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Expert Interviews

National HIV Curriculum Podcast

Priority Immunizations for People with HIV (Part 2)

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Dr. Shireesha Dhanireddy, an expert in HIV prevention and treatment, once again joins National HIV Curriculum Podcast Lead Editor Dr. Brian Wood to discuss vaccinations for adults with HIV. This episode focuses on optimal management of hepatitis A and hepatitis B vaccinations, as well as best practice strategies for measles immunization for adults with HIV.

Topics:

- vaccines
- hepatitis A
- HBV
- Heplisav-B
- MMR

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Transcript

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

In this episode:

- Hepatitis A Vaccine
- Measles Vaccine
- MMR Vaccine and CD4 Hello, everyone. I'm Dr. Brian Wood from the University of Washington in Seattle. 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 am back for another episode with Dr. Shireesha Dhanireddy. We will continue our discussion on immunizations for people with HIV. As a reminder, Dr. Dhanireddy is professor of medicine in the Division of Allergy and Infectious Diseases here at the University of Washington. She also serves as Associate Chief Medical Officer for UW Medicine and Section Head for the Division of Allergy and Infectious Diseases. She also helps lead the HHS Opportunistic Infection Guidelines Panel and is a member of the group that develops vaccine recommendations for those guidelines. Welcome back, Shireesha, and thank you again for taking the time to do this.Dr. DhanireddyThank you so much, Brian, for having me.Dr. WoodSo, let's jump into our discussion about vaccines, specifically viral hepatitis vaccines in this next section. And again, I'm going to frame it with a case, loosely based on a case I saw in clinic not too long ago. So, this is a 55-year-old woman who transfers care to your clinic. She was diagnosed with HIV approximately two years ago and started antiretroviral therapy shortly after the diagnosis. She has taken her ART [antiretroviral therapy] as prescribed. She's been excellent at taking it every day. Her viral load is undetectable. Her CD4 count is now 325. So, per the outside records, she did receive hepatitis A and B vaccines several years ago. You can't quite sort out from the records which type of hep B vaccine she received, but it is documented that she received a form of hep B vaccine, so as part of your routine lab testing, you check a hepatitis B serology panel, and the hepatitis B surface antibody (HBsAb) is under 10. And in addition, the hep A IgG antibody is negative, despite the report of receiving prior vaccines.Dr. WoodFirst, just to start, how do you interpret this, and what do you see as the most likely explanation?Dr. DhanireddyThis I think is not an uncommon scenario. And so there could be a couple of explanations here. So, I would want to know how low was her CD4 count when she was initially diagnosed and when she got the vaccines. Actually, one of our colleagues, [Dr.] Nina Kim, did a study a long time ago that showed that CD4 count nadir actually predicted response or nonresponse to vaccine. So, if she had a very low CD4 count, or she may not have responded, so that’s when we typically try to get our surface antibody repeated about a month after the vaccine series have been completed to document protection. We don't have that data to know is she a nonresponder, for one, or the second option is that she's had a waning surface antibody response over time, which can happen. And what that indicates is that if they were exposed to hepatitis B, or if they got another dose of vaccine, would that memory response come back?And so, we can't really distinguish those two at this point, so one thing you could do is actually give her a dose, a vaccine, and then repeat it. The tricky thing is we don't know what kind of vaccine she got. We usually like to maintain the same vaccine, but we don't know. So, you could either repeat her vaccination with Heplisav-B, which I'll refer to as Hep B-CpG, and give her two doses of that, or give her a dose and then check a titer, and then we can distinguish between the two options there.Dr. WoodAnd you mentioned regardless of which option you do, one dose or two doses of Hep B-CpG, you would repeat the titer about four weeks later, correct?Dr. DhanireddyCorrect.Dr. WoodSo then, what level are you looking for when you recheck?Dr. DhanireddyUnlike hepatitis A, which I'll talk about in a minute, we actually have a good correlative immunity for hepatitis B. So, greater than 10 has been associated with protection, but we have newer data from the BEe-HIVe trial, which looked at Hep B-CpG vaccination in people with HIV that showed, the higher their titers, the actual longer durability they could see in them staying antibody evidence of seroprotection. That being said, is there a clinical correlate for that? Do we know that the higher their level is above that 10 that they actually are more protected? We don't know that. And so, I generally use greater than 10, except in a separate situation where we see isolated core antibody, which is not the situation here, and I think there's a separate podcast about that, so I'll defer about that. But in that situation, we like to see titers greater than a hundred.Dr. WoodSo, if I'm hearing that right, if I can say that back to you, Shireesha, sounds like, in your practice, you check a month after hep B vaccination, look for a tighter above 10. Maybe there's long-term benefit to achieving a higher titer than that but sounds like we really just don't know. We don't have that data yet. Is that correct?Dr. DhanireddyThat's correct.Dr. WoodThe other question I'm eager to ask you, which may not have an answer, is let's say a person achieves a titer above 10 or

