Hot Topic

National STD Curriculum Podcast

Monkeypox: Key Recent Literature

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Season 2, Episode 11

This episode discusses recently published manuscripts on the monkeypox virus and clinical manifestations of this infection in the current outbreak.

Topics:

- MPX
- Monkeypox
- STDs
- STIs

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Disclosures

Disclosures for Meena S. Ramchandani, MD, MPH
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References

Paper #1 Paper #2 Paper #3a Paper #3b

Transcript

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

In this episode:

- Introduction
- Background
- Paper #1
- Paper #2
- Paper #3
- Summary
- Credits

[00:00] Introduction
Hello everyone. My name is Meena Ramchandani. I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STD [sexually transmitted disease] literature review for health care professionals who are interested in remaining up-to-date on the diagnosis, management, and prevention of STDs.

[00:21] Background
In this episode, we will review recently published articles on monkeypox. This is the second episode on

monkeypox, and we anticipate releasing a few episodes on this topic, given the global outbreak and increasing cases in the U.S. and worldwide. Vaccination, testing, and treatment for monkeypox have been rapidly implemented at sexual health clinics around the country as the number of cases seen in the community have increased. I think more providers and clinics will soon have the ability to evaluate patients with monkeypox symptoms, which will be helpful for patients to get the care they need. As of August 18, 2022, there have been greater than 14,000 cases of monkeypox infection in the U.S. and greater than 40,000 cases globally.

[01:07] Paper #1

Thornhill JP, Barkati S, Walmsley S, et al. SHARE-net Clinical Group. Monkeypox virus infection in humans across 16 countries - April-June 2022. N Engl J Med. 2022 Jul 21. **[PubMed Abstract]**

The. first article to review was published in the *New England Journal of Medicine* in July of 2022. It was published by Dr. Thornhill and colleagues and is titled “Monkeypox virus infection in humans across 16 countries – April-June 2022.”

1. So this was a case series of 528 monkeypox infections that were diagnosed between April and June from five continents, 16 countries, and 43 clinical sites. Patients were diagnosed with monkeypox virus by a positive PCR [polymerase chain reaction] assay that was taken from any anatomical site.
2. The authors found that overall, 98% of persons with infection self-identified as gay or bisexual men, 75% were white, 5% Black, 12% Latinx, 4% mixed race, and the median age was 38 years. In the cohort of individuals, 41% were persons with HIV; 96% of those with HIV infection were taking antiretroviral therapy, and the majority had an HIV viral load less than 50 copies [per mL].
3. Most transmissions were suspected to have occurred through sexual contact, for example, in 95% of the patients, and the median number of sex partners in the previous three months was four partners. Twenty-eight percent of persons reported recent travel abroad, 20% had attended large gatherings, 32% of persons had visited sex-on-site venues, and 20% reported engaging in *chemsex*—or sex associated with methamphetamine or other drugs. The authors had a clear exposure history on 23 persons and found the median incubation period was seven days, and this had a range of anywhere from 3 to 20 days.
4. Ninety-five percent of the persons with monkeypox presented with a rash, and the majority of people had less than ten lesions. Seventy-three percent had anogenital lesions, and similar to the patients that we’re seeing in our clinic, there was a wide spectrum of skin lesions, including macular, pustular, vesicular, as well as crusted lesions. Now, skin lesions could be present in multiple phases. For example, some patients had both macular and pustular lesions at the same time point. There were 54 persons in this cohort (or 10%) who presented with a single genital ulcer. Now, this is important to note because some of the patients we’re seeing in our clinic, especially those with a single, or very few genital lesions, have been misdiagnosed at other health care facilities.
5. The authors found the involvement of the anorectal mucosa was reported as the initial presenting symptom in 61 persons (or 12%) in their cohort, and this was associated with anorectal pain, proctitis, tenesmus, and/or diarrhea. Some patients did have oropharyngeal symptoms, and this included pharyngitis, odynophagia, epiglottitis, and oral or tonsillar lesions. Some patients did have systemic symptoms, which is what we’re seeing in our clinic as well, and the common systemic symptoms included fever, lethargy, myalgia, headache, and lymphadenopathy.
6. Overall, 70 persons (or 13%) were hospitalized for several reasons. Now, this included pain management, especially anorectal pain; soft tissue superinfection; pharyngitis, which was limiting oral intake; eye lesions; acute kidney injury; and—I haven’t seen this yet—but two patients in that cohort had myocarditis. A few patients were admitted for infection control, and that’s for those patients who could not isolate from others. Thankfully, no deaths were reported in this manuscript.
7. The authors did not find that the clinical presentation differed among persons with and without HIV infection.
8. And this is one of the few reports I have found documenting information on treatment. The authors

