Kendal Williams, MD (Host): Welcome everyone to the Penn Primary Care Podcast. I'm your host, Dr. Kendall Williams. So as of August 1st, there were over 4,600 cases of monkeypox in the United States. Over a hundred in both New Jersey and Pennsylvania each. It is a condition that we are gonna start seeing in our primary care practices.

And if you're like me, you don't know much about it. So the monkeypox virus is not a new virus, but it's new to us. And we Quite rapidly need to get ourselves up to speed. So, I put together a bit of an emergency podcast, looked for expertise within the Penn community and we have actually truly international expertise within the Penn community.

And we're happy to have it on the program today. So Stuart Isaacs is an associate professor of medicine at Penn and a member of the division of infectious diseases. He is an international expert on viral diseases, specifically pox virus. And maintains a lab studying Pox viruses. He did his undergraduate at Brandeis medical school at Yale, internal medicine residency at temple and ID fellowship at Tufts and the NIH. Stu, thanks for coming on.

Dr. Stuart Isaacs: Kendall. Thanks for inviting me. I really look forward to this conversation.

Kendal Williams, MD (Host): And with us again, it is Dr. Anne Norris. She is an associate professor of clinical medicine at Penn and a member of the division of infectious diseases. Anne did medical school at temple before residency at Pennsylvania Hospital in ID fellowship at Penn. Anne's podcast that she did with this on summer fever in Lyme disease was so popular that I asked Anne to come back and join us for this one as well. Anne, thanks for coming.

Dr. Anne Norris: Thanks Kendall.

Kendal Williams, MD (Host): So, let's start with the basic questions, Stu, I'll throw this to you. tell us a little bit about monkeypox the history of the virus and what it is?

Dr. Stuart Isaacs: Yeah. So monkeypox is in the same family of the virus that's most notorious and that's smallpox. So smallpox was a human disease that was caused by a virus called Variola virus. And that virus over centuries killed billions of people in epidemic and pandemics. And it was in the late, in the 1960s when the World Health Organization began an intensified program to eradicate smallpox.

And smallpox was the first and only disease currently totally eradicated. So

naturally occurring smallpox doesn't occur, but it was really during this time when smallpox was being eradicated that. Another pox virus was causing human disease and it was caused by a virus that was named monkeypox. Now the name monkeypox is really a misnomer similar to the cowpox virus that Jenner is credited as using as the first vaccine that was used to prevent smallpox.

So like, cowpox is not a cow specific virus. It's actually a virus that's in rodents. And then as a zooinosis, it would jump and infect cows. And the first disease was seen in cows. And so people back then called it cowpox. But it's actually a road in virus. And so similarly cowpox could incidentally infect humans and they would be called, said to have cowpox as the disease. So monkeypox is very similar in that the first animals the disease was noted in were monkeys. Actually monkeys in research labs in Europe. And so the disease was first found in monkeys and got the name monkey pots, but the actual animals where the virus hides out in and continues to grow and incidentally infect humans is rodent species in Africa. So, that's the history of monkeypox.

Kendal Williams, MD (Host): So, Veriola viruses are different than varicella viruses. But they have some common features, right. In terms of sort of a vesicular formation and so forth?

Dr. Stuart Isaacs: Yeah. So, and just to mention, so chickenpox, which is caused by varicella virus, so that's a herpes virus and which is a very different type of virus causes a different disease, a disease that hides out in neurons and can reactivate and it has the name of chicken. But it's not a pox virus like smallpox or monkeypox, which are acute viral infections that do not have a dormant state and can reoccur.

Kendal Williams, MD (Host): So monkeypox is really the first virus that we probably, as American physicians have seen since smallpox that's in this category.

Dr. Stuart Isaacs: Yeah. Yeah. And interestingly the U.S. was actually the first. Country out of Africa where monkeypox caused disease. And this was back in 2003, probably before you began your podcast days when some exotic animals were imported from Africa to be distributed as pets. And when they were in a distribution center, those exotic animals, which included something called the Gambian giant rat, which some people find very interesting to have as a pet.

