Expert Interviews

National STD Curriculum Podcast

HPV & Anogenital Warts

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Dr. Helen Stankiewicz Karita, Associate Professor at UCSF and a national expert on human papillomavirus (HPV)-related diseases in the anal canal, and National STD Curriculum Podcast Editor Dr. Meena Ramchandani discuss how to screen, diagnose, and treat HPV-related warts in the anal area.

Topics:

- HPV
- warts
- dysplasia
- HPV genotype

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Disclosures

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References

IANS Guidelines

Transcript

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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 STI [sexually transmitted infection] review for health care professionals who are interested in remaining up to date on the diagnosis, management, and prevention of STIs.

We welcome back Dr. Helen Stankiewicz-Karita to discuss HPV [human papillomavirus]-related diseases in the anal canal. Dr. Stankiewicz-Karita is an infectious disease physician and an associate professor at the University of California, San Francisco. Welcome back, Helen.

Dr. Stankiewicz-Karita

Thank you, Meena, for having me back.

overview**[00:39] Overview**

Dr. Ramchandani

So, let's discuss a big topic in sexual health, and that's anogenital warts, and let's touch on some areas that can be challenging for providers when seeing patients with anogenital warts. So why do patients get anogenital warts? Are they associated with acquisition of anogenital HPV infection?

Dr. Stankiewicz-Karita

This is a great question. Anogenital warts are caused by certain type of human papillomavirus, most commonly HPV 6 and 11, and they are considered low-risk HPV types because they don't cause cancer, but they cause visible warts over the skin or mucosal surfaces of the anogenital area. So, the answer is yes. The development of anogenital warts is directly associated with the acquisition of anogenital HPV infection.

Dr. Ramchandani

Now, how do anogenital warts present? How would a provider distinguish them between anogenital warts caused by HPV and wart-like lesions, for example, from other general infections, for example, for syphilis?

Dr. Stankiewicz-Karita

Great questions. So, the anogenital warts, I would say they are usually fairly easy to recognize on exam, and they have this typical appearance of like cauliflower or plaque-like appearance. But sometimes they can be just a little bit raised or elevated or tend to be flat rather than that typical pedunculated lesion. Most of the times, patients will not have any pain, they will be painless. When you palpate them, they should be soft to the touch. Now, there are other infections like syphilis, for example, secondary syphilis infection, that can cause a condyloma lata. They tend to be, or they can look exactly like HPV warts, but they usually are bigger in extension and moist. When you look under on exam, they are, instead of being that dry-ish warts from HPV, tend to be more moist, or the patient will also tell you that there are, or there could be systemic symptoms as well. So, in those cases, you need to get serology for syphilis, for example.

Another condition that I see, I saw one case, is herpes can also mimic genital warts, and they can look exactly like an HPV wart, but it's described that most of these patients are painful, and also, they have a kind of crusting or exudate on the top. But with our experience, I think we both know that the herpetic lesions are not always painful.

So, when there is a diagnostic uncertainty, I always recommend biopsy, and I want to emphasize that to the primary care providers who may be seeing these patients. There really is a relatively simple step that you can do to clarify the diagnosis and prevent an inappropriate treatment or delay a targeted treatment.

biopsy**[03:46] Biopsy**

Dr. Ramchandani

Who would do the biopsy? How is that done? I haven't done a biopsy before, especially the anogenital genital area.

Dr. Stankiewicz-Karita

I say relatively easy because we do it in our clinic all the time. But for primary care providers at the different sexual health clinics, sometimes you will use a punch biopsy. You can do a punch biopsy that's relatively straightforward and easy. You don't need to suture the lesion; you can do a three millimeter or something like that. It's tiny, it's small, you don't need a super big biopsy. But if you cannot do it, which is probably the majority of the audience, refer them to either their dermatology will do these biopsies fairly easily, especially if they are in the external genital areas or skin. And if there is something more deeper in the anal canal, for example, colorectal or general surgery, can see these patients. Or if you have in your clinic a high-resolution anoscopy provider, that will be the ideal person to evaluate for anal canal lesions. The OB [obstetrician] can look into the cervix or vaginal areas if there are lesions in that anatomical site.

