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Monkeypox: What Clinicians Need to Know

Dr. Russell:
The global outbreak of monkeypox in non-endemic countries may be surprising to us all. The virus has not mutated, and the WHO states that it can be contained. However, as more cases are popping up in Europe and North America, what do clinicians need to know to be prepared?

Welcome to *Clinician's Roundtable* on ReachMD. I'm your host, Dr. John Russell. And here to share insights on monkeypox and key points clinicians need to know about is Dr. Amesh Adalja, a Senior Scholar at the Johns Hopkins Center for Health Security at the Bloomberg School of Public Health. His work is focused on emerging infectious disease, pandemic preparedness, and biosecurity.

Dr. Adalja, welcome to the program.

Dr. Adalja:
Thanks for having me.

Dr. Russell:
So monkeypox is a brand-new illness for most of our listeners. When did it first emerge on the planet?

Dr. Adalja:
It's probably been with us for a very, very long time, but it really first was described in the 1950s in some captive research experiment, and that's why it got its name of monkeypox, but it started to be recognized as a human pathogen in the 1970s during the smallpox eradication campaign because they are really indistinguishable clinically in terms of the rash, so they had to determine if someone had smallpox or if they had monkeypox. And since the 1970s, we've seen sporadic outbreaks in about a dozen African countries with occasional importations in travelers to other parts of the world as well as a major outbreak in 2003 in the United States that was linked to the importation of African rodent.

Dr. Russell:
So by virtue of its name, one assumes that it's a spillover type infection. Besides monkeys, what are the other animal vectors?

Dr. Adalja:
It's interesting because monkeypox is kind of a misnomer because it's really not that much of a disease of primates. It's probably a disease of rodents, and many different animal species can get infected with it. They don't actually know what the real, true host of it is but not monkeys. It's probably some type of rodent. In the 2003 outbreak, it was African Gambian rats that harbored it. So they're still not clear what it is, but many people believe a lot of pox viruses have their origin in rodents.

Dr. Russell:
So how does this fit into the family of pox viruses?

Dr. Adalja:
So when we talk about the orthopox viral family, it's got a whole bunch of members: smallpox, horsepox, canarypox, camelpox. Monkeypox is part of that, and it is related to smallpox, and we know that because smallpox vaccination is protective against monkeypox. And as it's been decades since smallpox vaccinations ceased, you've seen more and more monkeypox because it was kept at bay by routine smallpox vaccination, but it's part of that orthopox virus family. It is less virulent and less contagious than smallpox.

Dr. Russell:

So the 2003 prairie dog import didn't get all the press that this seems to be having. How did that play out?

Dr. Adalja:
Well, what happened was there were implications of certain African rodent animals to the Midwest of the United States, and they were housed with prairie dogs, and this virus jumped from those imported African animals to domestic prairie dogs, and people that had exposure to those animals got infected. There were about 4 dozen or so cases. Only 3 of them were severe. The public health authorities were able to successfully deploy the smallpox vaccine to the contacts to halt the outbreak, and they did a lot of surveillance, and it didn't seem to take in any of the animal species in the United States. It disappeared after that, which is good, because there's a concern that if this spills in Europe to domestic animal species, it could become endemic there. It did get a lot of headlines there primarily because 2003 is only 2 years removed from the anthrax attacks of 2001, and we were on alert for smallpox being used as a biological weapon, so this was kind of in the press until they realized it wasn't smallpox; it was monkeypox. And then people lost interest in it. However, now in light of the fact that we're in the midst of a COVID-19 pandemic, the press and the public are really attuned to infectious disease threats, so this is getting a lot more coverage, and obviously, 2003 was a totally different news cycle than 2022.

Dr. Russell:
So how is it transmitted, and how transmissible is it?

Dr. Adalja:
So it's transmitted through close contact. Respiratory droplets are one way it can be transmitted, but also close contact, body-to-body or skin-to-skin contact is another way. In you're in contact with someone's lesions, you can get it. And it doesn't seem to be as contagious as smallpox. It's clearly not as contagious as a respiratory virus, so it isn't something that is easy to get. It's more something that requires prolonged close contact. However, based on the epidemiology of this outbreak, it makes sense that it's transmitting pretty efficiently in this network that it's gotten itself into.

Dr. Russell:
What's the R0? Do we know yet?