Those animals turned out to be carrying monkeypox, and they were either co housed or too closely housed or not really treated in a sanitary condition where

they came in contact with Prairie dogs, which are also animals that people use as pets. And it turns out the Prairie dogs turned out to be very susceptible to monkeypox. And the Prairie dogs got sick and were distributed to people and the Prairie dogs infected a whole host of people in the upper Midwest.

About 74 cases of suspected or confirmed monkeypox occurred during. Outbreak in 2003 and almost all the cases were associated with contact with sick Prairie dogs. There was not this human to human transmission that we're seeing now with this this current global outbreak of monkeypox.

Kendal Williams, MD (Host): Has there been human to human transmission in Africa?

Dr. Stuart Isaacs: Yeah. So, human to human transmission you know, so the initial infection is a zoonotic where someone comes in contact with a sick an animal may, but not always sick, but an animal carrying monkeypox. And they become the primary. And in Africa, human to human spread was most, if it happened, would happen within the household, people living together, sharing meals together, sleeping potentially in the same bed.

And so human to human transmission did occur, but the chain would quickly end. Most commonly a primary case would give a secondary case. Very rarely the secondary case would give a tertiary case. And the outbreak would then end very quickly because it was not spreading person to person.

Kendal Williams, MD (Host): So this experience is even different than what has historically happened in Africa, where you have an outbreak that seems to be growing to a greater degree than the African experiences. Am I hearing that correctly?

Dr. Stuart Isaacs: Totally. And I always say this has been unprecedented, many would not have predicted this type of global spread. An d it has been out of Africa. There's been cases where people get sick. Get exposed and infected in Africa, then travel through by plane or other means and show up in a country, and are diagnosed with monkeypox.

But then there hasn't been transmissions in those cases over the last decade or two. And so, this outbreak has been totally unprecedented and the mode of transmission appears to be different or not as described in the historical cases in Africa.

Kendal Williams, MD (Host): So something happened to the virus itself?

Dr. Stuart Isaacs: Yeah, so we're all familiar with SARS COVI 2, the cause of COVID, which is an RNA virus. RNA viruses replicate quickly, do not really care that much about the fidelity of their replication and therefore make mistakes. And as a novel coronavirus, it was the perfect laboratory experiment where this virus just grow hundreds and hundreds of thousands of people infected.

It was mutating. And has continued to mutate and found a way to increase its ability to spread. The pox viruses are DNA viruses, so totally different type of virus and it replicates using more higher fidelity or DNA polymerases that are more careful and don't make as many mistakes, but that's not to say there won't be mistakes made.

And especially in this unprecedented human to human transmission. There could be some mutations happening. Now, it's really not clear if the mutations that we're seeing in the virus are the explanation for why it's spreading to the extent that it's spreading today, or if the mode of transmission and the community that it's in and spreading, has just found the right niche to continue to spread. And that's not to say it won't continue to spread outside of that community.

Kendal Williams, MD (Host): So let's talk about the outbreak itself, because you're alluding to it. How did it start? Where are we at with it and so forth?

Dr. Stuart Isaacs: Yeah, we're gonna have to learn a lot more because the initial description and the first identification was just in May of 2022. So just a couple of months ag o. The odds are that this had been happening even prior to this and just was going undetected because it was presenting in a way that may not have looked like classical monkeypox. The disease that People would see in textbooks that described the disease in Africa.

So there was a good chance that this has been brewing for a longer period of time. And the community that it's been identified in and has continued to be the largest community where it's spreading, is in men who have sex with men.

And the transmissions are occurring through very close, intimate contact need not be sexual contact because it could occur from very close skin to skin contact and introduction of the virus through like micro abrasions in the skin. And then in that community, having a number of different partners have kind of allowed this virus to continue to.

Kendal Williams, MD (Host): And so the, of the 4,600 cases in the us most so far are confined to that community. Is that Right?

Dr. Stuart Isaacs: Right. Yeah. A very High percentage at 98% are male.

Dr. Anne Norris: Yeah.

Dr. Stuart Isaacs: Yeah, 98% are males of the information that the CDC has collected, and 94% of the 98% identify as having men who have sex with men.