above a certain level. Do you think we should be rechecking over time and revaccinating if the level then wanes to below 10? Is that something you've ever done in your practice, or what's your general thought around that?Dr. DhanireddySo, there is controversy around that, and some experts would say, "Repeat it." I have not been doing that in my practice, and mainly because many of my patients are on tenofovir-containing regimens, that I don't do that. And I guess in a situation where they're not on a tenofovir-containing regimen and they remain at high risk, that could be a consideration, but I generally don't because they're on a hep B-suppressing or -treating regimen, -preventing regimen.Dr. WoodMakes sense. And as far as I know, rechecking over time, revaccinating over time is not in any of the official guidelines, is that correct? Or am I missing something?Dr. DhanireddyThat's correct.Dr. WoodAnother area for potential further study. Dr. WoodSo, then in terms of the type of hepatitis B vaccine you recommend, you mentioned Hep B-CpG. Is that the one you favor these days? And can you just give us a couple sentences about pros and cons of that one compared to others?Dr. DhanireddyHep B-CpG, since the BEe-HIVe study came out, which was looking at this specifically in people with HIV, I think we really moved towards that vaccine. The benefits are it's a two-dose series four weeks apart. So, in terms of getting patients protected quickly, you can, and it's not spanned out over three doses over six months, which can be hard to complete for some people. So, I think that's one benefit.The other benefit is we know that, even prior to BEe-HIVe, there was actually observational data that showed that people, when they're nonresponders to the older recombinant vaccines, that they actually could respond better to Heplisav-B. And we have that data from BEe-HIVe now, so BEe-HIVe, they had a study looking at nonresponders, prior nonresponders, as well as people who are in vaccine naive. Both of those studies showed quite good protection.I will say that the BEe-HIVe study incorporated three doses rather than two. So, if you read that study, we'll notice that significant difference. But, when you look at data for protection after two doses, it's still quite good. And so, I don't know of anyone doing three doses standard. Based on BEe-HIVe, we're doing two doses, but there's an option to give a third dose in the setting of nonresponse.Dr. WoodAnd I'll just mention for listeners, we have a separate episode, a literature review on BEe-HIVe. So, if you haven't listened to that or aren't familiar with that study, you can check that out.Shireesha, that was a question I wanted to ask you. And just confirming, you recommend two doses of Hep B-CpG for anyone receiving that vaccine in your clinic. Is that correct?Dr. DhanireddyCorrect.Dr. WoodSo, what about another common scenario in which a person has received multiple doses of hep B vaccine in the past, but their surface antibody level is still not protective? What do you do in that situation? And how many courses of hep B vaccine until you will just say, "Look, I don't think we should repeat this."?Dr. DhanireddyYou know, in the past, I've done two courses with the older recombinant vaccines. And there were a number of different kinds of ways you could do this double dose, and actually the OI [Opportunistic Infection] guidelines do, if you're not using Hep B-CpG. It's a double dose of the traditional recombinant vaccines, and you can do a fourth dose of that double dose and see if you can get better protection. So, those are strategies I used to use. I will say, for those patients who were nonresponders, I was waiting for Hep B-CpG, and they did, the patients that I've had that were prior nonresponders, have responded to Hep B-CpG.Dr. WoodWhich is pretty amazing, and it kind of shows the value of that vaccine. I remember all of those strategies, as well, when a person did not respond to the older alum adjuvanted vaccines: giving double dose, giving extra doses, giving the hep A/hep B combo dose trying to stimulate a better immune response. There were a lot of things we tried. And now, it's really Hep B-CpG that has made such a difference and most people respond to. But Shireesha, not every clinic might have access to Hep B-CpG. In that situation, what do you think would be the optimal strategy for someone with HIV who does not respond to hep B vaccine, Dr. DhanireddySo, I think I would use a double dose of the adjuvanted recombinant vaccines that we used to use in standard practice in our clinic, and give that fourth dose if they are nonresponsive to the three doses. So again, checking the titer and then repeating the vaccine. I think you make a good point about if patients are on a tenofovir-containing regimen that I would feel much more comfortable even in the setting of nonresponse, if they're adherent with their therapy and their viral load is suppressed for their HIV that they're actually okay in terms of hep B, that they're likely not going to acquire hep B in that setting. For patients who are not on a hep B-active regimen, then I would be a little bit more concerned. And so patients, like patients who are on a long-acting injectable, cab-ril [cabotegravir and rilpivirine] for instance, who are hep B nonimmune, I do worry about those patients

