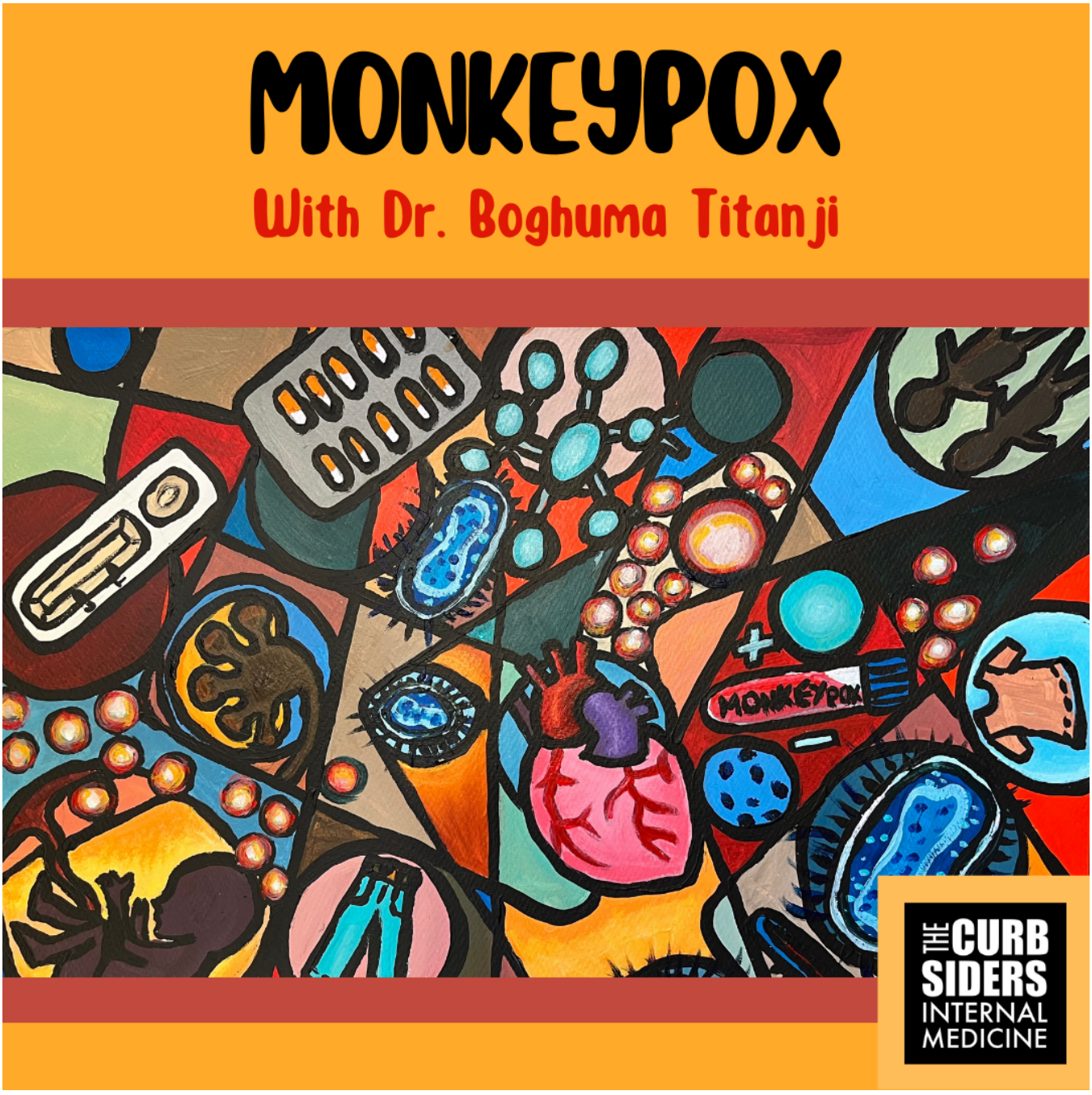
#359 Monkeypox with Dr. Boghuma Titanji



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[Curbsiders theme]

Matt: Welcome back to the Curbsiders. Tonight, we're going to be talking about monkeypox with returning guest. Dr. Boghuma Titanji. I'm Dr. Matthew Frank Watto, here with America's primary care doctor, Paul Williams. [Paul laughs] [crosstalk] you were going to forget about that, didn't you, Paul? I'm trying to make it stick.

Paul: You're going to be the only person who remembers it. But God bless and good luck.

Matt: All right, audience, on social please #PaulWilliams #AmericasPrimaryCareDoctor whenever you refer to Paul Williams. And, Paul, will you tell the audience what is it that we generally do on the Curbsiders?

Paul: Sure, Matt. Generally, and actually, specifically, tonight, we are The Internal Medicine Podcast and we use expert interviews to bring your clinical pearls and practice changing knowledge. I'm just going to get right into it. Tonight, we have, as you say the great Dr. Boghuma Titanji who talked to us all about monkeypox, how to recognize it, how to have a low threshold to worry about it, how to do the testing, fundamental management principles, just all the stuff that I think the basic internist would actually need to know, to be equipped to manage something that you are almost certainly going to see. It may feel a little bit niche right now, but it just sounds like the way things are progressing. It's something you're probably going to see in your primary care practices. I personally, found this to be an extremely helpful episode.

To remind you, she's been on the show, I think, you said 17 times before, it may have been four. But Dr. Titanji is a Cameroonian-born physician-scientist. She's at Emory University in Atlanta right now. She obtained her MD from the University of Yaoundé, and I probably mispronounced that in Cameroon and worked for two years after graduation as a medical officer, before pursuing postgraduate research training in London, United Kingdom. As an awardee of the prestigious Commonwealth Scholarship Program, she obtained a master's degree in tropical medicine and international health from the London School of Hygiene & Tropical Medicine, a diploma in Tropical Medicine and Hygiene from the Royal College of Physicians in London, and a PhD in virology from the University College of London just in case you were feeling a little bit accomplished, just compare your accomplishments to her and that should take you back down to size. [Matt laughs]

Doctor Titanji joined Emory in 2016 as a resident in internal medicine on the ABIM Research Pathway. She is currently an assistant professor of medicine and has four parallel career interests. She is interested in translational clinical HIV research. She is interested in science communication. She is interested in emerging infectious diseases and global health advocacy. Her clinical focus is specifically people living with HIV. Her current research, she just tells us that she actually just did grand rounds this week and we benefited from her research and expertise all about monkeypox for this episode. Matt, I'm going to peel back the curtain, you told me that you have a pun for us, so I'm just going to sit anxiously and awaited.

Matt: Well, Paul, they've been doing some work on my house. Specifically, the roof. They got to look up at the roof. And I've concluded after discussing with the contractor that my house has probably had chickenpox, Paul. Do you know why?

Paul: No.

Matt: Because, Paul, getting a look at the roof, it had shingles. [dramatic drum sound effect] So, it must have had chickenpox at some point.

Paul: Yeah, great. Do you know why they call the chicken coop, Matt?

Matt: Why is it called a chicken coop, Paul?

Paul: Because if it had four doors it'd be a chicken sedan. [dramatic drum sound effect] And, sorry, you can source your joke now.