Kendal Williams, MD (Host): And we all have this experience with COVID, which was 2% mortality when it first came out. And there was great fear. We were seeing coffins or not trucks lined up outside of New York emergency departments to handle the death toll. We're not seeing that with monkey PS, right. So far as I understand it, nobody has died of monkeypox.

Dr. Stuart Isaacs: Slight correction. So, and also to step back a little historically. So, it turns out there are two clades of monkeypox naturally occurring. Monkeypox in Africa, there's a central African strain, which we're now we're calling clade one. And the central African strain of monkeypox is a virus that we know has a higher virulence.

At least in central Africa has about a 10% mortality. There's another clade of virus out of west Africa which we call clade two. And we're fortunate if fortunate could be used as a word to describe an unprecedented worldwide outbreak that the virus that's spreading is a virus that came out of west Africa. And it's a less virulent, at most 1% mortality in west Africa.

And in the US, there's been no deaths from entering this current outbreak, although in two countries outside of Africa there, I believe there's been two cases, one in Brazil and one in Spain. I don't know any of the details of those other than one of the cases was in an immunosuppressed or immunocompromised patient.

Kendal Williams, MD (Host): Anne I understand you've seen cases of monkeypox. So I'm gonna now direct my questioning to you in terms of the clinical features. how do these patients present?

Dr. Anne Norris: Well, I have to say Kendall as a clinician, seeing these cases, this has been fascinating. Just riveting as an infectious diseases doctor, I'm literally learning about a disease that is unfolding before us, in a way that we've never seen before kind of like COVID. But a much less severe disease where I don't have to change my clothes in the garage before I go inside to see my family, I'm less terrified of this disease.

We have treatments, we have a vaccine. So, and it has become, I mean, I'm sure I'm gonna see lots of variations on it, but it is become a, you know it when you see it. And it largely looks exactly like the pictures in the books and the pictures online. So classically, and by that, I mean the 2003 outbreak and the outbreak in Africa monkeypox is said to start with a prodrome with a febrile prodrome with fever or headache, lymphadenopathy, myalgia.

Followed by the appearance of the rash. In the current outbreak, often the first sign is the rash. You'll get a message from a patient saying I have a couple of pimples on my body. Do I need to come in? And typically what patient's experience a, a lesion start as a macule that's maybe two to five millimeters in size that evolves into a papule, and then maybe a vesicle or pustule, they're deep seated lesions.

They often become umbilicated. And they often if you look people over carefully, you'll find a lesion that looks just like the lesions that have been described, true pox lesions. They're often painful. Patients have been admitted for pain control because these lesions can be so painful. We see them In the genitals, very commonly per anally on the scrotum, on the penis.

And we see them on the extremities and potentially on the face and some on the trunk. The lesions eventually crust and fall off. Their life cycle is something like 2, 3, 3 and a half weeks. They're not typically all in the same stage. That is another thing that differs from the previous African outbreaks. You can continue to see additional lesions over the course of a week or so. So a lot of patients do have systemic symptoms fever. Some patients have profound fatigue. Like I have a patient who went to bed for three days, just exhausted. And they often have painful lymphadenopathy as well.

Kendal Williams, MD (Host): The lymphadeopathy in the groin or the areas?

Dr. Anne Norris: It can be diffuse or can be regional.

Kendal Williams, MD (Host): Okay. Can I ask more about the lesions and just distinguishing them between say a primary herpes outbreak and also just Maluskan contagiocian from human papilloma virus and genital Wartz,

Dr. Anne Norris: Yeah. So compared to herpes, herpes, grouped vesicles on an [inaudible] base. So, herpes lesions are typically painful, but you typically don't see them diffusely all over the body. If they're just in the genital region, to actually get, to see the blister of a herpes lesion, you're lucky. Because they're transient. They last a couple of hours and typically they pop and you get this very shallow set of ulcers that sort of coalesce into a sorpiginous shallow based

lesion.

