adjust if you feel like you need more." So, every person's a little bit different, but that's maybe a good place to start.

Dr. Ramchandani

Thank you. And let's take a patient scenario. A patient has sex. They should take Doxy-PEP within 72 hours. So let's say they take Doxy-PEP the next day, but then that evening, they have sex again. When should they take their next dose?

Dr. Cannon

So, if people have sex multiple times within 24 hours, we would just go ahead and tell them to take it at the end of those multiple episodes of sex. So, say it was four times on a Saturday, they can take it that next Sunday morning, or they can take it a couple hours after they're done on Saturday night. We usually tell people it should be a maximum of one dose per day. However, I will say that there are some public health entities out there that feel like one dose a day is too much, and they're really trying to balance how many antibiotics people are taking. So, they have said, if someone's going to have sex Friday, Saturday, and Sunday, that maybe you just wait and take your dose on Sunday night or on Monday morning because then you would still have covered the entire weekend because all of that sex falls within a 72-hour window. So, it's up to the person, I think. You could do it either way. You could take it at the end of a 72-hour period if you had multiple episodes, or you could do it once a day if you're having sex frequently.

Dr. Ramchandani

Yeah, because this is a high dose of doxycycline, so it's 200 milligrams all in one dose. And while there were no significant adverse effects, it seemed like that was seen with a randomized control trial, those patients were taking up to 10 doses a month based on what you said earlier. Is that correct?

Dr. Cannon

Some of them were. The interquartile range went up to about 10 for some, so meaning a proportion of the total patients. Some of them were using it 10 times a month. So, depending on how frequently people are having sex, it could be that often, but I would say that the median seems to be somewhere between three and six for most people per month.

Dr. Ramchandani

So it's possible if people are taking it much more frequently, more potential adverse effects can occur.

Dr. Cannon

Correct.

Dr. Ramchandani

That's really helpful. Thank you.

allergic-reaction**[11:19] Allergic Reaction**

Dr. Ramchandani

We have time for a few more questions. Let's say you'd like to discuss with a patient about Doxy-PEP, but they have a severe allergy to doxycycline; they get hives, shortness of breath. Would you consider prescribing another antibiotic for STI prevention?

Dr. Cannon

Whew, that's a good one! This question actually came up again at CROI. Someone asked, not necessarily related to allergy, but saying, "If we're worried about pregnancy, is there an alternative that we could do for someone?" And honestly, we don't have data on that, so I can't say that we would recommend another antimicrobial to be used as STI prophylaxis. But I can say that historically, in the past, there have been studies that looked at other agents. So in the penicillin family, so some data with penicillin itself versus we know that amoxicillin has activity as an alternative like in pregnancy for things like chlamydia and

theoretically would work for syphilis, but I would not recommend that to a patient. We just don't have data to say what dose you need, how often you're supposed to take it. We don't even know what the efficacy would be to give people an estimate for them to make an informed decision. So, unfortunately, for a person with a severe allergy, you're a little bit stuck, but I would say you could always ask the STD Clinical Consultation Network [www.stdccn.org] and maybe speak to an expert to go through some options if you have to on a case-by-case basis.

Dr. Ramchandani

That's a fantastic idea, and that's what I would recommend as well to a health care provider. I would not recommend another antibiotic for STI prevention. We just don't have any data to support it.

Dr. Cannon

I agree.

counseling-patients-tips**[13:06] Counseling Patients Tips**

Dr. Ramchandani

Any key components of shared decision-making you'd recommend to providers to include in their patient interactions when discussing Doxy-PEP? I do think that providers should know about Doxy-PEP and feel comfortable discussing it with their patients.

Dr. Cannon

I think some of the things we've already discussed are important. So, number one, to talk about what the efficacy was in the clinical trials and which types of people were included in the studies. And one thing that I really emphasize is that even though we saw a pretty high efficacy, it wasn't a hundred percent. So you may take your Doxy-PEP exactly as it's indicated, but you may still get gonorrhea. And that's because we know it's not a hundred percent, so don't be sort of frustrated or think that you did anything wrong. This is just an intervention that reduces risk, but it is not completely protective. Also, it does not protect against any other pathogens. So, sometimes people think that they don't have to worry about things like herpes or HPV [human papillomavirus] or HIV, and this is only against bacterial STIs. So you still should be on PrEP if you are not using any other sort of methods for HIV protection, get vaccinated for other things like Hepatitis B and HPV. So, it does not protect against those things. So you may think about condoms for those if you want or other methods for prevention.