had 12 persons who received cidofovir and eight that received tecovirimat; one person received vaccinia immune globulin.
9. Now, 29% of persons that were tested were found to have another STI [sexually transmitted infection] at the same time as being diagnosed with monkeypox infection. There were also three new cases of HIV infection that were identified.
10. In persons with data on follow-up PCR testing, the latest time point at which a lesion remained PCR-positive was 21 days after symptom onset.
11. In their cohort, 49 patients, or 9%, reported having previously received a smallpox vaccination.

So overall, this is one of the largest case series I've seen published on monkeypox infection. Sexual activity was the most frequently suspected route of transmission. Common reasons for admission were severe pain and bacterial superinfection. Serious complications did occur, such as myocarditis and epiglottitis that were observed in this cohort of individuals, but these were very rare, and no deaths were reported. Patients with monkeypox infection are at risk of other STIs, so testing for STIs and HIV as well as administering empiric treatment when appropriate is an important part of the care and management of these patients. I encourage you to take a look at this article if you're interested in learning more, as there are some great pictures that I found helpful for future patient care.

[06:25] Paper #2

Patel A, Bilinska J, Tam JCH, et al. Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: Descriptive case series. BMJ. 2022 Jul 28;378:e072410. **[PubMed Abstract]**

The next article to discuss was published in *The BMJ* [*British Medical Journal*] in July of 2022 by Dr. Patel and colleagues. It is titled "Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: Descriptive case series."

1. This was a retrospective observational analysis of 197 people with confirmed monkeypox infection, and these persons were evaluated at a single site in south London that manages high-consequence infectious diseases. They were all evaluated between May and July of 2022. Seventy-nine percent of the participants had initially presented to affiliated sexual health and HIV clinics, 12% had presented to the emergency department, and 9% had previously been admitted to the hospital.
2. All participants were men, and the median age was 38 years; 196 of the 197 men identified as gay, bisexual, or other men who have sex with men; 41 participants (or 27%) reported a known close contact with someone who had suspected or confirmed monkeypox infection.
3. Now, *all* patients presented with mucocutaneous lesions, and the lesions were most commonly presented on the genitals or in the perianal area. The median number of lesions at presentation was five, and the interquartile range for this was 3 to 11; eight participants had more than 100 lesions, and 22 participants presented with just a solitary lesion. Twenty-seven participants (or 14%) described mucocutaneous manifestations as pruritic, and another 27 reported a widespread maculopapular rash. We've seen this in our clinic with a few patients who reported rectal itching as the presenting symptom and other patients who present with a widespread rash that looks very similar to secondary syphilis.
4. Thirty-six percent of participants reported rectal pain or pain with defecation. And 17% reported sore throat, and another 16% had penile edema. The majority of participants (or 86%) reported systemic symptoms, and most common were fever, lymphadenopathy, and myalgia.
5. The authors found a variable temporal association between mucocutaneous lesions and the systemic features. So, for example, while 62% developed systemic symptoms before the onset of lesions, 39% developed these symptoms after the onset of lesions. There were another 14% of participants who presented with mucocutaneous lesions who did not have any systemic symptoms.
6. In their cohort, 35% of participants were persons with HIV, and 91% of persons with HIV were receiving antiretroviral therapy; 79% had an undetectable HIV viral load, and the median CD4 count

was 664 [cells/mm3].
7. Thirty-two percent of their participants also had another STI at the time of diagnosis, and these included gonorrhea, chlamydia, HSV [herpes simplex virus]-1 or -2, and/or syphilis.
8. They did have some patients that were admitted to the hospital for a clinical indication, and this included 20 participants (or 10%) of their cohort. The reasons for admissions to the hospital were primarily due to rectal pain and penile swelling. Of the 20 participants that were admitted to the hospital, 15 of them (or 75%) were persons with HIV. Other complications included perianal or groin abscesses, tonsillar abscesses, eye involvement, urinary retention, a superimposed bacterial lower respiratory tract infection, as well as disseminated lesions.
9. There were no deaths reported in this article, as well, and the median length of stay in the hospital was eight days with an interquartile range of three to about ten days.
10. The authors describe several clinical manifestations of monkeypox infection that have *not* been commonly reported—but we have seen these clinical manifestations in our clinic, and I've heard the same from colleagues in the field. These manifestations include penile edema, some of which are quite significant. This includes paraphimosis or phimosis, secondary bacterial infections, rectal perforation, perianal abscesses, as well as other abscesses and confluent lesions. But these case presentations are rare, and it seems that the majority of patients do not have these complications, which is reassuring.