So, there may be a moment in time when you're looking at a genital lesion, that's a vesicle where you're thinking, I don't know which way this is gonna go, but a herpes lesion will not evolve into a monkeypox lesion over the next day. They'll be easily distinguishable. I actually sent Stuart photos of a patient with diffuse Maluskum about three weeks ago because This patient some of these lesions actually had pustules on them, which would be very, very, very unusual for Maluskum.

And it turned out the patient had immune reconstitution syndrome from HIV and that's what the pustules were from. It was Maluskum that became inflamed, but in most situations, Maluskum lesions again, they have that umbilication and if, you know, if you squeeze them, that little ball of wax might come out of the center, but it's not really a pustule. And they're not painful. Did I get that right? Stuey?

Dr. Stuart Isaacs: Yeah, yeah. Anne, a great, I should take a recording of this and use this ‘cause that was a great description of it. Yeah. I think Muluskum though, as we mentioned household contacts of the monkeypox cases are gonna happen. In fact, there's been two cases in children who were household contacts of monkeypox patients.

And, you know, Maluka is very common in P the pediatric community. And I think. That's gonna be you know, Anne had a great description and I think most a dermatologist would probably be able to tell that it's a moloka and not a monkey box, but I think it it's gonna be a difficult time going forward if this continues to spread as we're seeing.

Kendal Williams, MD (Host): So, what do I have to worry about if a patient comes in with monkeypox and you said that lesions are painful, people can be in pain, but what else should I be worried about happening?

Dr. Anne Norris: Well again what we're currently seeing is different than what has been described in Africa. And I imagine that's because this is clade two and not clade one. Previously the serious adverse. Events were as the virus involved organs and people developed hepatitis, encephalitis, pneumonia here so far the complications are largely pain related.

Patients developed nemis and I've had a patient with rectal prolapse and basically an inability to defecate. We've had patients have had to be admitted for pain control. They've had to be admitted for severe pharyngitis where they are at risk of developing dehydration.

Dr. Stuart Isaacs: And Kendall just to mention, and that the concern is that the monkeypox fortunately being this clade two a less ENT varialent much lower mortality, but in certain patients, it could be more severe. And the immunocompromised are at risk of complications from one of the small pots vaccines.

And we, I don't know if we'll have time to get into the vaccines, but even people from a vaccine, a replication competent vaccine In the immunocompromised could have a fatal outcome from that vaccine, as well as certain skin conditions could have very severe reactions to one of the vaccines.

And so since monkeypox is in the same family and. More ENT than the vaccine, for sure that there is concern that there could be some poorer outcomes here in the US, if this virus in gets into the wrong host.

Dr. Anne Norris: Stuart, how about pregnant women? I think that there's been some adverse events with previous monkeypox outbreaks in pregnant women. Should we worry about it with this plade?

Dr. Stuart Isaacs: Yes. And yes, pregnant women too, would potentially have a, a more serious outcome and even infections of the fetus from these pox viruses. But as Anne mentioned, we're fortunate in that the SARS COVI two the novel coronavirus that came when we had no vaccines and no therapeutics. There was some preparedness going on here in the United States and around the world to be prepared for a potential smallpox being a much more deadly virus.

And monkeypox and smallpox are such close family members that the vaccines and the drugs that were developed to treat potential smallpox, it is gonna be effective at hopefully preventing monkeypox and for treating monkeypox. And so in while most cases do not require treatment there will be cases that we use this drug it's called Tecovirimat or Tpox, which is a lot easier to pronounce. We use that drug in certain settings in patients with severe rectal pain or pharyngitis potentially.

And then certainly would be used in an immunocompromised host or someone else who's at a higher risk of a severe outcome. so the preparedness is one thing we have these drugs available, but part of the problem where experiences the implementation, the scale up and use. Anne, why don't you describe some of that?

Dr. Anne Norris: Yeah. So, I have had occasion to acquire Tecovirimat for patients and both the diagnostic algorithm and the acquisition of the drug. At

first to Stuart's point were phenomenally onerous just hours and hours of forms and paperwork to get these things. Both of them have gotten easier. Diagnosis has gotten much, much easier. And so, I think it's available to the primary care person to do these things now.

Kendal Williams, MD (Host): So Anne, you have a patient in front of you, you think may have monkeypox what do you do to diagnose it? What's the process?

