

## OPEN

# Current Evidence Demonstrates That Monkeypox Is a Sexually Transmitted Infection

Lao-Tzu Allan-Blitz, MD\* and Jeffrey D. Klausner, MD, MPH†

The rapidly developing global outbreak of monkeypox, declared a Public Health Emergency of International Concern by the World Health Organization,<sup>1</sup> has demonstrated transmission dynamics uncharacteristic of prior outbreaks. Historically, outbreaks of monkeypox have been short-lived, mostly limited to already endemic tropical rainforest regions, with infections transmitted through predominantly animal-to-human contact, as well as human-to-human transmission via close contact with an infected individual.<sup>2</sup> Over the past several months, however, the current outbreak of monkeypox has spread more rapidly and pervasively than any previous outbreak<sup>1</sup> and with mounting evidence that sexual contact is the most common mode of transmission.<sup>3–6</sup> But whether monkeypox constitutes a sexually transmitted infection, or simply one that is transmissible via sex, and why that distinction is important are subject to ongoing debate.

## WHAT CONSTITUTES A SEXUALLY TRANSMITTED INFECTION?

Sexually transmitted infections are typically defined as being caused by an infectious microorganism that can be transmitted from one person to another through bodily fluids (blood, semen, vaginal fluids, rectal fluid, or saliva) during oral, anal, or vaginal sex with an infected partner.<sup>7</sup> Direct inoculation via skin-to-skin contact during sex is another mode of transmission common to other sexually transmitted infections such as herpes simplex virus type 2.<sup>8</sup> Furthermore, the World Health Organization identifies 30 pathogens that are *transmissible* through sex but reserves the label of sexually transmitted infection for those that are predominantly transmitted through sex.<sup>9</sup> But does monkeypox virus meet the aforementioned criteria for a sexually transmitted infection?

First, the evidence that monkeypox virus is transmissible during sexual activity is numerous. Monkeypox viral DNA has been identified in seminal fluid,<sup>4,10,11</sup> rectal swab specimens,<sup>10</sup> tests of

respiratory secretions,<sup>2,10,12</sup> and blood.<sup>12</sup> Furthermore, a recent study isolated monkeypox virus from the semen of an infected individual and demonstrated infectiveness of that virus *in vitro*.<sup>11</sup> Thus, bodily fluids, in particular semen, may transmit monkeypox virus. In addition, direct inoculation by skin-to-skin contact during sex may explain the numerous reports documenting index lesions occurring at the genitalia, rectum, and oropharynx<sup>4–6,13,14</sup> before subsequent clinical dissemination.

Whether or not sexual contact is the predominant mode of transmission is more challenging to establish. From reports during the current monkeypox outbreak, 84% to 100% of cases have endorsed sexual activity, often with a new sex partner, before the development of monkeypox, providing evidence of a temporal association between sexual contact and the disease.<sup>3–6,10,14–16</sup> Furthermore, practices conferring elevated risk for other sexually transmitted infections are frequently reported among cases of monkeypox; such practices have included attending sex-on-site venues, group sex, multiple recent sex partners, and condomless receptive anal intercourse.<sup>3,4,6,10,15</sup> In addition, there seems to be an anatomic association between sexual practices and the location of lesion development. One series reported that the risk of proctitis due to monkeypox was 5.5 times higher among those who recently engaged in receptive anal intercourse compared with those who did not engage in receptive anal intercourse, and that 95% of patients who presented with tonsilitis reported receptive oral sex in the preceding days.<sup>6</sup> Finally, such transmission dynamics would further explain the vastly disproportionate burden of disease among gay, bisexual, and other men who have sex with men who constitute 92% to 100% of the currently reported monkeypox cases,<sup>3,4,6,14</sup> as well as the high prevalence of concurrent sexually transmitted infections (17%–29%) among the patients with monkeypox.<sup>4,6,10</sup>