Dr. Ramchandani

I guess one could also swab the area if you're thinking about herpes on your diagnosis and sending for an HSV [herpes simplex virus] PCR [polymerase chain reaction], and then, if one had access to a dark field microscope, they could also put a slide on those mucousy lesions and look for treponemes.

natural-history**[05:25] Natural History**

Dr. Ramchandani

Do you find that persons who have anogenital warts from HPV tend to have those warts for a longer period of time than someone, for example, for syphilis or herpes, or is there a variety?

Dr. Stankiewicz-Karita

I would think that probably the timeline will be different in more slow and may be slash chronic for the HPV. There are some studies, some of them done at the University of Washington back in the days that after the exposure to the HPV 16/11, there is incubation per se, we can call it incubation period of like couple weeks to a few months before the lesions will appear, then the warts. The warts just tend to be present for at least a couple of months before they disappear, so it involves 3 to 4 months. And again, a lot of the time, because they don't cause any other symptoms, patients may not seek care or evaluation immediately. So, I will think that HPV wart-like lesions will probably be there for a little longer than herpes or syphilis, for example.

anal-dysplasia-or-precancerous-lesions**[06:42] Anal Dysplasia or Precancerous Lesions**

Dr. Ramchandani

Let's say you have a patient who presents with some anal lesions that he said has been there for several years. He's not concerned as he has a history of anal warts, and so you do an anoscopy to evaluate the lesions a bit better. What features would you be concerned about for anal dysplasia or precancerous lesions?

Dr. Stankiewicz-Karita

This is a great question, and it is something that I really encourage providers to keep in mind when you are seen or evaluating patients with warts. So, when I examine warts, the features that are concerning for dysplasia or, most importantly, cancer can be bleeding, ulceration, having these atypical or unusual pigmentation like grayish or darker pigmentation, for example. If I'm seeing them in my clinic with a high-resolution anoscopy exam, I will look for atypical blood vessels. We can see that on the exam as well. And those can be highly concerning, particularly for cancer. If those features are present, I strongly recommend a biopsy, and if you cannot do those biopsies in your clinic, I will refer them to the high-resolution anoscopy clinic or colorectal genital surgery for an evaluation.

Now, the high-grade lesions or precancerous lesions they usually don't look like warts, and they are flat and they can be very subtle. So, that's why when we look with a high-resolution anoscopy, we really have to pay a very close attention because they sometimes can be really hard to see or distinguish from the regular mucosa. And that's why we use the vinegar or acetic acid and use the Lugol's iodine to kind of help us differentiate those lesions and look at these lesions with light and magnification. So that's kind of what we do with the high-resolution anoscopy. I tell My patients that ask me sometimes, “I just had a colonoscopy, why they didn't see these?” And I say unless these lesions are bumpy, like warts, they won't be noticeable on a regular exam when we do it in the clinic or even during a colonoscopy exam. So, in patients with a prior history of anal warts or if there's a new or persistent wart, I really want to perform the high-resolution anoscopy not only to evaluate for a recurrent or the current warts, but most importantly to rule out precancerous lesions.

And again, the warts itself are not a direct precursor of cancer, but they are thought to be more markers of their risk, meaning the presence of a wart signals a higher likelihood of developing these precancerous lesions somewhere else in the anal canal. The main concept is that there could be co-infection with different genotypes, and a person can have benign HPV types, represented by warts, but also oncogenic types, and they can develop high-grade lesions. And I think that's why the International Anal Society guidelines specifically address, in their anal cancer screening considerations, that patients who have a history of anal warts should be screened for anal cancer just again, because that can be the signal for higher risk of anal cancer development.

external-warts-treatment**[10:25] External Warts Treatment**

Dr. Ramchandani

Let's say, for this patient scenario we just discussed, there are no concerning features of his anal warts. Nothing's bleeding, nothing looks bigger, no new lesions. It's pretty much the same. What are some of the

ways to treat anogenital warts from HPV that a provider could do in the office? And, if there were no concerning features of his anal warts, would one need to do a high-resolution anoscopy, especially if not all centers have that available to them.