Matt: Thank you to *nineunstoppablepuns.com, poxpuns.com* for that shingles joke. And let's get on with it. A reminder that this and most episodes are available for free CME through VCU Health at *curbsiders.vcuhealth.org.* Boghuma, so excited to have you back. Is this the fourth time now, at least a third?

Boghuma: No, it's the fourth.

Matt: Fourth, yeah. Okay. Welcome back, remind the audience, for the audience members that don't know you, tell them a little bit about yourself maybe a hobby or interest you have outside of medicine. I know you have many.

Boghuma: Yeah. I really love to cook Cameroonian food. When I don't want to talk about infectious diseases, for example, when I go to the hairdresser's and they ask me what I do for a living. I am a personal chef, which is technically not lying, because I cook a lot for myself, and I enjoy it. And so that's one of my hobbies.

Matt: Fantastic. And, Paul, anything you want to ask? We're going to get right into it, talk about monkeypox, but anything you wanted to ask before that time?

Paul: This is a very specific question, but since you mentioned Cameroonian food, is there a particular cookbook or source that you would recommend if someone who has no familiarity with it would like to learn more about it?

Boghuma: I am trying to talk my mother into writing a cookbook because she's the best Cameroonian cook, I know. Unfortunately, there are no Cameroonian cookbooks out on Amazon that I can recommend. But there is actually a very good Cameroonian food blogger who has excellent recipes. And I think people can check out Immaculate Bites to see some Cameroonian recipes. Yeah.

Matt: It's a great question, Paul.

Paul: Thank you.

Matt: Sounds like there's a market for your mom to become a celebrity chef.

[laughter]

Matt: Paul, did you want to give a quick pick of the week before we get into the main topic here?

Paul: Sure, always happy to. I feel like if you follow me on Twitter, and there's no reason to do that. You probably have a sense of the things I'm excited about. But I just discovered a band that's been around for a while. Matt, have you listened to Sleigh Bells at all? Are you familiar with them?

Matt: I think I actually, yeah. I actually have heard. I know something of a song, Sleigh Bells. Yeah, I think I have.

Paul: It's not the Christmas song. It's not the one with the horses and then [unintelligible [00:05:58]. It's a duo out of Brooklyn. And I just happen to stumble across their 2012 album *Reign of Terror*. And Wikipedia describes them as noise pop. But it's like these metal guitars and these thumping drums and these ethereal vocals. It's danceable and sing-along-able too. It's my absolute new favorite, the song *Demons*. I can't think of a song better right now. If you're not familiar with it, I would recommend checking out the band Sleigh Bells and the album of *Reign of Terror* from 2012.

Matt: Yeah. I think Spotify has fed me some of their songs on one of those playlists they make for you. Yes, thank you, Paul. As always, I appreciate your recommendations. I actually think I will like this one.

Paul: I think maybe so.

Matt: This sounds good. Sometimes your recommendations terrify me.

Paul: [chuckles] Yeah, appropriately.

Matt: Yeah. What was the movie recommended recently *Naked Lunch*? I'm not going to watch that. That's not going to--

Paul: Terrific.

Matt: All right, let's get into a case here, Paul.

Paul: Sure. So, Boghuma, happy to talk to you about Mr. S. He is a 41-year-old gentleman who presents to your primary care office for the evaluation of a genital lesion. His medical history is noteworthy for HIV on ART and his viral load has been undetectable for years. He states that he initially noticed this red spot on his penis approximately five days ago. And this eventually developed into something that looked kind of a pimple. Maybe it had some fluid in it, it's hard to tell. But he does note that the lesion is extraordinarily painful, and he's worried that he might have an STI. He has been sexually active with four male partners over the past month, and he endorses intermittent condom usage. He does have a prior diagnosis of chlamydia approximately five months ago. He's not aware of any STIs in his recent partners. But because you are a good doctor, and because you've been paying attention to the news, you are obviously potentially concerned for monkeypox. Before we get into the case, what your work have a look like and if we even should be concerned, I would love if you could just talk us through basic biology of monkeypox that we actually need to know to get started here.

Boghuma: Yeah, absolutely. Monkeypox is a DNA virus. It's the genus of viruses known as Orthopoxviruses. And it's a close cousin to the more well-known a smallpox virus that was caused by the variola virus, which is now eradicated. And monkeypox for a long time has been well established to cause human infections. It was first noted to cause human infections in the early 70s, in the Democratic Republic of Congo, and has circulated in Western Central Africa since that time. And it wasn't until recently that we had an explosion of cases and we're currently in a global outbreak of monkeypox. So that is just the gist of the pathogen and a little bit about its origins.

Matt: I was trying to get a sense of why were we initially so alarmed about this? Was there something about the way that we started finding cases that made this so alarming early on when there was still a really small number of cases?

Boghuma: Yeah. I think it was mainly the patterns along which the cases started appearing. Remember, I said that monkeypox has been a known pathogen that causes human disease and this is [unintelligible [00:09:14] pathogen that circulates in an endemic fashion in countries in West and Central

Africa. And for many years, a lot of the outbreaks that have happened in that part of the world, primarily happened when you had a zoonotic exposure to either animal reservoirs or animals that were infected with the virus. And humans came in contact with these animals, either through hunting or manipulating the animals. So just living in close proximity with the natural flora in forested parts of Africa. When you had an introduction into human populations, you had very restricted outbreaks primarily in household contacts of whoever the index case was.

Now when the outbreaks were noted happening across Europe, the first cases in the current outbreak were noted in the United Kingdom. And they seem to be clustering in people who had no contact to travel linking them to an endemic country. So, the question, obviously arose, these are people who had not traveled to Western Central Africa, where we know that this virus circulates, how were they coming in contact with the virus? And why were they seeing cases in people that also didn't really seem to be connected to each other in any way. So, cases started popping out in the United Kingdom, in Spain, and across Europe. So, it was the manner, in which the cases was spreading. It was the fact that the cases were happening outside of an endemic region. And it was also the fact that they started making connections between the cases, linking them to sexual networks, which seemed to suggest that the virus may be spreading in a new way that we had not noted it to spread before. So, all of these factors were a different pattern of behavior for zoonotic virus infection, which of course raises the question of, has it adapted? Is it spreading better between humans? Or, is this just the result of multiple introductions into networks that are somehow facilitating the transmission of this virus?

Matt: And, yeah, Paul, are you confused after reading? Do you understand how it's transmitted? I mean, obviously, skin-to-skin contact. But beyond that, I feel I'm a little bit confused.

Paul: Yeah, that was my exact follow-up question. Yeah, so what do we think is happening with transmission at this point? What's our best guess?

Boghuma: Well, let's start from what we knew about the transmission of monkeypox prior to the current outbreaks. Monkeypox is a virus that doesn't transmit very efficiently from person to person, that we know from the multiple outbreaks that have happened in endemic countries through the years, through the last five decades that we've known that this virus is capable of infecting humans. However, the way in which transmission has been described, human-to-human transmission really requires prolonged skin-to-skin contact, that appears to be the most favorable mode of transmission, but the virus can also be transmitted through contaminated inanimate materials or objects that have been utilized by individuals who have active lesions of monkeypox. And I'm thinking specifically, clothing, bedding, if you have prolonged contact with that, that also has been well described as a way in which the virus can be transmitted.