Taken in context, the temporal and anatomic association with various sex practices, the high prevalence of sexual risk behavior among patients with monkeypox, and the *in vitro* infectiousness of monkeypox virus isolated from semen strongly suggest that monkeypox can be and is predominantly transmitted through sexual activities. Indeed, one report concluded that all secondary cases of monkeypox were likely due to sexual transmission—that conclusion was based on anogenital and perineal localization of the rash in 72% of cases, associated inguinal lymphadenopathy in 72% of cases, and frequent report of sexual activity including condomless anal intercourse and sex with multiple partners within the preceding 3 weeks among 84% of cases.<sup>15</sup> Another report of more than 500 cases globally similarly noted that the clinicians seeing patients suspected sexual transmission in 95% of cases,<sup>4</sup> although the specifics on how that determination was made were unavailable. Further supporting the nearly exclusive sexual spread of infection in the current outbreak is the infrequency of reported household transmission of monkeypox (1%–3%).<sup>4,6</sup>

Worth highlighting; however, the recent findings are predominantly derived from the United States and Europe. The role of sexual transmission among cases in Africa is less clear. An unpublished report of cases of monkeypox presenting to a hospital in the Democratic Republic of the Congo between 2007 and 2011

From the \*Brigham and Women's Hospital, Boston, MA; and †Keck School of Medicine, University of Southern California, Los Angeles, CA

Conflict of Interest and Sources of Funding: L.-T.A.-B. served as a consultant for Curative Inc., J.D.K. has received consulting fees from Curative Inc.

Correspondence: Lao-Tzu Allan-Blitz, MD, Department of Medicine, Brigham and Women's Hospital, 75 Francis St., Boston, MA 02115. E-mail: lallan-blitz@partners.org; Jeffrey D. Klausner, MD, MPH, Department of Population and Public Health Sciences, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033. E-mail: jdklausner@med.usc.edu.

Received for publication August 12, 2022, and accepted September 8, 2022. DOI: 10.1097/OLQ.0000000000001705

Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Sexually Transmitted Diseases Association. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

identified exposure to wild animals and handling of uncooked meat as the primary source of exposure for the majority of cases.<sup>17</sup> Data from cases of monkeypox in Nigeria from 2017 to 2018 noted that the rash localized to the genitalia in 47% to 68% of cases.<sup>18–20</sup> Sexual risk factors were not explored in those studies, but the authors speculated on the possibility of sexual transmission. Finally, a report from the current outbreak in peer review documented 6 linked cases of sexual transmission in Nigeria.<sup>16</sup> The data on the transmission dynamics of monkeypox virus within Africa during the current outbreak, however, remain limited. Thus, the actual proportion of cases being transmitted globally via sexual contact is unknown.

### WHY DOES IT MATTER?

The ramifications of classifying monkeypox as a sexually transmitted infection instead of an infection that is *transmissible* via sex are important to acknowledge. On the one hand, the stigma surrounding sexually transmitted infections limits health care seeking and partner-notification behaviors,<sup>21,22</sup> directly subverting our primary means of outbreak control—namely, early identification and behavior change in infected individuals. Furthermore, such stigma can fuel homophobia, particularly in areas without human rights protections for individuals who engage in same-sex relationships.<sup>23</sup> Conversely, failure to appropriately identify and disseminate to the public the predominant mode of transmission will likely perpetuate behaviors that are driving transmission. Identifying high-risk subpopulations, in this case gay, bisexual or other men who have sex with men, who have multiple partners, or who participate in group sex will facilitate targeted awareness and education efforts, exposure reduction, and other disease intervention activities such as testing, treatment, and vaccination, which in turn may augment control efforts and prove to be cost effective. Such efforts are analogous to what was eventually implemented in combating the human immunodeficiency virus pandemic with notable success.<sup>24</sup>

Furthermore, the current guidelines recommend isolation of individuals infected with monkeypox virus until complete resolution of symptoms and healing of the rash, which can last for up to 4 weeks.<sup>25</sup> We have already observed the numerous socioeconomic consequences of 14 days of isolation recommended during the SARS-CoV-2 pandemic in the form of lost productivity, missed school days, and disruptions in supply chain and agriculture production.<sup>26</sup> If monkeypox is in fact predominantly transmitted through sex, which the evidence suggests that it is, that prolonged duration of isolation and thus the consequent socioeconomic burdens may be unnecessary.