Dr. Stankiewicz-Karita

So, if no cancer concerns and we're just dealing with benign anogenital warts, there are several treatment options that can be done right in the office. And the choice really depends on the number and size of the lesions, where they are located, the patient preference, and also what we have in our clinic or things that we are comfortable to offer, right? So, one common option is the cryotherapy (or freezing the warts), and that just mainly involves applying liquid nitrogen to freeze these warts and cause these tissue damage by ice, the formation of ice crystals, and that leads to cell death. So, that I will say can be done easily and is fairly cheap to do it in the office for single or multiple warts that are in the pre-anal area.

I will say here in the U.S., we typically don't use that for the anal canal, although I know that some European colleagues are using that in the anal canal. I usually apply three freezing cycles in a visit and then ask them to come back in one or two weeks and tell them that they may need several cycles to get rid of the warts. Most patients do find they may have a little bit of burning after the freezing, but usually no major side effects, and the successful rate is about 45 to 75%. So, I will say it could work pretty nicely.

We also can offer an application of a topical acid. It's called a trichloroacetic acid (or TCA). And this is something that we can just use a tiny little bit with a Q-tip and directly apply to the warts. Usually, I will use this when there is just one or very few warts and when they are fairly small. So I know that it doesn't work for larger lesions because it doesn't really penetrate like the bigger, you know, thickness of the skin. I will do this, I think once a week for a couple of weeks until the lesion is completely gone. Most patients, again, will tolerate this burning without any issues, but sometimes can cause that burning sensation for a couple of hours after the application.

In our clinic, we will use more commonly the hyfrecation or electrocautery ablation of this lesion. This is something that we can do fairly quickly as an outpatient procedure without general anesthesia. We usually just inject a little bit of the lidocaine at the side of the lesion and then burn off that spot or the warts. We can use this in the anal canal, in the pre-anal area, and most patients will tolerate the exam or the treatment and the posttreatment recovery just fine, although can cause a little bit of bleeding and discomfort because it basically causes or creates a tiny open wound at the site of the treatment. And, for those who have more larger warts or newer warts, sometimes it's hard to ablate them in the office, and mainly because we have to numb it up this lesion individually and that can be a lot for the patient. So, colorectal surgery or general surgery can take care of them in the operating room.

Those are the most common, I will say, treatment options that we offer. Regardless of the method that we use or offer, I always tell them upfront that the recurrence is very common, and so one treatment is not one-and-done. And again, these lesions can come back, and we see these even in patients undergoing for like a surgical excision, and I see them again in our clinic, and just after a couple of months, the lesions can be all back again. So, follow-up is important. Education is key for discussing the treatment options.

internal-warts-treatment**[15:07] Internal Warts Treatment**

Dr. Ramchandani

So, if a provider were to do an anoscopy for a patient and sees *internal* anal warts, how would you recommend treating these? Are these the same types of methods you just described for external anogenital warts?

Dr. Stankiewicz-Karita

So, when I find internal anal warts during the exam, I usually explain that these are benign lesions, so they don't turn into cancer, and we don't necessarily need to treat them. Unless they are either causing some symptoms for patients, because remember they can be highly vascularized and sometimes can cause a little bit of benign bleeding I will say, or they can be prolapsing to the pre-anal area. Some patients who have receptive anal sex they can also express concerns about that, so aesthetic and things like that. But if they don't have any symptoms and they don't want to receive any treatment, we can watch them and monitor. Now, if the patient wants to get rid of them, we have a few options, as we just discussed more commonly, and I think, in my experience, more effectively, will be the hyfrecation in the office. So, ablating those spots and remove these lesions. And again, if they are circumferential or larger that we cannot treat them in the office; we may send them to the colorectal or general surgery for an out-treatment in the operating room.