To a much lesser degree, airborne transmission and droplet transmission are possible routes of transmission, but very much thought to not be the most efficient modes of transmission. And when you think about droplet and airborne transmission, you're really thinking about spaces that are not well-ventilated, where people are in crowded spaces and in contact with someone who has an index case of monkeypox or who has active lesions of monkeypox for a prolonged amount of time for that to be a viable mechanism of transmission. Now, what is unusual with the current outbreak is like I mentioned before, we're seeing clustering in sexual networks. And what that really amounts to is that sex in itself facilitates the type of close and intimate contact, that would essentially make it easy for a virus that requires close contact to be transmitted.

Paul: So, that's all incredibly helpful, but a couple of questions. In terms of respiratory transmission, you mentioned prolonged exposure. As soon as you describe the situation might happen, I immediately thought of a clinic waiting room where people were packed in like sardines at the busiest times. So that

obviously was a little bit nerve-wracking, but how long exposure are we talking about, and in what situations where we typically see the possibility of respiratory transmission?

Boghuma: We're talking about hours. So, we're talking about two to three hours of that exposure and sharing the same air in a clustered, enclosed space with someone who has to be highly infectious at the time when that exposure is happening. So, I would not worry too much about casual or short-lived contact, face-to-face contact with someone who was infectious. Technically it is possible but that is not the most efficient mode of transmission of this virus.

Matt: Do you think the PPE is going to be scaled back because right now it sounds like it's full and what they call enhanced droplet, the face shields, the KN95, N95 and the gown gloves? Do you think that all will ever be scaled back as we learn more about this? Right now, I was just thinking that it seems like it's a lot first if you're just going in brief encounters with the patient.

Boghuma: Well, then I'll give you some perspective of what it looks like to actually manage cases of monkeypox in western Central Africa, where PPE is actually scarce. So here, we obviously have the full PPE, as you mentioned with the N95, and the face shields, and the gloves and the gowns. But in clinics in West Africa and in Central Africa, where we see this in an endemic fashion, this is not usually available. And a gown and gloves are pretty much sufficient if all you're doing is examining the patient, making your diagnosis, and then probably discharging them home. But if you have that PPE available, you should definitely use it because oftentimes, people are not using this because they don't have it available. But I'm just mentioning that just to highlight the fact that even when people do not have access to all the PPE that may be available in more resourced settings, you're not seeing massive nosocomial transmission of monkeypox, just because individuals are not wearing full PPE. Really, it is a virus that transmits through prolonged skin-to-skin contact.

I really want providers who are listening to this, to feel really comfortable with knowing that if they're wearing their gown, and they're wearing droplet protection, and they have gloves on, they should feel fully confident to go ahead, examined these patients' collect swabs without worrying that they would get infected themselves.

Paul: And before we move on from transmission, I was wondering what the current thinking is about, transmission through sexual fluids, it sounds like be part of the sexual-- part of the skin-to-skin contact that comes along with sexual encounters is just sort of like the going in theory. But in terms of fluid transmission, I feel like there are varying opinions about that. I'm just wondering so what the current state of thought is in terms of that as a mode of transmission.

Boghuma: There is actually emerging literature that's helping us clarify what the state of that is. We now know that monkeypox virus has been detected in the semen of individuals who had a diagnosis for monkeypox. There's actually been a published paper in the Lancet that looked at a patient up to 19 days out of their initial presentation with monkeypox. And they found virus that was isolated from that patient's semen, that also was able to cause infection of cells in vitro in the lab. So that would mean that the virus that was isolated was viable to infect cells, that tells you that that semen is infectious. And it is for this reason that as a measure of precaution, the WHO now recommends that individuals who have recovered from monkeypox, that they continue to use barrier protection, such as condoms for up to three months after recovery. And I'm sure that we will have more data emerge to fully characterize for how long virus is viable in semen. But for right now, we do not know. And that's an area that we need to gain better understanding on, because it has implications for seeding new transmission chains and for onward transmission in an asymptomatic patient who has recovered, but may still be carrying virus in their semen or in their bodily fluids.

Matt: It's interesting because I'm sure Paul gets this question all the time too, when you have patients with the COVID pandemic, patients were always asking, "How do I know if I'm no longer infectious?" And I will just be like, "Well, at 10 days we say you're probably not infectious. If you're still really sick, consider yourself so infectious and go another 10 days." I think it's hard for people to wrap their head around the fact that as advanced as we are, we still don't have that quite down yet to say who's infectious and who's not. If we did, it would be super convenient.

Paul: A lot of people don't realize that virus is called the lunar calendar. That's I think an important thing we don't really describe well enough.

Boghuma: Yeah, but I would also want to add to that other studies have also shown that the peak or the lesions that shed the most virus are the cutaneous lesions, that's really where a lot of the virus is being isolated from. And in patients who have been sampled from their oropharynx as well as sampled from their rectum and sampled from their skin lesions. It's really those active skin lesions that are very infectious. And what I do tell patients is that you are less infectious or you're less of a risk to pass this on, when your skin has fully healed and there's a new layer of healthy skin over those skin lesions. And the whole guidance about continuing to use condoms is an extra measure of precaution until we know fully whether this virus persists in the semen for any length of time for you to be able to pass it on to your sexual partners.

Matt: And we don't know about reinfection yet either, I imagine, for this.

Boghuma: We do not know about reinfection yet. That is correct.

Matt: So maybe we can move on to the next part of this case, Paul? I wanted to get into the presentation, and I do want to talk about how we're going to collect for this patient that we have here. How are we going to actually test them because that's something that I haven't seen in, at least I don't think I've seen anybody with monkeypox yet. When I do, I need to know how to click the sample.

Paul: Before we get there. Matt, do you mind if I actually ask about pretest probability? I would like to know who especially should I be worried about. For instance, our patient is someone who we obviously build some potential risk factors into the case. I think before we get to, what it looks like and how to test, Matt, do you mind if we start just talk about background risk factors?

Boghuma: When you describe the case, you actually highlighted some risk factors that I think it's very important for providers to think about. The patient in this case had had multiple sexual exposures in the month leading up to his symptoms. It's a patient who has had a history of having sexually transmissible infections, which to me as a clinician simply tells me, this is someone who's having a lot of sex. And then thirdly, they're not using protection consistently. And all of these factors, raise in my mind a risk for does this patient present with a sexually transmissible infection. So, running the differential through my mind, I'm obviously thinking about syphilis, I'm thinking about herpes, I'm thinking about monkeypox because we are in the midst of an outbreak. And one of the emerging features that has come out as we learn more about the epidemiology of the ongoing outbreak is that because it is transmitted through sexual contact as one of the main mechanisms of transmission in the current outbreak, we are seeing it track very closely with other sexually transmissible infections.

And actually, in the cohorts that have reported on monkeypox cases in Europe and in North America, about 20% to 30% of individuals who test positive for monkeypox also have a concomitant positive test for another sexually transmissible infection. That is how I'm approaching this case, already thinking that on my list of differentials besides monkeypox, you're going to have a lot of other STIs on that list as well.

Paul: And mechanistically, is there some synergy there or is it just the shared risk factors that you're seeing concomitant sexually transmitted infections?