a little bit more, and I'd want to think about ways that we could get them immune.And so, if you don't have Hep B-CpG in your clinic, is there an outside pharmacy that they could get it at to offer that better protection? And I'm saying that because some clinics see a combination of pediatric patients and adult patients, and that's a scenario where you may not see Hep B-CpG in that clinic because it's not approved for individuals younger than 18 years old. And so that is an important consideration if you're stocking vaccine in your clinic and you want that to be a vaccine that most of your patients across the age spectrum can use, and that there's not confusion and mix up of vaccine. So, that actually, in one of our clinics in our system, that did come up because I didn't have access to Hep B-CpG because of that issue.Dr. WoodThanks, Shireesha. There's so much to consider around hep B vaccination but, for time, I want to switch us to hepatitis A. So, let's think about hepatitis A vaccine for people with HIV. Let's start with, when do you recommend hepatitis A vaccine in your HIV primary care clinic?Dr. DhanireddyTo everyone. I think it's been much more simplified. When I first started in clinic, it was people with additional risk. And now, the issue is that everybody should get it, right? And even more so now, we are seeing recommendations about making sure they're immune, so that's a little bit new in the last couple of years. So not only screening everyone based just on the fact that they have HIV, and not necessarily having any additional risk on top of that, but then also ensuring that they have an antibody response to that vaccineDr. WoodClarifying for listeners. So, checking a hepatitis A IgG as part of baseline labs at entry into care for everyone who has HIV, and for everyone who has a negative or not detected IgG recommending vaccine. Is that correct?Dr. DhanireddyThat's correct.Dr. WoodAnd so then, to your other point about rechecking or monitoring, to make sure there's been a response, what are you doing in your practice Dr. DhanireddyI am checking an antibody, the IgG response to the vaccine. I will say, unlike hep B, there's not as good of a correlative of immunity, and most of our labs don't do a quantitative titer, right? We just get, is it there or is it not there, and what does that really mean for durability of protection? We've always thought of hepatitis A being a lifelong vaccine, so you get your doses and then you're done for good. We know that it's a universal vaccine in infancy, but we don't know how long the protection necessarily is. And we have seen cases, even in our own community here, of people getting hepatitis A despite having been vaccinated. So, it is a concern that there may be some waning immunity. So, for patients who have ongoing risk with hepatitis A, and you've not checked a previous titer before, I would definitely check a titer to make sure that they have evidence of protection.And when I mean additional risk, I mean men who have sex with men; people who are living in congregate settings, in tent cities, supportive housing potentially; people that are living homeless for sure, because we have had large outbreaks in metropolitan settings in homeless communities... that we would want to make sure that they do have protection.Dr. WoodIf you are seeing someone who received hep A vaccine and you recheck their serology, their IgG level, and it is still negative, what do you do?Dr. DhanireddyI repeat the series.Dr. WoodAnd what if, as in the case scenario we described, a person received hep A vaccine years ago and you checked now and the IgG is negative? Give one dose of hep A vaccine, repeat the whole series, then recheck? What's your practice?Dr. DhanireddyThat's a good question, and I don't think there's a really good answer around that. One thing I will say is that I don't give the combination hep A and hep B in that setting. I will just give the hep A, and I typically do the two doses.Dr. WoodActually, that's a great point, and I'm glad you mentioned that. It seems like nowadays, especially for practitioners and clinics that have access to Hep B-CpG vaccine, which you were talking about all the value of that, if a person needs hep A vaccine and hep B vaccine, instead of doing the combination hep A-hep B, you will do hep A vaccine and then separately Hep B-CpG. Is that correct?Dr. DhanireddyThat's correct. I've really moved away from doing the combination just given the data around Hep B-CpG being very effective, and then the hep A vaccine only having two-dose series rather than a three-dose series for that, I've just moved to doing them separately.Dr. WoodTotally makes sense. I'm glad you mentioned that. That's become my practice too. Shireesha, that is so excellent and helpful regarding hepatitis A and B vaccine.I'm going to switch gears now and bring up another really important topic that I think has some clinical questions conundrum. So that is measles vaccine. So let me frame this again with another case, again, loosely based on someone I saw in clinic not too long ago. So, this is a 64-year-old man born in 1961. He has taken ART for many years, maintained an excellent CD4 count, maintained an undetectable viral load, and he asks you, "Should I get the measles vaccine?" As far as he is aware, he received all recommended childhood vaccinations,