Dr. Adalja:
No, I don't think we know the R0. And remember, when people use the concept of R0, they often think of it as some kind of intrinsic, you know, 10 commandment written-in-stone number. R0 is an average, so someone could be infected with monkeypox and have an R0 of zero because they noticed the lesion and they say, "I'm not going near anybody," whereas somebody can have a lesion and then be a superspreader and have an R0 of 7. Less than 1.5 is probably where people are putting it when they're trying to model it, but I think it's less important to focus so much on the R0, just that it's less transmissible than smallpox.

Dr. Russell:
So you mentioned skin-to-skin contact. But this is not an STI, correct?

Dr. Adalja:
There's no evidence that this spreads through reproductive fluids or body fluids in the way that, for example, HIV might or herpes might, even though herpes itself can spread from skin to skin as well, so this may be more of a virus exploiting the close contact that occurs during sexual encounters to be able to get from one person to another rather being a strictly sexually transmitted infection. I think it's important to understand is this in any of those body fluids? Can they isolate it? And I suspect they probably will find it, but that may not be the main way that it's spreading. It may just be skin-to-skin contact because a lot of the lesions that people are seeing in these patients are concentrated in the genital area, which tells me this might be just direct inoculation from one person to another, but for public health control measures, it probably doesn't matter either way because it's still the same type of response that you would have whether it's spreading through body fluids during sexual intercourse or through the close contact that happens during sexual intercourse.

Dr. Russell:
So what should clinicians be looking for? And what kind of historical questions might we add to the usual history questions we take?

Dr. Adalja:
So clinicians should keep in mind fever, rash, and lymphadenopathy. Those are 3 things to keep in mind, also that the rash is characteristic, but it doesn't always look like the pictures that you find on the CDC website. It's going to start off with macules, papules, but the one thing about it is that they all look the same. So when you have a patient with chickenpox, if people can remember what chickenpox look like or remember from their own life, they all look different. With monkeypox everything is going to look the same, so that's important.

One of the things that we're seeing is that this is clustering in men who have sex with men, so be on the alert for genital lesions, not just lesions that are on people's arms and legs and face that you might see in the textbook if you look up monkeypox. And some people, at

least anecdotally, only have a couple of lesions kind of in their genital region, so it may be atypical. So if you're thinking someone is coming in with sexually transmitted infection type of symptoms, lymphadenopathy and some kind of skin lesion, you should be thinking about monkeypox.

Traditionally, we always thought, have you traveled to the DRC? Have you traveled to countries where monkeypox is endemic? Have you been handling animals that were imported from Africa? Those historical clues are not so operative with this outbreak. It right now seems to be men who have sex with men, genital lesions, inguinal lymphadenopathy, and atypical presentations.

Dr. Russell:
So what's the overall incubation period of this virus?

Dr. Adalja:
It's relatively long. The incubation is about 12 days or so, which gives you time to do things because that's where we intervene. That's when we vaccinate contacts and cases during that long incubation period because if you vaccinate them, you can abort or attenuate the infection. And the other thing is monkeypox is not contagious during its incubation period. You have to have symptoms to be contagious from all of the other outbreak investigations, so that also allows you a lot more ability to contain something like monkeypox versus something that's contagious during its incubation period.

Dr. Russell:
For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. John Russell, and I'm speaking with Dr. Amesh Adalja about monkeypox and the recent spread that we are seeing across the globe. So some of us are old enough to have received the smallpox vaccine pre-1972. How much are we at risk, and how much is the generations after us at risk?

Dr. Adalja:
It's unclear, but when you look at the epidemiology in places like Africa where this is endemic, many of the cases are in unvaccinated individuals, people who were not vaccinated during the smallpox vaccination campaigns, so I suspect that people that are older that have been vaccinated or maybe they're in the military and they got vaccinated recently likely have some level of protection. It may have waned over time, but it's clearly more protection than someone who's never been vaccinated against smallpox. But if you or someone gets exposed to it, they would still likely vaccinate you again because there's probably been some waning even though you probably have some residual immunity in place.

Dr. Russell:
So there's a newer better-tolerated vaccine, correct?