Boghuma: I think that to a great extent, it is a question of shared risk factors. So, again, people with the opportunity and the exposure to come in contact with sexually transmissible infections, and who have shared sexual networks tend to be the individuals that we are seeing present with monkeypox. And I also think that it is important to highlight emerging higher risk group individuals that we are noting in the ongoing outbreak. 98% of the cases of the over 62,000 cases that have been recorded in the ongoing outbreak have been in men who have sex with men. And this is a reflection of shared social and sexual networks. And I think that it is important for providers to be aware of this, not to stigmatize, but to make sure that we are offering the appropriate testing based on an individual's risk profile.

And in addition to that, I would also want to say that, although the higher risk group right now and the concentration of cases has been among MSM, the outbreak is not only happening among MSM, and we are also seeing cases in heterosexual networks from individuals who have reported their exposure as being sexual contact. If you have someone who has risk factors for a sexually transmissible infection, you really should be including monkeypox on your list of differentials if you're considering some of the more common sexually transmissible infections as well.

Matt: Why don't I recap a little bit, Paul, and then we'll move on with it? So, what we said was monkeypox since the 1970s, it's been around what piqued the interest this time is that it started to-- usually, there was clear exposure to an animal and it would spread in households. But now this time it was popping up and it was in these networks of people and there wasn't that clear exposure, and it didn't seem to be like burning itself out the way it sounds like prior outbreaks had where it was just a couple of isolated cases. And then we think that you should wear full PPE, the face shield, N95 mask if you have it, gown and gloves at the bare minimum, because we do think there may be some respiratory or even aerosol droplet spread of this, but we know the primary mechanism is skin-to-skin contact. And you just have to be prolonged close exposure to somebody else, maybe even on the order of hours. And then the pretest probability right now, a lot of it is in the men having sex with men community, but we have seen it start to spread to heterosexual groups as well. And we do expect that this will start to see cases outside of those initial communities where we were seeing it. Anything to modify there, I probably bit off more than I could chew with that recap.

Boghuma: [laughs] I think you captured a lot of the salient features of the epidemiology of what we know about monkeypox in the current outbreak so far.

Matt: Okay. Paul, let's go to the next part of the case.

Paul: All right. We decided to take more history, again, because we're very good doctors. And Mr. S tells us that he felt pretty awful four days before he even noticed the lesion on his penis. So, in fact, he actually felt feverish, he felt achy. He didn't take his temperature, it was a subjective fever. And he's just been feeling tired and washed out lately. He's not having a penile discharge, he's not noticed a rash anywhere else. He does not have any proctitis or diarrhea or lesions or anything else. It really is just a solitary lesion that he's experiencing right now. When you examine him, he has these two solitary papulopustular lesions on the gland's penis, and because we're doing a very thorough examination, we also note bilateral inguinal lymphadenopathy as well. And there are no other anal general lesions that we've noted. So, I'm wondering, again, as we're considering monkeypox, is this a fairly typical presentation? Or could you at least talk us through the spectrum of presentations we might be seeing in our offices?

Boghuma: I think the approach that I would like to set up to address this is to talk about the spectrum of presentations because that's one of the key features that's emerging in this outbreak. And I think that it's very important that providers be aware of what that spectrum is because we're seeing a lot of diagnoses missed because people are not thinking about it, and are thinking about all the classical textbook presentations of what monkeypox should look like. So, starting from what monkeypox should look like and what we know about monkeypox from previous outbreaks, generally, people have presented with a prodromal phase where they have fevers and nonspecific flu-like symptoms with muscle aches and pains and maybe just generalized fatigue, preceding the emergence of the rash. And the incubation period from the initial exposure to you beginning to develop some of this prodromal symptom has been anywhere between five to 17 days, even up to 21 days, historically.

After that prodromal phase, individuals start to present with a rash, and the rash evolves in five phases. So, it initially starts out as a macular, and then progressively becomes a little more vesicular-papular, and then evolves into more what looks like a postural with that classic central umbilication that is quite distinctive for Orthopoxviruses. And as that postural erodes, it forms some sort of like an ulceration, and then ultimately scabs over and heals, and then that scab sloughs off. So, these are the classical five phases of the development of the rash, and the rash can last anywhere between two weeks up until four weeks for it to fully heal.

Now, in terms of what has been the distinguishing features in the past, to say, for instance, distinguish between exanthem that you get with monkeypox and for example, what you would expect with chickenpox, which is a common differential, another viral exanthem with which this could be confused. Monkeypox lesions were typically thought to be all in the same phase of development. So, if an individual presented with a rash, it would tend to all be in the papular phase or all be in the vesicular phase or all be at the healing phase.

Also, individuals with monkeypox traditionally were thought to present with lymphadenopathy, which you don't usually see with chickenpox. So, lymphadenopathy was considered one of the more distinguishing features, and the rash tended to be a lot more generalized. So, this is what you would see if you were to open up an infectious diseases textbook and read about the presentation of monkeypox. How does the presentation of monkeypox in the ongoing outbreak differ? What we have seen is actually a shortening of the incubation period. And really right now, the incubation period is anywhere between five to up to 12 days with a median of about seven days before individuals start presenting a rash. The prodrome is not always present, a lot of people are paucisymptomatic. And they will tell you, "I didn't feel any flu-like symptoms, I didn't have a headache. I didn't have a fever." And they just present because they have a rash.

We're also seeing people present with singular lesions. So, in the case that we're discussing at the clinic, this patient presented with isolated two genital lesions, as opposed to a more generalized rash. And individuals who don't present with any rash, we've also had cases of just proctitis. So, individuals presenting with rectal pain and tenesmus and no rash, and getting treated for hemorrhoids and rectal abscesses with no one thinking to collect the sample for monkeypox.

And then the last feature that I think it's very important is also isolated pharyngeal presentations, presenting with just a sore throat. A severe sore throat, negative for strep throat, and you can't figure out why this person has such a sore throat that they can't swallow anything. You get a sample, you test it, and they come back positive for monkeypox. And I highlight these features because one of the things that has also emerged as we learn about the epidemiology and the clinical presentation in the ongoing outbreak is the fact that the symptomatology also appears to track with the sexual exposure that people are reporting. So in individuals were reporting on protected oral sexual exposure, they're presenting more with oral and pharyngeal lesions, whereas individuals who may be reporting receptive,

unprotected anal sex are more likely to be presenting with proctitis lesions. So, really important to ask the history and think about that diagnosis, even if the patient doesn't have the classic textbook presentation that you would expect for what you knew about monkeypox.

Paul: In terms of the cutaneous lesions, the rash specifically, is it typically described as pruritic? Is it painful? How are patients actually describing the symptoms that come along with the appearance?

Boghuma: It is a mixture of both, so it can be intensely itchy, depending on what phase of development the rash is. It starts getting itchy in the more papular and ulcerative phase when parts of it are beginning to heal, it gets really intensely pruritic. But there is also considerable pain associated with a lot of the rash. And particularly for patients who are presenting with mucosal lesions, those-tend to be the most painful of the lesion. So, like I mentioned, very severe pharyngitis, with severe sore throat and patients presenting with inability to control their saliva and to swallow anything, and also patients presenting with such severe rectal pain that they require admission into hospital for pain management.

Matt: Yeah, that was not on my radar. I did not realize pain was such a major component. It sounded like that was the main reason people were admitted to the hospital was just uncontrolled pain. And I guess in the case of pharyngeal, they maybe have trouble swallowing. I heard that was a big issue as well.