In some patients, we can also use a topical cream to decrease those bulky lesions and then aim to ablate or hyfrecate whatever is left over after the topical treatment. Some of them, just to mention, for example, the imiquimod, or 5-FU [5-fluorouracil], or *Efudex*, is the name. These are not HPV-directed therapy. So, these creams are not antivirals, and we don't have any antiviral treatments or cream-like for HPV. These creams will just cause an inflammation in the anal mucosa and really allow for the immune system to get rid of the lesions. That’s how they work. Particularly in patients who do not have a strong immune system, like patients living with HIV or transplant patients, this approach may not work. But again, it's an option that we can use to shrink them down. And then with the hyfrecation, just get rid of whatever is left after the topical treatment.

Dr. Ramchandani

Yeah, that's helpful. I've found that the imiquimod cream does really help for patients, including my patients with HIV. But I guess it depends on the burden of how many warts they have and the length of time, potentially.

Dr. Stankiewicz-Karita

Right. And it's hard to predict, and some patients are willing to try and do a trial, and for the audience, the imiquimod or the 5-FU are intended to be applied for 16 weeks. So, one of the main concerns that I hear sometimes is like those who are sexually active or are having receptive anal sex, the cream application can cause irritation and burning. So, doing this therapy for 16 weeks can be sometimes not realistic for some of the patients. So, what I do, because we don't have a way to know who will or not respond after starting the treatment, I bring them back in about two months or so to see if there's any response. And if I don't see any response, I just move on to the next step or offer something else instead of continuing the treatment when I may predict that won't have any effect on the warts.

natural-history**[18:59] Natural History**

Dr. Ramchandani

What is the natural history of a person with anogenital warts? For example, does natural or spontaneous clearance of anal HPV occur?

Dr. Stankiewicz-Karita

That's a great question. After exposure to HPV, the typical incubation period before the clinical development of a wart, it's about three weeks to a few months. And once the warts develop, they may increase in size and number. Because once you have an established lesion, that skin or infected lesion can shed new viruses or viral particles to the healthy skin. So not infrequently you may see one wart and then in a couple of weeks you may see a bunch of new satellite warts around that initial lesion. And there are studies saying that about 30% of these warts will resolve spontaneously within the three or four months after development. That's visible warts, right? What we're seeing, and I think that doesn't mean that the HPV infection is completely gone. And, in fact, we used to think that our immune system will get completely rid of them in a year or two

after the initial acquisition, but I think we now, as a field, we think that this HPV infection can persist in this latent state and hide in that basal layer of the skin. We may not see necessarily clinically or we may not pick up with the swab or when we test for the DNA that clears up the visible warts, doesn't mean that the HPV is completely gone. I think that's something that the provider should be aware of, and the patients as well.

I always give this example with my transplant patients: that they may not have or they may have a history of warts back in the days and then nothing for many, many years. Then they receive an organ transplant and after a couple of years of immunosuppression, they may start dealing with anogenital warts and they tell me "I didn't have any exposure. I'm not even sexually active, how is possible to have new warts if I'm not sexually active?" So, the truth is, the viral particles were probably dormant there all the time. And whenever our immune system is not controlling them, they may show up later in life or after our immune system is being hit, for example, with immunosuppression or with an HIV infection.

Dr. Ramchandani

That's really interesting. That's a change in our understanding or what I've been taught about HPV warts historically.