Dr. Adalja:
Right. So smallpox is actually the first vaccine that humans ever developed. Edward Jenner developed this in the late 1700s, and we basically used Jenner's vaccine until the last 10 or so years when the second-generation vaccine became available because the original vaccine is a live vaccine; it has a lot of reactogenicity; it even can cause serious illness in certain individuals; it's contraindicated in people with bad skin diseases and pregnant women; so it wasn't something that people wanted to continue to use in everybody. So a second-generation vaccine, one that is more of an attenuated virus, was developed, and that is now something that also has an FDA label for prevention of monkeypox, so that's sort of the preferred vaccine to use. We could use either one, but certainly in people with high-risk factors for severe disease from smallpox vaccination, this one makes sense. And this is more tolerated, and I think it likely is going to be the one that is the mainstay of how we contain this outbreak.

Dr. Russell:
So if a patient has this, what would we treat them with? And what lethality do we expect from this infection?

Dr. Adalja:
There are no specific treatments for monkeypox; although, we have a couple of antivirals that are approved for use in smallpox. However, they haven't been used so much in human monkeypox cases, so it would probably be in severe cases immunocompromised patients. Maybe it would be under an investigational new drug application. I think it will be important if we can see how well these work in monkeypox to do clinical trials on these patients, as many as we can, but it's probably not something that every patient is going to need. A lot of it is going to be supportive care. Many of these patients aren't even being hospitalized, so it's just the routine stuff, you know, fever control, making sure they're hydrated, making sure that they don't get a secondary bacterial infection of their skin lesions if they're starting to get infected or they're bothersome and people are scratching them, for example.

And the mortality rates have been quoted, you know, ranging between 1 and 10%, but those are often from outbreaks that occurred in Africa where there may not have been access to routine supportive care. It's probably much lower in this outbreak. We know from 2003 that there were only 3 serious cases in the United States out of about 4 dozen cases, and there was zero mortality, so it may be closer

to 1%. The other point is that there are 2 different strains of this, and the strain that's spreading in this European outbreak is known to be less virulent than other strains as well, so I don't suspect you'll see a major mortality rate with this.

Dr. Russell:
And diagnosis is really from unroofing some lesions and sending off some material from them. Is that something that Anytown USA's lab should have, or do they have to go through the state department of health or the U.S. Government's department of health?

Dr. Adalja:
It's more of any state's public health laboratory can do this. So what has to happen is, yes, you unroof the lesion or you get a swab of that lesion and it's sent for PCR testing. Some labs can say this is an orthopox virus, but they can't identify which one it is, so then it goes on to CDC for confirmation testing. But for all intents and purposes, if you've got a positive orthopox molecular diagnostic test, it is monkeypox. The confirmation test isn't going to add much to it other than making it official. So this is something that you should be in contact immediately with your local or state health department depending upon where you live.

Dr. Russell:
So you live in the public health, you live in the emerging infectious disease space—how much of an issue do you think this is going to be in the United States?

Dr. Adalja:
For the general public, it's not going to be a major issue. This seems to be confined, to men who have sex with men, although anybody can get infected if they are exposed, and in prior outbreaks it hasn't clustered in this group, so I think the general risk is low. However, it's very important for clinicians in the United States to be aware of this. Most of them including myself have never seen a case of monkeypox, so they have to think about it first, because if they miss it and say, "Oh, this person has chancre or this person as syphilis, that person can then go on and spread it, and then it becomes harder to contain, so it's really important that every doctor, especially primary care physicians, have a high index of suspicion to think about monkeypox when they are dealing with sexually transmitted infections and have a low threshold to call someone. Phone a friend, call an infectious disease doctor and say, "Should I be thinking about monkeypox?" because the quicker we identify these cases and identify their contacts, the quicker this disappears from our headlines.

Dr. Russell:
So, Dr. Adalja, any final thoughts you'd like to share with our audience?

Dr. Adalja:
I think that any time a virus is behaving differently, it's important, and you must take notice, and that's why this is important. It's not a reason to panic. Monkeypox is something we know how to contain. It does not have pandemic potential, but we want clinicians to be alert to the fact that infectious diseases are going to continue to be part of our life, and they're going to become more and more common as we travel more as more and more people are exposed to animals, to different environments, to each other. This is really important, and I think it underscores the fact that just because we came out of COVID-19 doesn't mean the threat of infectious diseases is now over.

Dr. Russell:
So that's a great note to leave our audience with. I want to thank my guest, Dr. Amesh Adalja, for sharing his expertise in this infectious disease space. Dr. Adalja, it was great speaking with you today.

Dr. Adalja:
Thanks for having me.

Dr. Russell:
I'm Dr. John Russell. To access this and other episodes in our series, visit reachmd.com/cliniciansroundtable where you can be Part of the Knowledge. Thanks for listening.