Boghuma: Yes, absolutely. And when we mentioned pharyngeal cases, I think it's also important to highlight the fact that sometimes these can be complicated with bacterial superinfection. And at Kashlak Memorial, we have actually seen patients admitted with pharyngeal abscesses that were only diagnosed as monkeypox once the infectious diseases team was consulted, took a history and thought about it and collected the sample, and did the appropriate testing. So, very important to keep this in mind as well.

Matt: Well, so, let me recap, the main, contrasting between the two. So, there was the classic presentation was there was a prodrome, then the rash, the incubation period tended to be longer and the rash tend to be more generalized when people got it. Usually, they had lymphadenopathy. Did you say the lesions all seem to be in the same stage in the [crosstalk] presentation?

Boghuma: Yes. All seemed to be at the same stage of development.

Matt: In the current outbreak, they may or may not have a prodrome. The incubation periods seem shorter five to 12 days, maybe seven days seems to be common. And then they could have singular lesions or they don't have that generalized lesion appearance necessarily. And then we were talking about proctitis and the mucosal lesions, pharyngeal lesions are the lesions causing proctitis have been severely painful. So, I guess the next thing I wanted to get to here is, how are we going to test this person? You mentioned that you would test for coinfection? So, can you be specific, like which labs would you order and then tell us about how we would go about testing for monkeypox?

Boghuma: I will start by talking a little bit about how we test for monkeypox. So, like I mentioned at the beginning of our discussion, this is a DNA virus. And when patients have lesions, a lot of these lesions are just teeming with virus, so they are shedding virus from these skin lesions or mucosal lesions, if they have monkeypox. And in order to make the diagnosis, we have to collect swabs of virus DNA from these lesions and send them to the lab for basically, what is a PCR test to detect that virus DNA.

Now, some labs would implement a two-step testing where they do an initial generic PCR test that would detect any Orthopoxvirus. So, these are other viruses that are of the same group as monkeypox,

but it's not specific tests for monkeypox itself. And if that Orthopoxvirus PCR is positive, then a confirmatory PCR is run which is specific for monkeypox testing.

Now, in the context of an outbreak if the Orthopoxvirus PCR is positive, that is considered a presumptive diagnosis of monkeypox while awaiting the confirmation testing. So, how does one collect the swab? I would say you collect the swab from the site where a patient has symptoms. Remember, I've mentioned before that we are seeing a typical presentation. So, some patients may not present with skin lesions that you're able to swab, they may just have the oral ulcers or have pharyngeal pain, or they may just be presenting with intensely rectal pain that makes you think about proctitis. If they have skin lesions, you collect the lesions using a dry swab. So, a sterile dry cotton swab, and I would recommend using one swab per lesion.

Normally, although the lesions are described as pustular or vesicular in certain phases, they don't always contain a lot of fluid. So, what I do when I collect these samples is you take a scalpel or just scrape the top of the lesion to make sure you're getting inside the lesion and then really vigorously swab the surface of the lesion to make sure that you're collecting enough virus DNA on that swab. Now, depending on where you're sending the testing sample to, if you're sending to a state laboratory, they may accept the dry swab. Some of the labs may require that you place that swab in virus transport media before you conduct that swab to the laboratory. And make sure you collect swabs from at least two lesions if the patient has multiple lesions, and if they have symptoms elsewhere, collect a pharyngeal swab if they have pharyngeal symptoms and collect a rectal swab, if they have rectal symptoms.

Now for rectal symptoms, because those are associated with a lot of pain. Sometimes it's very difficult to get a proper sample. And what I do If I get the patients to self-collect, because that way, you're not causing more pain, and there's actually a publication that just came out this week, it's still in preprint, it's not been peer-reviewed yet. But that showed that self-collected swabs for monkeypox are just as good as provider-collected swabs. So, you should feel quite confident, we already do it for other sexually transmissible infections.

Matt: So, for the proctitis lesions, if you can't see it. This is all extra, they're just swabbing the rectum externally.

Boghuma: They are just swabbing the rectum; they're just putting a swab into their rectum and turning it 360 degrees.

Paul: I thought I had heard earlier that unroofing lesions was not necessary. Is that something that has changed recently or [crosstalk] misremembered?

Boghuma: Yeah, actually, if you look at the CDC guidance, they say it's not necessary. But just based on the lesions that we've seen in the clinic. Some patients present at the stage of the lesion where you still see quite an epithelium above the lesion and you really have to scrape the top of it to get into the lesion to make sure you're sampling it properly. So, I would say this should be a matter of clinical judgment. If they're presenting with lesions that are already ulcerated and are open, then you don't need to unroof the lesions. But if they're presenting with a papule that still has a healthy layer, that has its layer of skin on it, then you want to gently scrape the top of it so that you can get into the lesion and actually sample it properly.

Paul: I see.

Boghuma: And then coming back--

Matt: I had the same question, Paul. I was just going to say, it just seems weird to be swabbing dry skin where you generally were told not to do that, like, we want some moisture on the swab, you want the swab to be dirty when you're sending it off, Paul, most of the time. Unroofing it makes sense to me.

Boghuma: Yes, and unroofing it is the right thing to do. And you're absolutely correct, Matt, you do not want to send a swab that you can't visibly see what it is that you swabbed. So you do want to make sure that you're getting into the secretions in the lesion, or at least getting below the skin. It's not like doing surgery, this is really just gently scraping so that you can get into the lesion and make sure you get a good DNA sample. And then coming back to the additional testing that you do. Obviously when people present with ulcers or papules, and you're thinking about sexually transmissible infections, some of the other things that are on that differential that I would send for in this patient would obviously be an RPR to make sure I'm testing them for syphilis. And I will also collect swabs for herpes simplex virus testing, as well as collect swabs for chlamydia testing by DNA sampling, because they can be presenting with LGV lesions or any of the other ulcerative STIs that we commonly identify in the clinic.

And not to forget, in individuals who are presenting, unlike the patient in the case that we're talking about, who do not have a documented HIV status, remember to screen them for HIV. We have seen at Kashlak Memorial, a new diagnosis of HIV that have been made in the context of a new diagnosis of monkeypox. So, very important to remember to screen individuals who are presenting with any STI for the first time and don't have a documented HIV status.

Matt: So, for the monkeypox part of this, we're going to be swabbing at least two lesions. And if they have multiple sites involved, let's say proctitis and pharyngitis, we would swab both those areas, patients can self-swab, especially very painful areas, it seems like that's going to be a way to go very patient-centered. And we may need to gently unroof the lesion to make sure that we're sending a swab getting a good sample. And then the other testing that we might send for, if there's papular ulcerated lesions would be syphilis, swabbing for HSV or chlamydia by DNA, in case, you said LGV is present.

Boghuma: Yes, lymphogranuloma--[crosstalk]

Matt: And don't forget to test HIV.

Boghuma: Yes.

Matt: Yeah, I was just forgetting the full-term terminology of it. So, Paul, what's next for our patient here? So, we're sending off all this testing and what's happening next?

Paul: Well, I guess, I'm going to turn the question to Boghuma. How long does this testing usually take? I realize there's going to be some variation depending on lab practices and where you practice. But in general, how long are we waiting for results and what should we be telling the patient in the meantime?