And, the other thing that is often a challenge to counsel patients about is the microbiome because it's tough for even providers to explain, and some patients have never heard about this. And so generally speaking, I just kind of tell people, "You have good bacteria that are in your body that kind of interact with your immune system and keep you healthy. And we just don't know to what extent that doxycycline may change the number of good bacteria in your body or cause other sort of impacts down the line. And so you should just understand if you're taking this, that there could be unknown effects in the future." And I know it feels a little sort of nebulous to leave it that way, but it is true. We just don't know. So, the challenge with the shared decision-making is telling people what we know, what we don't know, and then hopefully what we will get more information about in the future.

Dr. Ramchandani

Those are really great counseling points to remember. And I think that over time, more data will be published on some of these key points, we'll have more information that I think will evolve that we can use in our provider-patient discussions.

differing-guidelines**[15:40] Differing Guidelines**

Dr. Ramchandani

There are some different guidelines on Doxy-PEP available for different jurisdictions in the U.S. Can you highlight some of the guidelines and review either overlap or discrepancies?

Dr. Cannon

So there are a lot of jurisdictions out there who have made guidelines, but I think in terms of some of the larger organizations, so San Francisco of course, was the first to do it in October 2022, and theirs is a little more broad where they kind of have a tiered approach and they recommend it for the same population that was in the studies. But then they also say that you can offer it to other people who may have not had an STI in the last month but may be at risk. And then I think, perhaps, the broadest is the California Department of Health, where they basically say you can offer it to any person who's non-pregnant, who's at risk of a bacterial STI. And I think it varies all the way down to organizations that have really opted away from it and kind of recommended against it.

So, the German STI Society just released guidelines a few months ago. They are pretty strict in saying that this should be used on a case-by-case basis. You really should only reserve it for people who have had one or more episodes of syphilis. And they also highlight that, at least in Germany, that Doxy-PEP use is off-label, and so if you agree to do this, basically, the potential consequences of this are on you as the provider. The language is a little cautious. I think that generally speaking, that goes kind of from more restrictive all the way to the broadest use. And everywhere else kind of falls in between where people say there are these populations like MSM [men who have sex with men] and other populations who have had an STI where it seems more consistent that we would recommend it and everyone else, it's kind of case by case or they say prioritize people specifically who have had multiple STIs.

key-takeaways**[17:41] Key Takeaways**

Dr. Ramchandani

I'd like to highlight an article that Dr. Chase Cannon just published in *Topics in Antiviral Medicine* in November of 2023, and it reviews doxycycline post-exposure prophylaxis. The title is Doxycycline Post-Exposure Prophylaxis Prevention of Sexually Transmitted Infections. And I'd recommend it for our audience if they're interested in learning more. Any takeaways from this article that you'd like to discuss, Chase?

Dr. Cannon

I think we've covered a lot of it. I think that the main takeaways I would say is people should recognize that this is one of the first novel sort of biomedical interventions and really solutions that we've had to this rising epidemic that has been going on for the past 20 years. And so we should think about what else we have, nothing really right now, so this is something important that we should talk with our patients about because they want it.

Of course, we need to have measured caution and think about resistance and potential side effects, but I don't want that to keep us from offering an intervention to people that could be beneficial and improve their sexual health just because we, as providers, are concerned about it. And one thing that I hope will add at least some comfort to providers' minds and give them some guidance is when CDC releases their guidelines, which are hopefully coming out later this year. They had a draft that was released in the fall of 2023 and went out for public comment. I think they're working on those right now. So everyone stay tuned for those to come out later this year.

Dr. Ramchandani

Very well said. The 2022 STI Surveillance Report was just released showing a great increase in STIs, especially in syphilis. And the syphilis epidemic continues to grow in the U.S., and so it's really nice to have this STI prevention tool to help patients and the community.

Dr. Cannon

Yeah, absolutely.

Dr. Ramchandani

Thank you so much, Chase. This has been such an informative session, and I learned a lot from speaking with you. I really appreciate you being here with us today.

Dr. Cannon

Thank you very much.

new-hiv-podcast**[19:50] New HIV Podcast**

Listeners, we have an exciting announcement! Our *National HIV Curriculum* team just launched a podcast about HIV diagnosis, management, and prevention. Please check it out on your podcast app or at www.hiv.uw.edu/podcast.

credits**[20:10] Credits**

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