Dr. Anne Norris: Yes. It's gotten easier. The first thing you do is go put on your PPE, your gown, gloves, your eye protection, and your N 95, which is all the things that CDC recommends to keep that virus in the room and not on you. It no longer requires approval to get monkeypox testing. And in fact, here at Penn, if you make your way to the order entry box in Penn Chart and type in monkeypox, you'll see an order for orthopox non variola PCR parenthesis.

Monkeypox. And that's the one you want. It's already been prepopulated with all of the important information. There had been some concern about whether this test would be covered when sent to commercial labs. But I have been assured that patients are very unlikely to face a bill and that they would be able to successfully adjudicated if for some reason they did, if they're their particular payer gave them some trouble.

The turnaround time for the test is. Supposed to be about 48 hours. I haven't had one come back yet using this methodology because prior to this week, we had to send all these tests out to the department of health and that there was this very onerous approval process and paperwork that was required.

So I've sent a few this week, nothing's come back yet, but I'm optimistic that this much simpler process will make it much easier for us to manage these growing number of cases.

Dr. Stuart Isaacs: Kendall, if I could just add some additional info to what Anne was describing. So, because these lesions are so deep seated, a lot of people trying to diagnosis think that they need to somehow unroof and get some of the puss out of it, which is almost impossible to do, unless you are a dermatologist doing a biopsy.

And so, using a swab and you could use any type of swab except a cotton swab. You wanna vigorously just rub the lesion with the swab and it's the skin cells coming off that lesion that has virus in it. And it's just swabbing the, and get collecting enough of the cells that just naturally are being decimating off of that lesion. That the PCR is very sensitive and specific to then amplify and determine whether monkeypox is present.

Dr. Anne Norris: If you're a Penn person ordering the pen order, you use the usual universal viral transport media, the same thing that you use to do, for instance, a respiratory panel or a herpes swab, and you only need one specimen per lesion. And CDC recommends that you swab at at least two lesions and try to get them at different stages.

Kendal Williams, MD (Host): So inside the Penn community, we're using the same tubes that we would use for a respiratory viral panel. Outside of Penn, there may be some other collection system you just don't know. Right?

Dr. Anne Norris: Yeah, it depends on the lab. If you're sending it to the Department of Health, it's a dry swab in a sterile urine cup. It's just a cotton swab, like as if you're doing a bacterial culture.

Kendal Williams, MD (Host): Okay. So, through that, we're able to diagnose it in 48 hours. I'm curious what are you telling your patients in that time? So they're leaving your office and maybe they're not feeling poorly enough to be hospitalized, but you're saying them home, what are you telling them? While you're waiting for this to come back.

Dr. Anne Norris: Yeah, this has been very interesting. Where people are used to the COVID lockdown. And so I have told patients go home, you should wear a mask when you're around other people, you should isolate from other people, you should keep all of your lesions covered. So bandaids on the ones that are on your hands or your legs if you're wearing shorts. Don't share bedding, don't share clothing. And that goes well at first, virtually all the cases that I've sent have been confirm. And then you have to tell people that they have to remain isolated until all of the lesions have scabbed over. The scab has fallen off and new skin has formed. And that is a two-to-three week process. And people are less compliant with that advice.

Kendal Williams, MD (Host): I would imagine. And they're not feeling that sick at some point. Right?

Dr. Anne Norris: Many of these people, aren't feeling sick.

Kendal Williams, MD (Host): Yeah.

Dr. Anne Norris: For many of these people, this is just a rash and nothing else.

Kendal Williams, MD (Host): Okay. So let's get back to treatment. The, you mentioned that the drug I've forgotten the name. I'm sorry. I should know it. I'm

the host of a podcast, but I've forgotten it.

Dr. Stuart Isaacs: Kendall it's Tecovirimat or Tpox. You could call it.

Kendal Williams, MD (Host): Okay. And so we had some old stores of it available. Still. You were going over this and let's say we do instead of 4,600 cases, we have 46,000 cases. what's the future of getting this available to others?