Boghuma: Normally, a PCR should have a pretty quick turnaround time and should not take longer than 48 hours for you to get a result. Unfortunately, we're still dealing with some issues and barriers around testing, probably, which has to do just with the logistics of transmitting the sample to an outside facility and then getting those results back. So, the meantime to getting testing results back is still anywhere between five days to up to seven days for a lot of sites.

Paul: Well, let's say we have an extraordinarily efficient lab system at Kashlak for change and we get our results back a mere two days later, and the patient is positive for Orthopoxvirus DNA. So, what do we do with this poor gentleman?

Boghuma: Yes, so first of all, we start by counseling the patient and providing reassurance about the fact that this is not a new disease, and we are getting familiar with it and we know how to manage it. So, the first thing is a lot of patients with a new diagnosis of monkeypox also have a lot of anxiety around whether they can pass it on to their family members, and what they should be doing to make sure that they're protecting themselves. So, the first thing I start out with is always providing that counseling.

Now in terms of what we can offer from a therapeutic standpoint, a lot of patients with monkeypox would recover, just with supportive care. So basically, what you're going to be doing for these patients is making sure that if they have fevers, you're treating that, you're making sure that they're staying hydrated properly, and you are controlling and treating their cutaneous symptoms. So, for patients who have associated itching with these lesions, you can certainly consider antihistamines to help deal with some of the pruritus that can be associated with this. For those who are presenting with lots of pain associated with their lesions, you can certainly use non-steroidal anti-inflammatory medications to help alleviate some of that pain. If the pain is severe, even consider opioid-based medications to really address some of the very painful syndromes.

Now in terms of patients who present with more severe disease, and by severe disease, we're generally thinking about patients that have greater than 10 cutaneous lesions or who have lesions on mucosal surfaces such as pharyngeal lesions or rectal lesions, or patients who are presenting with complications of monkeypox, either bacterial superinfection and things like that. Those are some of the patients that we would start to consider whether they would be an appropriate candidate for an antiviral medication.

Now, it's important for the audience to be aware of the fact that the antiviral medications that we currently have available for monkeypox, we do not have randomized controlled clinical trial data on any of these medications. A lot of the medications we have basically animal data, based on animal models of monkeypox, indicating some measure of efficacy and also in vitro data supporting that this medication may be efficacious.

The first medication that I want to talk about is the antiviral drug called tecovirimat. And this is a medication that acts by inhibiting an important protein in the replication cycle of the virus and so blocks the formation of new virion particles and inhibits viral replication in that way. It is currently available in certain countries through emergency use authorization processes, and we are offering it to patients who present with severe disease as a way of hopefully reducing the viral load and the viral replication with the goal being to shorten the course of that illness. It's given in a weight-based dosing and the duration of therapy is 14 days for the full course of the treatment. And that is anecdotal evidence that some patients report that they feel that they have fewer lesions emerging once they start using the medication, or that they feel there's some alleviation in terms of their symptoms. But, again, without a randomized control trial, one can't really say whether this is the natural course of the disease itself, or really an effect of the medication. Fortunately, there are multiple clinical trials right now recruiting, and hopefully, we would get additional information on some of these studies to really tell us what the utility of this medication is.

Matt: Paul, I believe the STOPM trial is going on. And I think that's the tecovirimat trial that's going on in the US and maybe a platform trial, Paul. So, what do you think? How do you rate them, as a trial-head, Paul, what do you think?

Paul: Like the cardiologist, I feel like it just have its beat in on almost every domain. STOMP is even--

[laughter]

Paul: It doesn't make sense. I just want to ask, in terms of the administration, did I recall there's some dietary considerations too? I, feel in one of the quick facts sheets I saw like, they have to eat a certain way-- it's recommended to eat a certain way I should say while you're taking medications? [crosstalk]

Boghuma: The medication is better absorbed with food, and actually, a fatty-rich meal would help with absorption of the medication. And now that we're talking about the dietary considerations, I think it's a good time also to mention some of the common adverse effects that are associated with the medication. Some patients do complain about nausea or abdominal pain, and a few patients have reported headaches while taking the medication. But overall, it is really well tolerated and very few patients have had to discontinue because they had such bad side effects. Now, before we continue, there are two other antivirals that we can talk about. Do you guys want me to talk about those or not?

Paul: Absolutely.

Boghuma: Because they would really be-- you would need ID involved to get any of them prescribed, but they are antivirals that can be used for monkeypox. So, it's up to you guys, sure. [laughs]

Paul: I certainly don't mind making more for ID. I mean, that's what we have you for. So, yeah, by all means, [crosstalk] horizon.

Boghuma: So, there are, other antivirals that could be considered for the treatment of monkeypox. The second antiviral, that can be considered is a medication called Brincidofovir which is of the same class and a prodrug of the medication cidofovir. Both of them act by inhibiting DNA synthesis, and they are medications that have been used to treat other DNA viruses as well. Now Brincidofovir has FDA approval for treatment of smallpox and can also be used for treatment of other Orthopoxviruses. It is orally bioavailable and is usually prescribed by infectious diseases doctor, so if you're considering Brincidofovir, then I'm assuming that your patient would have gotten an infectious diseases consult at some point to be considered for this medication.

Much like with tecovirimat, we do not have randomized controlled trials in humans, assessing its efficacy for the treatment of monkeypox. But an important consideration to remember if your patient is going to receive Brincidofovir is that there are teratogenic effects that are well documented in the animal studies that have been done with this medication. And there are also, considerations that have to be made for male fertility if you're prescribing this to a male patient because that could also have an impact that you would have to consider it for a certain number of months after the patient discontinues the medication. Ensuring that you're counseling your patients properly before you prescribe these medications.

The most common adverse effect is association with elevation of liver enzymes, which in certain cases have led to the medication being discontinued. So, an important thing to monitor if you do get your hands on Brincidofovir and that is something that your patient ends up being prescribed for their monkeypox treatment. Now cidofovir, as I mentioned, Brincidofovir is the oral formulation and it's the prodrug of cidofovir. Cidofovir is available in topical formulation and it's also available in IV formulation. It tends to be very nephrotoxic and has to be co-administered with probenecid to reduce some of that nephrotoxicity. Again, it's only a medication that you will be considering after discussing this with infectious diseases experts. It has spectrum and activity against Orthopoxviruses, but also no

randomized control trials really informing us of how beneficial it is in the treatment of monkeypox. It's given as an IV infusion once a week for two weeks. And Brincidofovir is also given in oral formulation once a week for two weeks. So those are the antiviral drugs that we do have available for treatment.

Matt: Tecovirimat is it's IV or oral formulation, is that correct?

Boghuma: It has both IV and oral formulations. Yeah, correct.

Paul: Okay, that's helpful, it's nice to hear there are treatments that will not be coming from me. So that's wonderful. [laughs] I did want to touch on something in the stem of the question we have talked about the patient is living with HIV but is undetectable, untransmissible. I guess I'm wondering, does HIV status impact, I guess, diagnosis and then I think, since right management, would that change in any ways that you might actually treat this patient just given his HIV status?