Dr. Stankiewicz-Karita

It's very similar to HSV, actually. To me, I think more as a chronic infection and again, we can have this kind of latent type of state and later on they can just replicate and create these lesions. As a field, we read about this type of thinking in terms of like the natural history, but I think back in the days, the thought was once we get it, we get rid of them, and then it's gone. I don't think they behave quite like that, but again, it's an area of ongoing research. And as you know, Meena, you have done a lot of work on this, on HPV, natural history with HSV, and other pathogens. It is hard to study, particularly viral infections, but yeah, the field is still learning and understanding about the natural history, particularly in the anal canal.

Dr. Ramchandani

It speaks even more of how important the HPV vaccine is.

Dr. Stankiewicz-Karita

Absolutely. You're absolutely right, yes. And all the efforts for those who are able to provide the vaccination as soon as it can, be over 9 to 12 years old, it's really, really important to get those shots to all the arms that are qualified and before people get exposed to the virus.

follow-up**[23:10] Follow-up**

Dr. Ramchandani

So, along those lines, can anal warts turn into anal dysplasia or precancerous lesions in the future? And how would you recommend a provider or patient follow their anogenital warts?

Dr. Stankiewicz-Karita

So that kind of goes aligned with what we were just discussing in like the natural history. So, I think now we recognize anogenital warts as a separate type of HPV infection caused by these benign types. And again, they are a morphologically distinct lesion compared to the high-grade lesions or precancerous lesions. In the past, we used to think them as a continuum or like a spectrum of disease that the low-grade will progress to the high-grade. I think you will still see and hear from some groups that that's still the case.

But in our practice in particular, we think about the low-grade lesions or warts as just benign lesions that do

not turn into a cancer. And separately, the high-grade lesions or precancerous lesions are definitely the precursors to cancer and the ones that we want to monitor or watch over time. So, for the provider in the clinic, having those warts now or having a history of genital warts are *not* necessarily a concern that those lesions will develop into a cancer, but again, just consider as a marker of increased risk rather than a direct precursor to anal cancer. And again, that's where that international guidelines, [International] Anal Neoplasia Society (IANS) guidelines include in their recommendations that having the history of genital warts will put you at slightly higher risks than the general populations for anal cancer in the consideration of starting the anal cancer screening when they turn 45 years old. That is not a very solid, I will say, a recommendation, but as a provider, you should have a discussion with your patient about having the anal cancer screening in those patients with prior or current anogenital warts.

hpv-testing-warts**[25:30] HPV Testing of Warts**

Dr. Ramchandani

So that gets me to my next question, and this was actually asked by a provider. In a patient with anogenital warts, would you do HPV testing of the warts to find out what serotype of HPV is causing those anogenital warts? For example, would you do an extragenital swab for HPV, similar to what we do for gonorrhea or chlamydia?

Dr. Stankiewicz-Karita

That's a great question. So, for genital warts itself, we don't typically perform any HPV swab or testing themself. They are usually a clinical diagnosis. And again, in a few cases you may require the biopsy, but swabbing those lesions will not help with the diagnosis. If you really want a histopathological diagnosis, you really have to biopsy the lesions. So, swabbing the lesion won't be helpful. Now, if you think about the anal cancer screening, if you are thinking, okay, this patient has genital warts, is 45 and older, and he meets the criteria for the consideration of anal cancer screening. In those patients, you could do the HPV swabbing of the anal canal, but for anal cancer screening, not for a wart diagnosis. So, I just want to make sure that's clear and separate. And that's why now that we have these guidelines, when I see these patients, that again, we have a ton of patients be referred for anogenital warts or anal warts, and I usually separate these two components when I provide my guidance or recommendations. One is the HPV itself, the other is the anal cancer potential or risk, and how we deal with that, and how we monitor or screen for that.

ians-screening-guidelines**[27:25] IANS Screening Guidelines**

Stier EA, Clarke MA, Deshmukh AA, et al. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702. [**PMID**]

Dr. Ramchandani

Tell us a little bit more about the guidelines, just briefly, if you could communicate that for our audience.