Dr. Stuart Isaacs: Yeah. So, fortunately this drug which was developed and got FDA approved for treatment of smallpox was FDA approved in 2007. And my understanding is that the strategic national stockpile has plenty of this drug available. Now I say my understanding because previous to this outbreak of monkeypox, I would've said that the vaccine that was recently approved for prevention of smallpox. And monkeypox a vaccine called Ginios.

Would've also said that that vaccine was in the strategic national stockpile and there was plenty of. And during this outbreak, we have heard that it wasn't as plentiful as most of us in the field thought it was although the supplier and the government is quickly acquiring hundreds of thousands of doses. If not by next year, millions of doses.

Kendal Williams, MD (Host): Let's go to vaccines too. I know it's become available. Penn. I thought, I think I saw received a hundred doses to something from the department of public health. As this gets rolled out, what are the priorities for vaccination? Who should we be vaccinating and so forth?

Dr. Stuart Isaacs: Yeah. So, the vaccine, there's actually two smallpox vaccines available. There's a vaccine called Acam 2000, which is a replication competent vaccine and more similar to the vaccine that was used during the time of smallpox eradication. The problem with that vaccine is that the number of adverse events and potentially serious adverse events with it is gonna be very high.

And so in weighing the risk benefit of using that vaccine To try and prevent or to give as post exposure prophylaxis in to prevent monkeypox disease. At the moment that risk benefit ratio makes it seem that the risk of that replication competent vaccine to be higher than the benefit. So we fortunately have a second vaccine that was FDA approved in 2018 called Ginios.

And the beauty of this vaccine is it's a much safer vaccine. it it's a live virus vaccine, but when it's injected into mammalians or mammalian cells, it doesn't form infectious variance. So you inject the virus. Makes all the proteins it needs to make. And that immune response would wanna be developed to. But the

virus never assembles into a new infectious verion and therefore doesn't spread within the host.

And is much safer and can be safely used in a lot of populations where the replication competent vaccine that Acam 2000 vaccine would be more dangerous to use. So the Ginios vaccine, which is the one that most people are talking about and wanting to get it's certainly available as post exposure prophylaxis, meaning that a case is identified, there's contact tracing. And if you vaccinate someone within the first four days after exposure, you could potentially prevent development of monkey pox, or certainly modify the disease.

And so similarly people within the first 14 days after an exposure, you could give postexposure. Prophylaxis with the vaccine to modify the, the outcome of the infection. So that's the first group and there's vaccine available for people who are known contacts to monkeypox cases. The CDC has now begun a second phase of vaccinating through something they're calling enhanced post exposure prophylaxis.

Because you may have been exposed, but don't know you were exposed, but within the last 14 days did activities that put you at risk of monkeypox and you're in a community where there's monkeypox disease happening. And so that's the second group that is being offered vaccines through the public health channels. And the public health channels have been now distributing these vaccines to various centers to make sure it's being equitably provided to the communities that are in need of this.

Kendal Williams, MD (Host): Once you've had the vaccine or once you've had monkeypox what's the duration of immunity of protection?

Dr. Stuart Isaacs: Yeah, that's a great question and something we're gonna learn during this current outbreak. We know for smallpox that if you survived smallpox, you had life, what we would say would be lifelong immunity to getting small pox again, meaning. If you were exposed to smallpox later in life, you would not die from smallpox if you got it again.

But as we've learned with COVID and the vaccines that we're using to prevent COVID is that these vaccines really don't provide what's called sterilizing immunity. They just change the scales more on the side of the. To respond to the virus and clear the virus. So with monkeypox it would be expected that you would have pretty good lifelong immunity to monkeypox, but I still, I'm not sure.

And will learn if you could get reinfected. And if you get reinfected, do you have symptoms? Do you have a mild case? Fewer lesions? I think that's something we're gonna learn from during this current outbreak.

Kendal Williams, MD (Host): So Stu eventually we'll get to the stage where, maybe we're at that stage now where we're doing a formal vaccination program. It becomes a routine aspect of primary care and among at risk populations, which I'm sure will evolve and to be defined better as this proceeds through the community. Right?

