

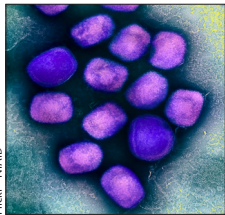


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Does it matter who is spreading monkeypox?



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Recently, many cases of monkeypox were reported worldwide. Although most of these cases seem to be associated with the community of men who have sex with men (MSM), not all of them are.¹ Cases with west and central African monkeypox virus clades have been rising in the past 20 years.² The current spread, due to the less transmissible and less virulent west African clade, was unexpected because observations on earlier outbreaks, mostly in African villages,³ indicated that monkeypox outbreaks are self-limiting. In technical terms, the basic reproduction number (R_0) was less than 1. R_0 is the average number of secondary cases produced by a single case during the whole infectious period in a community without immunity and without interventions. The low transmissibility, obviously, must have changed during this current emergence of cases. Whether this change was due to mutations in the virus or due to a different type and frequency of contacts is interesting, but not necessarily relevant when contemplating how to stop the outbreak. The main question simply is how to reduce the average number of secondary cases per infected person to below 1. In this context, it also does not matter whether the infection mainly spreads within an MSM community or finds its way into other groups of the population. We can only speculate about the current value of R_0 for monkeypox.

Monkeypox used to be far less transmissible than smallpox, the R_0 of which lay between 3.5 and 6.⁴ The R_0 has not been estimated for the west African monkeypox clade,⁵ but the effective reproduction number (the average number of secondary cases per infectious case in a population made up of both susceptible and non-susceptible hosts) of a more transmissible clade in the Congo Basin was estimated to be about 0.3, while its R_0 was estimated to be between 1.46 and 2.67.⁴ New estimates are urgently needed, particularly because these estimates date back to a time when smallpox vaccination coverage was high, which might have led to an underestimation of the R_0 . Using $R_0=3$ for monkeypox might still be considered a very large (highly pessimistic) value. As with smallpox, individuals who are infected take rather long to develop symptoms and they have—compared with influenza or SARS-CoV-2—a rather long infectious period.⁶ Therefore, the average generation time of monkeypox is rather long (about 20 days).⁶ This

renders monkeypox highly vulnerable to interventions: even with $R_0=3$, it takes months until a few thousand cases occur. With the raised awareness, cases will be detected much quicker now than in the beginning of the outbreak. Even if it takes 1 week from onset of symptoms to detect and isolate cases, the contagious period (15–27 days after the onset of rash) is reduced by over 50%. If the infection is not predominantly passed on during the prodrome or early enanthem periods, the assumed reproduction number of 3 drops to less than 1.5. The standard practice of most public health systems is to initiate contact tracing for all confirmed cases. As the latent period of monkeypox is long (7–17 days),⁶ cases among known contacts can be contacted before they spread the infection. They can either be quarantined or, at least, they will be aware of the infection as soon as they develop first symptoms. Importantly, unlike for SARS-CoV-2, there seems to be no evidence of asymptomatic *Orthopoxvirus* infections in humans, or at least this is believed to be true for smallpox;⁵ studies for monkeypox are still ongoing. Because oropharyngeal lesions are necessary for airborne transmission and skin rash is required for transmission by physical contact, it is plausible that at least some symptoms must be present before the infection can be passed on. Therefore, awareness or quarantine of contacts should further reduce the spread of infection considerably, bringing the remaining reproduction number close to or below 1. Data from the 1980s suggest that smallpox vaccination provided 85% protection against monkeypox.⁶ In the 1970s, smallpox vaccination programmes were starting to be discontinued and, by 1984, all countries had ceased vaccinating the general public against smallpox.⁷ Studies suggest high seropositivity of *Orthopoxvirus* antibodies in the smallpox-vaccinated population.⁸ This further reduces the effective reproduction number of monkeypox. Using the newly available monkeypox vaccines, post-exposure vaccination of known contacts—or more generally the social environment of cases (this was termed ring vaccination⁹)—can even protect people who have already been infected if applied soon after infection.¹⁰ Additionally, increased awareness might lead to earlier detection of new cases, and the prophylactic vaccination of risk groups and of individuals who are immunocompromised can also be considered.

We declare no competing interests.

*Kristan A Schneider, Martin Eichner

kristan.schneider@hs-mittweida.de

Department of Applied Computer Sciences and Biosciences, Hochschule Mittweida, Mittweida 09648, Germany (KAS); Institute for Clinical Epidemiology and Applied Biometrics, University of Tübingen, Tübingen, Germany (ME); Epimos, Bischofsheim in der Rhön, Germany (ME)

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Monkeypox virus isolation from a semen sample collected in the early phase of infection in a patient with prolonged seminal viral shedding



The unexpected increase in human monkeypox cases in non-endemic countries that began in May, 2022, is raising concerns of a novel global infectious threat. Since the first human case in 1970 in the Democratic Republic of the Congo, the virus has become endemic in several countries in central and western Africa.¹ Imported cases have been sporadically reported outside Africa (in England, the USA, Singapore, and Israel), with the majority of cases associated with travellers returning from endemic countries, or due to nosocomial contact or contact with infected imported rodents.^{2,3} As of July 22, 2022, 16 016 laboratory-confirmed monkeypox cases have been reported from 75 countries worldwide, and the WHO Director-General has declared the escalating global monkeypox outbreak to be a public health emergency of international concern.⁴ The vast majority of cases have been reported in Europe and other non-endemic countries, mostly diagnosed in young men, self-identifying as men who have sex with men (MSM). Monkeypox virus transmission might occur through close contact of mucosa or non-intact skin with infectious material, or large respiratory droplets during prolonged face-to-face contact.⁵ Whether monkeypox virus can be sexually transmitted via genital fluids remains under investigation. Monkeypox virus transmission during sexual intercourse has been documented in the UK in two men with no travel history

to endemic countries and evidenced by the temporal association of symptoms with sexual contact and the location of primary lesion sites matching those of sexual contact.⁶ Viral DNA detection in semen samples has been reported in three cases in Italy and subsequently in two patients with monkeypox in Germany.^{7,8} Furthermore, monkeypox DNA was detected in the seminal fluid of 29 (91%) of 32 people affected by monkeypox in a large case series on the 2022 global outbreak.⁹ However, to date, no evidence is available on the infectiousness of monkeypox virus in semen. Therefore, we investigated viral shedding in longitudinal semen samples collected 5–19 days after symptom onset from one confirmed monkeypox virus case diagnosed at the National Institute for Infectious Diseases ‘Lazzaro Spallanzani’ (Rome, Italy; appendix p 1).

The patient was a 39-year-old man, who travelled in Austria during the first 2 weeks of May, 2022. He self-identified as an MSM and sex worker and reported condomless sexual intercourse with several male partners during the previous month. The patient was HIV-infected, treated with dolutegravir and lamivudine, with viral suppression and immune recovery, and reported a history of sexually transmitted infections. He was admitted to the hospital 5 days after symptom onset. His symptoms included fever, followed by the appearance of clustered itchy papular lesions in the anal region and

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