Boghuma: Well, what we know again, from the emerging epidemiology and the ongoing outbreak is that there is quite a very strong emerging association between individuals who are testing positive for monkeypox and having an existing diagnosis of HIV. Actually, in the US, 38% of people who have been diagnosed with monkeypox also happen to be people with HIV. And we're still trying to understand what is driving this very strong association, is it just a reflection of similar risk exposures that are making these two infections track quite closely together? Or is there something about living with HIV and being immunocompromised that may predispose these individuals to have a higher chance of acquiring monkeypox if they are exposed to the virus. That aspect is still an area where we need more research to tease that out.

Now, in terms of management, in our case, the patient has HIV that is well controlled. So, I'm assuming that the CD4 counts are above 500 and they have an undetectable viral load and they are taking their ARVs properly. In these scenarios, I would manage them exactly in the same manner as an individual who did not have HIV because we know from cohorts that have reported on individuals with HIV who tested positive for monkeypox, that the outcomes were pretty much similar in individuals who had well-controlled HIV compared to the HIV negative population.

Now, coming back to HIV, individuals who are more immunocompromised, so I'm thinking about that individual who is not on antiretroviral therapy or struggles to take their medications, and has a very profoundly depleted CD4 count and undetectable viral load. There has historically been reports that have demonstrated that this particular category of patients are at a higher risk for more severe and disseminated infections from monkeypox and also at a higher risk for complications. And we are also beginning to see this in our practice at Kashlak Memorial where we have had to see lots of other people with HIV and AIDS who have presented with monkeypox and have required hospital admission because they've presented with more severe infections than individuals who do not have HIV or have presented with complications as well.

And in the report recently published by the CDC looking at almost 4000 cases of monkeypox in the US, in that particular cohort, they also reported higher rates of hospitalization among people with HIV compared to people who do not have HIV. So again, emerging data that there may be some more severe disease considerations in this patient population. In terms of what we offer for treatment, certainly, this would be someone that we would be considering for an antiviral drug, like tecovirimat, because you're really trying to make sure that you're controlling viral replication. And as I mentioned before, all the good supportive care things that we've talked about, so making sure that we're caring for the skin properly, using skin protectants where indicated thinking about petroleum jelly, that protects and adds a layer on the skin, and also thinking about the insensitive losses that can happen when someone has multiple skin lesions and really treating these patients almost like burn patients, making

sure they're properly hydrated, etc. When they present with bacterial superinfection, really considering the necessity of adding anti-microbial's to treat any additional bacterial superinfection that may be further complicating their case. And, of course, because they have AIDS and HIV, having a conversation with your infectious diseases physicians as to whether it's appropriate to initiate antiretroviral therapy and treat their HIV as well.

Paul: In terms of other supportive management, so you talked about like Vaseline and maintaining hydration [unintelligible [01:00:25] and that kind of stuff. For the pruritus, what is the current thinking about, you mentioned antihistamines for that before, I think what about topical steroids? Good idea, bad idea?

Boghuma: I think that in this case, topical steroids are not a good idea at all because they actually would impede on the ability of the skin that has the lesion to heal properly. It thins the skin, it's really bad for skin healing. So, it's not something that we should be using for these patients. And another question that I get frequently as well as for patients with proctitis, whether there's any role for using enema based or suppository-based preparations of steroids. I also strongly discourage against that because you're thinking again about a mucosa that is irritated, and putting in steroids in there would not only promote viral replication but would also impede on the healing. Things could work well in patients who have a lot of inflammation and a lot of pain, we have found in our experience, and this is an expert opinion that using IV nonsteroidal anti-inflammatories can be very helpful in decreasing that inflammation. And also thinking about using alternative local anti-inflammatory agents such as mesalamine suppositories can also really have a very good anti-inflammatory effect locally, and avoiding the use of steroids.

So, these are some of the things that people can consider as ways in which to address that really severe pain that's associated with proctitis. And also not forgetting lidocaine-based preparations for patients who have perianal lesions, thinking about sitz baths and things that improve vascular circulation. And really just ease the pain by virtue of the fact that you're using a warm-- I'm spacing out in the word but using warm water as a sitz bath that can have a soothing effect on the perineum. That's what I'm trying to say.

Matt: Outside the antivirals, which we talked about, a lot of the treatments are in our wheelhouse, which is if it's mild, maybe we can get by with some antihistamines and some NSAIDs. If the pain is more severe, in some cases, opioids may be okay. As far as mucosal treatment, we just talked about sitz baths, we talked about lidocaine preparations that may be appropriate. And then IV NSAIDs seem to help maybe with inflammation and pain as well if patients are on the more severe side of things. Even mesalamine suppositories are being experimented with as an anti-inflammatory. And then the antivirals, tecovirimat were one of the ones that's available oral or IV and then there's Brincidofovir and cidofovir, we're going to be having ID involved probably for all of those agents, at least in the near term because I imagine most people listening don't have familiarity with them. I think the next curveball that we wanted to throw you is, if our patient was a pregnant woman with genital lesions, how would that change our management here?

Boghuma: If this was a pregnant woman who presented with genital lesions and she did have exposures that made me worried that these genital lesions may be associated with an STI, obviously, I would still have monkeypox on my differential and I would do the screenings that of how we have described in terms of screening her both for monkeypox and for other sexually transmissible infections.

Now with regards to the management as pertains to a pregnant woman, I mentioned before that two of the antivirals that we do have at our disposal have teratogenic effects. So, a pregnant woman with monkeypox will not qualify for Brincidofovir or cidofovir. Now, in terms of tecovirimat, there is no

evidence of teratogenicity in mice, but we also do not have enough human data and that would have to be a decision that would have to be shared between the patient and an expert consultant to weigh the risks and benefits of providing antiviral in that scenario. Now pregnancy is considered an immunosuppressed state, so that would qualify for consideration for an antiviral treatment for this pregnant person if they were confirmed as having monkeypox.

Now, if this pregnant person says, "I don't want to have tecovirimat because there's no data. What are some of the other things that we could consider?" There's vaccinia immunoglobulin, which is essentially antibodies that are collected from individuals who have received a smallpox vaccination, and can be used as passive immunity for individuals with severe of the Orthopoxvirus infections. Now, we don't have data on whether it's effective for treatment of monkeypox or not, but it's again, one of those therapeutics that is in the realm of things that we can consider for immunocompromised hosts that we cannot offer antivirals to, or who needs some form of treatment, but we're running out of ideas on what we can offer. And again, that would need an expert consult and a risk-benefit conversation to make some of those decisions.

Now, if this pregnant woman had an exposure to someone with monkeypox, but she did not have any lesions, and she showed up in the clinic, and she was worried because her roommate has tested positive for monkeypox and they share the same bed because it's a really tight apartment, and she has no lesions. What could be considered for this patient is post-exposure prophylaxis with vaccination. And that gives us the opportunity to talk about some of the vaccines that are currently available and being used both as pre-exposure prevention and post-exposure prophylaxis for monkeypox. So, the monkeypox vaccines that are available are really vaccines that were developed for smallpox and were able to use these vaccines because Orthopoxviruses share a feature of immune cross-protection or immune cross-reactivity. And this just means that if you've been infected with one virus appeal of the Orthopox genus, if you encounter another virus of that same class, then the immunity you gained from your exposure to another Orthopox virus would give you some protection against another Orthopoxviruses.