but he is unable to find records, does not have confirmation, does not know if they were given on time, what ages he received them, or which versions of the vaccine he received.So, given all of that, how would you counsel him? What would you do? Would you go right to recommending vaccine? Would you not recommend vaccine? Would you check a serology titer first? What would your strategy and counseling look like?Dr. DhanireddyThis is a great question, and it's obviously a very timely question given the significant increase in measles cases in the last year, and the decrease in measles vaccine uptake in general. And there's definitely pockets in our community where people have not gotten this vaccine in particular. They may have gotten their other vaccines, but this vaccine in particular. And there's a lot of vaccine misinformation about this one in particular, which I always am concerned that even though they got their other vaccines, did they Couple important points about this particular patient. This person was born after 1957. In 1957 and before, we assume natural immunity to measles. So, we are going to be relying on whether this person had a history of measles potentially, or if they got the vaccine, and we don't have documentation of that. Given the concern for potential disease outbreaks, and for this person who has HIV, although an excellent CD4 count, I think it's very reasonable to check a titer.There have been some studies recently, in the last couple of years, and then series over time, that show that when they've screened patients at HIV primary care clinics, that a significant percentage actually are measles nonimmune. What does that mean? We don't know. Does that mean that they have waning antibody response but maintain protection if they were exposed, like an anamnestic response, a memory response that they would have? Or is it true that they're really not protected? So, there's some controversy around that.There was a study, two studies from the Midwest, that actually showed it's about 20 something percent of individuals screened had a negative antibody to measles. So that's significant, I would say. And so, clinics like ours have decided for new patients, particularly patients where we don't have any records of vaccines, and because we're seeing a lot of patients who are immigrating and may not have vaccine data for them, or don't have vaccine data for them, that we are offering screening, we are doing screening for measles in that situation.So, for this individual, I think it's reasonable to have that discussion and say, "We're going to screen you," particularly if there's an outbreak situation, or cases. In our community, we don't have cases frequently, but I feel like every month or so we get a public health alert about measles in our community from an imported case. And so, this is one where the vaccine is very effective, and the disease is highly infectious. And so, I think those two things compel me to do more screening than I would say probably for other diseases. Because the vaccine has a tremendous impact and the majority of cases of measles in an outbreak are going to be from unvaccinated or unknown vaccine status patients.Dr. WoodSo, what I'm hearing you say, Shireesha, is you have a very low threshold to check a serology titer for the majority of individuals in your primary care HIV clinic. I guess let me flip the question around, for whom do you Dr. DhanireddyI think if they're born before 1957, you don't have to. If we have documentation of the two MMR [measles, mumps, and rubella] doses, we don't have to. And then if they've had antibodies checked before. And then otherwise, I'm checking.Dr. WoodGot it. That's helpful. And then let's say you check and the titer is negative, sounds like there's a possibility that the titer simply waned and there would be an anamnestic response, but as long as the CD4 counts above 200, there's really low downside to recommending vaccine. Am I understanding that correctly?Dr. DhanireddyThat's correct. It is a live vaccine, so we wouldn't give it in low CD4 count settings. But otherwise, I would go ahead and give that vaccine, and the two doses.Dr. WoodThat's where I was going. So, titer's negative, you counsel someone about their risk of measles infection, and then you recommend two doses, not one.Dr. DhanireddyThat's correct. Because we don't have documentation of that vaccine.Dr. WoodSo, you do two doses of vaccine and then do you recheck the titer after the two doses or not?Dr. DhanireddyI do not recheck the titer after the two doses of vaccine. Now we have documentation of those two doses, and that's sufficient.Dr. WoodGot it. Dr. WoodNow a challenging question, but one that has come up for me in clinic. What if an individual has no documentation, unknown history of prior MMR vaccine, you check an IgG and it's negative, but their CD4 count is below 200. What do you recommend, or how do you counsel an individual in that situation?Dr. DhanireddyIn patients who have CD4 counts less than 200, it is a contraindication to give the measles vaccine. That is because, in the pre-HAART [highly active antiretroviral therapy] era, there was a report of vaccine-derived measles. We are in a very different era in terms of our HIV treatment than we were back then, but we don't have safety data. No one's