In summary, this article describes the characteristics and clinical features of monkeypox infection in 197 people. There are important differences in clinical manifestations in this current outbreak that providers should be aware of. It is reassuring that the majority of patients do fine, and the main presenting symptom is a rash or a mucocutaneous lesion. But there does seem to be a wide spectrum of clinical manifestations, and some patients, unfortunately, do get severe disease, which is important for a health care provider to recognize. Penile swelling and rectal pain were the most frequent indications for hospital admission, but the severity of symptoms did not always correlate with a high lesion burden. A portion of individuals tested positive for another STI, indicating the importance of keeping a wide differential diagnosis to ensure prompt diagnosis as well as treatment of coinfections. Thankfully, there were no deaths from this infection in this series as well.

[11:53] Paper #3

Peiró-Mestres A, Fuertes I, Camprubí-Ferrer D, et al. Hospital Clinic de Barcelona Monkeypox Study Group. Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022. Euro Surveill. 2022 Jul;27(28):2200503. **[PubMed Abstract]**

Ferré VM, Bachelard A, Zaidi M, et al. Detection of monkeypox virus in anorectal swabs from asymptomatic men who have sex with men in a sexually transmitted infection screening program in Paris, France. Ann Intern Med. 2022 Aug 16. **[PubMed Abstract]**

So what has been published on monkeypox viral shedding thus far? This leads me to a third article to discuss, which is titled "Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022" by Dr. Peiro-Mestres and colleagues. It was published in *Eurosurveillance* in July of 2022.

1. This is a small study of viral shedding in 12 patients with confirmed monkeypox infection. They collected saliva, rectal, and nasopharyngeal swabs; semen, urine, and fecal specimens.
2. All patients were young adult MSM [men who have sex with men]. Three patients had another STI at the time of diagnosis. Four were persons with HIV, and all persons with HIV had an undetectable HIV viral load and CD4 T-cell counts between 400 and 860. Four patients reported a history of smallpox vaccination.
3. The authors found that monkeypox DNA was detected in the swabs of skin lesions in all 12 cases. In

nine of these cases, high viral loads were observed with quantification cycle value ranges in 16 to 21.
4. They also found that monkeypox virus was detected in saliva from all 12 patients. Eleven patients had positive rectal swabs, ten patients had positive nasopharyngeal swabs, nine patients had positive urine samples, and eight patients had positive fecal specimens. There were nine patients who had semen that was tested for monkeypox virus, and seven were positive.
5. When follow-up samples were taken, monkeypox DNA was detected in several follow-up samples taken between 4 and 16 days post symptom onset. For example, one patient was positive in saliva, rectal, and nasopharyngeal swabs; semen, urine, and feces specimens at 16 days since symptom onset.

So this is a small study but one of the first few I've seen detailing shedding of monkeypox virus. It suggests shedding of monkeypox virus at non-lesional sites is possible. Now, actual culture of the monkeypox virus was not obtained in this study, so it's unclear if these are active virions and if the shedding data is associated with transmission of the virus. If you're interested in learning more about viral shedding, including asymptomatic shedding, a brief research report was published in the *Annals of Internal Medicine* in August of 2022, and it was titled "Detection of monkeypox virus in anorectal swabs from asymptomatic men who have sex with men in a sexually transmitted infection screening program in Paris, France." Now, whether viral shedding in asymptomatic persons can lead to transmission is still unknown.

[14:39] Summary

To conclude, I'd like to summarize some key points from this session:

1. Case series of monkeypox infections suggest most transmissions occur through sexual contact. The median incubation period is seven days. The majority of patients present with a rash, and there's a wide spectrum of skin lesions.
2. Involvement of the anogenital mucosa is common, and some patients have systemic symptoms either before or after the onset of lesions.
3. No deaths were reported in this case series. Severe complications can occur, but the majority of patients do not have severe disease.
4. Patients may be at risk for other STIs or HIV, so testing for other infections and empirically treating when appropriate is helpful for the care and management of patients.
5. Shedding of viral DNA can occur at non-lesional sites. Whether this is a factor in transmission of the virus remains to be determined.

[15:32] Credits

This podcast is brought to you by the National STD Curriculum, the University of Washington STD Prevention Training Center, and is funded by the Centers for Disease Control and Prevention.

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