But monkeypox is not exclusively transmitted through sexual contact.<sup>2</sup> A related poxvirus, molluscum contagiosum, has similar transmission characteristics, which can be transmitted via skin-to-skin contact and sexual contact.<sup>27</sup> Human herpes simplex viruses similarly can be transmitted via close contact and through contact with bodily fluids during sex.<sup>8</sup> Similarly, *Treponema pallidum*, the cause of syphilis, is predominantly transmitted through sexual contact,<sup>28</sup> yet historical reports before the routine use of protective gloves frequently noted syphilitic lesions on the fingers of physicians acquired via nonsexual skin-to-skin contact,<sup>29,30</sup> and via human bites.<sup>31</sup> Thus, universality of sexual transmission is not a requisite of sexually transmitted infections.

### CONCLUSIONS

The transmission dynamics of monkeypox in the current outbreak are highly consistent with a sexually transmitted infection. We must therefore, incorporate a sexual health framework into our response to the current outbreak while destigmatizing both the disease and its route of transmission. Targeted screening among pop-

ulations with high risk for other sexually transmitted infections may be important strategies for case identification. Finally, further work should evaluate formally the transmissibility of monkeypox from different bodily fluids through experimental studies and careful epidemiologic analyses with particular attention to the possibility of differing transmission dynamics in different regions of the globe.

### REFERENCES

- World Health Organization. Second Meeting of the International Health Regulations (IHR) Emergency Committee Regarding the Multi-Country Outbreak of Monkeypox—23 July 2022. Available at: [https://www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-\(2005\)-\(ihr\)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox](https://www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox). Accessed August 28, 2022.
- Titanji B, Tegomoh B, Nematollahi S, et al. Monkeypox: A contemporary review for healthcare professionals. *Open Forum Infect Dis* 2022; 9:ofac310.
- Philpott D, Hughes CM, Alroy KA, et al. Epidemiologic and clinical characteristics of monkeypox cases—United States, May 17–July 22, 2022. *MMWR Morb Mortal Wkly Rep* 2022; 71:1018–1022.
- Thornhill JP, Barkati S, Walmsley S, et al. Monkeypox virus infection in humans across 16 countries—April–June 2022. *N Engl J Med* 2022; 387:679–691.
- Antinori A, Mazzotta V, Vita S, et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. *Euro Surveill* 2022; 27:2200421.
- Tarin-Vicente EJ, Alemany A, Agud-Dios M, et al. Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain: A prospective observational cohort study. *Lancet* 2022; 400:661–669.
- National Institutes of Health: National Cancer Institute. Sexually Transmitted Infection. Available at: <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/sexually-transmitted-infection>. Accessed August 10, 2022.
- Jaishankar D, Shukla D. Genital herpes: Insights into sexually transmitted infectious disease. *Microb Cell* 2016; 3:438–450.
- World Health Organization. Sexually Transmitted Infections (STIs). Last Updated November 22, 2021. Available at: [https://www.who.int/en/news-room/fact-sheets/detail/sexually-transmitted-infections-\(stis\)](https://www.who.int/en/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis)). Accessed August 28, 2022.
- Peiro-Mestres A, Fuertes I, Campubi-Ferrer D, et al. 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; 27:2200503.
- Lapa D, Carletti F, Mazzotta V, et al. Monkeypox virus isolation from a semen sample collected in the early phase of infection in a patient with prolonged seminal viral shedding. *Lancet Infect Dis* 2022; 22:1267–1269.
- Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox: A retrospective observational study in the UK. *Lancet Infect Dis* 2022; 22:1153–1162.
- Patrocinio-Jesus R, Peruzzi F. Monkeypox genital lesions. *N Engl J Med* 2022; 387:66.
- Girometti N, Byrne R, Bracchi M, et al. Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: An observational analysis. *Lancet Infect Dis* 2022; 22:1321–1328.
- Inigo Martinez J, Gil Montalban E, Jimenez Bueno S, et al. Monkeypox outbreak predominantly affecting men who have sex with men, Madrid, Spain, 26 April to 16 June 2022. *Euro Surveill* 2022; 27:2200471.
- Ogoina D, James IH. Monkeypox among linked heterosexual casual partners in Bayelsa, Nigeria. *Qeios*. August 22, 2022. Available at: <https://www.qeios.com/read/2Z4ZH4.2> Accessed August 30, 2022.
- Pittman PR, Martin JW, Kingebeni PM, et al. Clinical characterization of human monkeypox infections in the Democratic Republic of the Congo. *medRxiv* 2022. doi:10.1101/2022.05.26.22273379.
- Yinka-Ogunleye A, Aruna O, Dalhat M, et al. Outbreak of human monkeypox in Nigeria in 2017–18: A clinical and epidemiological report. *Lancet Infect Dis* 2019; 19:872–879.
- Ogoina D, Iroezindu M, James HI, et al. Clinical course and outcome of human monkeypox in Nigeria. *Clin Infect Dis* 2020; 71:e210–e214.