There are two vaccines currently available. And they are all based on a vaccinia virus, which is another Orthopoxvirus, which is not as virulent as variola or as smallpox. We have an inactivated form of vaccinia virus, that is not replication competent, but it is a live vaccine. And this particular vaccine can be used in immunocompromised individuals. And for this patient, she would be able to get an inactivated vaccine as post-exposure prophylaxis if she had a credible high-risk exposure to someone with monkeypox.

Now, the modified attenuated live vaccine is given in two doses. And those doses are spaced 28 days apart. It is a subcutaneous vaccine, although it can also be given intradermally. And in that case, we use a fifth of the dose to administer intradermally. So that would be something that I would consider for someone who was exposed, but didn't have lesions yet. And we are hoping that if you immunize them within four days of their exposure, then they can develop enough of an antibody response that they essentially catch up with that long incubation period and prevent the virus replication from actually causing an infection. And even if the first person develops an infection, then you're also hoping that it would not be quite as severe as someone who had no antibodies already present Orthopoxviruses. And then that brings us to the second vaccine. Do you want me to launch into that or you want to ask a question?

Matt: No, I think we can launch into the second vaccine. So, the first one was the attenuated, it was the inactivated vaccine, but not a live vaccine.

Boghuma: The inactivated vaccine. And then the second option that we have for vaccines is a live vaccine. These are not attenuated. They're replication-competent vaccines, and they contain the vaccinia virus, and they are administered with a special needle, that's called a bifurcated needle, which essentially allows the person administering the vaccine to make little puncture marks on the skin and inoculate the virus into the upper layer of the skin. So, what you're doing is making 10 to 15 puncture marks and actually inoculating a live virus vaccine into the skin. And that area of the skin forms a pox, it forms what we call a vaccine take which is a local infection in the skin, and that infection triggers an antibody response that is then protective. I know this may sound a little bit barbaric to the people listening to--[laughs]

Matt: Is that scarification, because I was reading--

Boghuma: It is a scarification technique, and was used in the latter days for the eradication of smallpox. So, a lot of people who got vaccinated for smallpox are quite familiar with the scarification and the fact that it can leave a scar

Matt: Can't argue with results, Paul. [Boghuma laughs]

Paul: Yeah, this just feels like Edward Jenner level stuff. But I'm glad that we have something but that is wild.

Matt: I'm not sure if we're going to be using the video for this one, Paul. But Paul's cat is on his chair behind his head right now. [Boghuma laughs] I had to mention that. Boghuma, Paul's cat records with us most weeks. [Boghuma laughs]

Paul: Yeah, he's a usual picture. He's very smart.

Boghuma: [laughs] Yeah. And I think that, important things for providers to remember about live vaccines is that they are completely contraindicated in people who are immunocompromised because they are replication-competent and can actually cause disseminated vaccinia infections and individuals who do not have a competent immune system. And also, after vaccination, individuals have to cover the vaccination site, because that site, remember has a replication-competent virus.

Paul: Oh, jeez.

Boghuma: And you can actually transmit vaccinia virus to other people if you don't protect your vaccine site appropriately. This is a vaccine that has a single administration. It's not dual administered, like the modified inactivated vaccine. And both vaccines have been compared in a phase three trial and have been found to generate equivalent antibody-level responses.

Matt: Boghuma, it seems like this virus, there was a couple of contraindications for-- sorry, the vaccine for the live one, that if people had really bad eczema, pregnancy, a lot of cardiovascular disease then maybe that wouldn't be the one for them. It seems like this one had more adverse events than the inactivated virus.

Boghuma: That is completely correct, Matt, because the live vaccine is actually a second-generation smallpox vaccine and these live vaccines have been very well described to be associated with more severe and significant adverse effects. Notably, myocarditis has been one of the adverse effects that has been a concern with the life replication competent vaccines. And in individuals who have pre-existing skin conditions like eczema or atopic dermatitis, they can develop a complication from these live vaccines that we call eczema vaccinatum, which essentially is just a disseminated cutaneous

infection with vaccinia. And in these individuals, having an existing skin condition like that would be an absolute contraindication to getting a live vaccinia vaccine.

Matt: I don't want to go too far down this rabbit hole. But are we worried that like giving the smallpox vaccine where there's replication, is smallpox going to like come back because of this?

Boghuma: Well, the virus in the vaccine is vaccinia. And the virus that causes smallpox is variola. So, vaccinia is a much milder Orthopoxvirus that really doesn't cause severe infections, even when those infections happen. So far as you're administering it to individuals who are immuno-competent. Remember, smallpox was eradicated using vaccinia-based vaccines. And these vaccines were given to millions of people around the world, and only became discontinued towards the end of the eradication process where it was obvious that it was riskier to be vaccinating hundred million people to prevent a single case of smallpox that was becoming vanishingly rare, as opposed to not vaccinating and really just targeting the pockets of residual smallpox that still existed around the world.

Matt: Oh, Paul, I think we might be at the end of this one. What do you think?

Paul: I think we've done hero's work as per you. I would like to know, Boghuma, if you have any final thoughts or summary statements that we should really-- what should we be taking away from this episode specifically, that is the most critical thing for, let's just say the general internist to know that as we're starting to think and worry more about monkeypox?

Boghuma: I think that the point that I would like to drive across is that although we've seen the case numbers leveled off and even start to decline in a lot of places, we are still quite far from elimination., and eradication is going to be challenging. So, I really want the general internist to think about monkeypox as something that they are likely to encounter in their practice, either, in their clinical practice when they screen patients for STIs or think about viral exanthems or if they're in the hospital medicine side may have to care for a patient who's admitted with one of the complications of monkeypox.

The take-home message would be, be aware that we are in an outbreak. And I think it's important to know the many varied presentations of the virus. And to be proactive about testing. If you don't think about it, you're not going to test it. And if you don't test for it, you're going to miss it. And lastly, also be aware of what the risk factors are, and know to recommend the vaccines to your patients who may meet some of these risk criteria because for once we're dealing with an outbreak of an infectious disease for which we do have vaccines available. So, prevention is always better than cure. If we vaccinate the highest-risk group individuals, then we stand a better chance of making sure that this doesn't spread and become a bigger problem than it already is. And I'll stop with that.

Paul: This has been another episode of the Curbsiders that bring you a little knowledge food for your brain hole.

Matt: Yummy.

Paul: That’s just being you, buddy.

[laughter]

Paul: Get your show notes at *thecurbsiders.com* and while you're there, sign up for our mailing list to get our weekly show notes in your inbox, plus twice each month, you'll get our new Curbsiders Digest recapping the latest practice changing articles, guidelines, and news in internal medicine.

Matt: And we're committed to high value practice changing knowledge. To do that, we want your feedback. So, please subscribe, rate, and review the show on Apple Podcasts or on Spotify. You can also send an email to *askcurbsiders@gmail.com*. A reminder that this and most episodes are available for CME through VCU health at *curbsiders.vcuhealth.org*. I wanted to give a special thanks to Dr. Paul Williams for helping to write and produce this episode. And to the team at Pod Paste who helps to produce and edit our show. Elizabeth Proto runs our social media, Stuart Brigham composed our theme music. And with all that, Paul, until next time, I've been Dr. Matthew Frank Watto.

Paul: And as always, I remain Dr. Paul Nelson Williams. Thank you and goodbye.

[Curbsiders theme playing]

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