Dr. Stuart Isaacs: Yeah, it's still early and I'm not sure yet if we're at that stage, that there's still some hope that this might be contained and not require continued. Routine vaccination similar to what's being done with like a papilloma virus vaccination, which is definitely needed to prevent the cancers that result from papilloma virus.

Hepatitis B virus, is it definitely a routine vaccination that's needed to prevent the problems of hepatitis B. Still think we may be early enough to potentially prevent this from moving into just becoming another viral disease that we have to deal with. But there are others in the field who are saying, it's it, we're too late already at this point.

Kendal Williams, MD (Host): yeah, that was a question I had wanted to ask Stu and that is can we put the genie back in the bottle? is it too late to do that? Or, and I guess you're saying varying opinions on that, but you're still hopeful.

Dr. Stuart Isaacs: Definitely varying opinions and. That the public health responds that, the communities where this is spreading, and we've learned this from also the COVID pandemic and the great hope of the vaccine and how the vaccine was gonna allow life to go back to normal. It's just one of the tools of public health and the current outbreak of monkeypox we, the vaccine is gonna help, but we're also gonna need to identify cases, isolate them, prevent further transmissions and ask communities to potentially decrease any risky behavior. At least for a period of time, until we could get better control of the outbreak.

Kendal Williams, MD (Host): Anne in your population or in the patients you've seen, I assume there's been some contact issues that have become up from patients you've diagnosed. And how are you handling that vaccination piece?

Dr. Anne Norris: We have been provided with a small supply, a vaccine here at Penn. And so, we have given both post exposure prophylaxis and we have given Pep plus is what Stu was getting at, which is post exposure prophylaxis

for people who are at highest risk of of coming down with monkeypox. So we have offered vaccine to patients that for instance, have had a sexually transmitted disease within the last three months.

And Penn Chart's great with that. We can actually run reports and find out who we need to call and invite to come in. And we've also given vaccine to patients who have been known contacts to patients with monkeypox, it's a well-tolerated shot, you don't get sick like you do with a COVID shot.

Kendal Williams, MD (Host): It's one shot?

Dr. Anne Norris: It's meant to have a second shot a month later, but it remains to be seen. We're not currently anticipating that we're gonna have adequate supplies to give that second shot CDCs, not making that promise yet. Eventually people will get a second shot, but it probably won't be within a month because we have so many people that need their first shot.

Dr. Stuart Isaacs: although I do think the goal is for the prime and boost, it's a two shot regimen for this Ginios vaccine to get the best immunity from it. And so, with limited supply, the goal was to get as much vaccine out in those initial vaccinations, but then additional supplies are coming and jurisdictions are getting enough supplies to do that second vaccination. So the real hope is to get that second dose in, within a month plus or minus seven days.

Kendal Williams, MD (Host): So I have two residual questions just to clean up some things from before. And forgive me if I use the wrong terms, it's been a while since medical school, but the latency from exposure to clinical manifestations forgotten exactly what that's termed, it may be latency?

Dr. Stuart Isaacs: Yeah, incubation period. Yeah.

Kendal Williams, MD (Host): Stu what is that? So somebody's exposed and then they show signs of symptoms. Could you say what that is?

Dr. Stuart Isaacs: Yeah. so someone's exposed and it really depends on the mode of exposure. And that's, what's been a little different in this current worldwide outbreak where some of the exposures happen and then diseases manifested within days of the exposure. And the commonly seen in like, genital lesions or per rectal lesions.

And when it begins to be more heterosexually transmitted into women I believe vaginal lesions could potentially come up very quickly. In other cases, depending on the exposure, you get the incubation period where there's a period

of time where the virus has gotten in, and it's now traveling to a regional lymph node replicating.

And then there's a viremic phase where the virus then spreads and that's when you then get these diffused few skin lesions in various parts of the body as Anne was describing on the arms, on the potentially on the trunk, potentially on the face. So that the incubation period is a period of time when the virus has initially gotten in.

You're presumably not infectious during that period of time. then you get the prodrome during this viremic phase where the virus then spreads and you get these lesions popping up in other parts of the body.