20. Ogoina D, Izibewule JH, Ogunleye A, et al. The 2017 human monkeypox outbreak in Nigeria—Report of outbreak experience and response in the Niger Delta University Teaching Hospital, Bayelsa State, Nigeria. *PLoS One* 2019; 14:e0214229.
21. Morris JL, Lippman SA, Philip S, et al. Sexually transmitted infection related stigma and shame among African American male youth: Implications for testing practices, partner notification, and treatment. *AIDS Patient Care STDS* 2014; 28:499–506.
22. Fortenberry JD, McFarlane M, Bleakley A, et al. Relationships of stigma and shame to gonorrhea and HIV screening. *Am J Public Health* 2002; 92:378–381.
23. Hagopian A, Rao D, Katz A, et al. Anti-homosexual legislation and HIV-related stigma in African nations: What has been the role of PEPFAR? *Glob Health Action* 2017; 10:1306391.
24. Sullivan PS, Carballo-Dieguez A, Coates T, et al. Successes and challenges of HIV prevention in men who have sex with men. *Lancet* 2012; 380:388–399.
25. Centers for Disease Control and Prevention. Isolation and Prevention Practices for People with Monkeypox. Updated August 2, 2022. Available at: <https://www.cdc.gov/poxvirus/monkeypox/clinicians/isolation-procedures.html>. Accessed August 12, 2022.
26. World Bank. *Global Economic Prospects*, June 2020. Washington, DC: World Bank. © World Bank, 2020. License: CC BY 3.0 IGO. Available at: <https://openknowledge.worldbank.org/handle/10986/33748>. Accessed August 12, 2022.
27. Meza-Romero R, Navarrete-Dechent C, Downey C. Molluscum contagiosum: An update and review of new perspectives in etiology, diagnosis, and treatment. *Clin Cosmet Investig Dermatol* 2019; 12: 373–381.
28. Stoltey JE, Cohen SE. Syphilis transmission: A review of the current evidence. *Sex Health* 2015; 12:103–109.
29. Epstein E. Extragenital syphilis in physicians. *Calif Med* 1952; 77: 149–150.
30. Meyer GS. Occupational infection in health care. The century-old lessons from syphilis. *Arch Intern Med* 1993; 153:2439–2447.
31. Fanfair RN, Wallingford M, Long LL, et al. Acquired macrolide-resistant *Treponema pallidum* after a human bite. *Sex Transm Dis* 2014; 41: 493–495.