going to do a study to look at the safety of giving MMR to people with CD4 counts less than 200. This question came up to me recently and I'd say that if they don't have an immunologic response to their ART, meaning their CD4 count remains persistently low, but they're virologically suppressed and it's an outbreak situation, I think there should be shared decision-making about giving the measles vaccine in patients with CD4 counts between 100 and 200.Dr. WoodAnd what if their CD4 count does seem to be responding? Let's say it's on an upward trajectory, what would you do then?Dr. DhanireddyThen I would wait.Dr. WoodWait until above 200 then vaccinate.Dr. DhanireddyYeah.Dr. WoodAnd what if it's on the border? Actually, this came up for me in clinic not too long ago. What if it's stably 180 to 190, it's not going up, the person's taken ART for a long time, their viral load suppressed?Dr. DhanireddyI would give it. I mean, there's no magic about that count of 200 being less. So, I think I would just give it in that situation.Dr. WoodAnd that's what we ended up doing with some shared decision-making, and this was an individual who may have had, let's say, higher than average risk of being exposed to measles, but there was a lot of shared decision making about it.Dr. WoodShireesha, this has been so excellent and educational. I really, again, just want to thank you for sharing your time and expertise. I'll give you the final word. Any last take-home message for listeners that you would like to emphasize?Dr. DhanireddyI think when we're taking care of people with HIV, we often focus on the HIV itself, and that has become a lot easier to treat. There's a lot of other discussions about prevention, and I think we think about that with cardiovascular disease prevention, cancer prevention. But I think vaccines are a vital part of that process, and normalizing that at every visit, and talking about vaccines is going to be really important for our patients.Dr. WoodSuch an important take-home message. Shireesha, thank you so much for your time.Dr. DhanireddyThanksTranscripts and references for this podcast can be found on our website, the National HIV Curriculum at

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