Kendal Williams, MD (Host): And that time delay, that incubation period is typically how long?

Dr. Stuart Isaacs: Yeah, it could potentially be like two weeks. And that's part of the reason why the postexposure prophylactic vaccine has some efficacy that during that incubation period, while the virus is growing, if you give the vaccine, which gives a lot of the antigen load to say hey body, this is a foreign thing, develop an immune response to it.

And then the immune, both the innate and adaptive immune responses kick in and can alter the progression of the monkeypox during that incubation period.

Kendal Williams, MD (Host): The other cleanup question I had just from our discussion previously, what are the criteria that are informing your decision to treat with the viral medication you mentioned?

Dr. Anne Norris: We're offering treatment to patients that are immunocompromised. So in my practice for patients with HIV over a CD four count less than 200. We're offering treatment to patients who have the potential to have severe disease. So, particularly the per anal lesions tend to be very painful.

And so, for many of those patients they're so uncomfortable that we're offering treatment for them. For patients who are at risk with oral lesions, where they might develop dehydration. It's gotten a little easier to get the drug. It's a well-tolerated drug. And so we're getting more comfortable giving it to people.

Where we think that, I have to admit, I'm thinking maybe they'll be less contagious. Maybe they'll be able to get out of isolation sooner because they're not staying in isolation as long as we want them to. So I have liberalized my

criteria somewhat, but I'm not offering it to people who are like clinically well, with just a rash.

Kendal Williams, MD (Host): Is it orderable in Epic?

Dr. Anne Norris: Yes, it's orderable in epic, but you can't get the drug. You have to, if you have a patient that needs Tecaviramat, you have to reach out to one of us or to the pharmacy to get it. commercial pharmacies don't have it.

Dr. Stuart Isaacs: Yeah, just Kendall. I could add to that on. So one of the problems again with being prepared and then being able to roll out medicines and vaccines in a public health crisis like this in the population where this is in is the implementation has been difficult. So Tecaviramat has FDA approval for treatment of smallpox. Even though we know that it will work against monkeypox, it has to be done under an investigational new drug.

And the CDC has a protocol and emergency access IND. And that creates some of the cumbersomeness of using the drug because you require written, informed consent to use the drug. And then there are some additional logistics with the CDC, which they have simplified over time. But this is not like the emergency use authorizations that we had with some of the COVID drugs and vaccines, one's clinical trials showed that they were safe and efficacious. We know this drug is safe because it's been tested in humans and it's safe. But it doesn't have FDA approval for treatment of monkeypox.

Kendal Williams, MD (Host): I'm also gathering that it's not something primary care physicians will be ordering as of yet?

Dr. Stuart Isaacs: Yeah. So I think it will be very similar pro depending on how this epidemic goes. It's gonna be similar to what we've experienced with COVID. At the beginning, it was just the specialist kind of seeing and treating. And then more cases came and drugs became easier to access and prescribed, that it could someday become a disease where primary care doctors are both diagnosing and treating. Because it's gonna be mainly an outpatient disease as we're currently seeing it.

Kendal Williams, MD (Host): Well, that's wonderful information from both of you. I wanna give you an opportunity to say something to the primary care community. If there's additional points you wanna make.

Dr. Stuart Isaacs: I would just say, testing has become much easier as Anne described and that. At this point where we're learning about the disease and trying to see where it is and who has it, that if you have a question, if you're not

sure of the diagnosis. And frequently monkeypox could occurs with other sexually transmitted infections, that it may be worth doing more testing. At least initially to see if the case you are seen in front of you is a case of monkeypox.

Kendal Williams, MD (Host): so thank you both for coming on. This was really timely and very important. I learned a lot and I'm sure the members of the primary care community did as well. This is something that were all sort of struggling to figure out, and you've answered many of the most important questions. So I really appreciate you both coming on.

Dr. Anne Norris: My pleasure.

Dr. Stuart Isaacs: Kendall, thanks for the invite. I really enjoyed it and I hope it's helpful.

Kendal Williams, MD (Host): It will be Stu. Thank you so much. So please join us again next time for the Penn Primary Care Podcast.