Dr. Stankiewicz-Karita

Basically, we aim with the guidelines is really to try to emphasize the anal cancer prevention, because this is a highly preventable cancer, by finding these precancerous lesions and treating them before they progress into a cancer. And what the society is putting together, the different group of people that are at the highest risk of anal cancer. So, fortunately, anal cancer is relatively rare in the general population. So, we can really center on those smaller groups that will benefit the most for anal cancer screening, like patients living with HIV, patients who have HPV lesions at other genital sites, for example, the vulva or the cervix, and patients who are immunocompromised, for example, solid organ transplant recipients. So, now the first component is defining those different groups that are at higher risk. And the second component is what tools we can use to do the screening.

And that will highly depend on what you have available in your clinic. So, the anal PAP (or anal cytology), is the most commonly available tool, so that's what people will usually use. As we were discussing, we can do that same swab to test for the HPV DNA. And, just to make sure for the audience, what the type of HPV genotype that we will look in that test are these oncogenic types. So actually, most of the tests that are available will not test for the HPV 6 or 11, which are the ones related to the anogenital warts. So those two are the two main tests that we can use for screening. And then, depending on, again, your access to high-resolution anoscopy, if any abnormal cytology or HPV DNA testing will be referred to high-resolution anoscopy, which is really the gold standard for diagnosing high gradations.

counseling-patients**[29:42] Counseling Patients**

Dr. Ramchandani

How would you counsel your patients about transmission of HPV, especially when they have anogenital warts?

Dr. Stankiewicz-Karita

This is a very common question when they see patients, and always patients worry about their partners, right? But the truth is, this is a very common virus, right? We think that we all get exposed at least once in our lifetimes, but it's important to emphasize that patients that have clinical lesions or warts, those tend to be the lesions that have the highest viral particles that can be passed or transmitted to the partner. But in reality, I always tell them, if there are no lesions, there could be some HPV reactivation or detection in the genital area, but it shouldn't prevent you from having your normal sexual life or having your partner. More likely, the partner is also infected with one or more types, and also, most importantly, it’s impossible to know who the original person was who transmitted the virus to the partner.

Dr. Ramchandani

Do you recommend condoms to prevent or decrease transmission of HPV?

Dr. Stankiewicz-Karita

Condoms can be helpful, especially if there are visible lesions, but because we don't have a full protection of all the genital mucosa, the effectiveness is not a hundred percent; they help decrease but not protect a hundred percent.

key-messages-patients**[31:20] Key Messages for Patients**

Dr. Ramchandani

What are some key messages you tell your patients about HPV? For example, what questions do they ask, or what things do you want them to know?

Dr. Stankiewicz-Karita

I always tell my patients that almost every sexually active patient will be infected with at least one or multiple HPV types in their lifetime. So, extremely common and most commonly asymptomatic. But HPV can definitely have a broad range of outcomes, right? So, from nothing or no symptoms to symptoms like genital warts or precancerous lesions or, in rare cases, invasive cancer, including in the cervix, vaginal area, anal canal, the mouth. That said, it's important to reassure the patients that having this HPV infection doesn't mean that you will go and have cancer. Most people won't. And the good news is that we have a great HPV vaccine that prevents, I will say, almost 90% of all these infections in precancerous lesion, warts, and a cancer. But for those who were not vaccinated before exposure, that can be the older or later generations, I always say that the genital warts are benign and treatable. And we can definitely catch a lot of these precancerous lesions

before they become a cancer through the cervical screening in the cervix, the anal cancer screening in the anal canal. So, we definitely have tools to find them before they turn into a cancer.

Dr. Ramchandani

Thank you, Helen. This has been a wonderful discussion on anogenital warts and HPV. I really appreciate your time. I learned a lot from you.

Dr. Stankiewicz-Karita

Thank you for having me, Meena.

credits**[33:10] Credits**

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