

An opportunity seized: rapid clinical research provides insights into monkeypox virus dynamics and durations of infectiousness

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Monkeypox (mpox) is not a new disease, having first been detected in humans in the Democratic Republic of the Congo over fifty years ago. Clinicians and scientists in countries in West and Central Africa have previously reported the course of disease and virological findings from a number of clade I and clade II monkeypox virus (MPXV) outbreaks.¹⁻³ However, the unprecedented international outbreaks in 2022, caused by clade IIb MPXV and driven by human-to-human transmission, have provided additional opportunities to describe clinical manifestations and investigate viral dynamics in individuals with MPOX.

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24 In the Lancet Infectious Diseases, Suñer and colleagues⁴ report their study of 74
25 outpatients with mpox during Spain's 2022 clade IIb MPXV outbreak that has mostly
26 affected gay, bisexual, and other men who have sex with men. Participants provided
27 a variety of sample-types at six time points up to two months from enrolment. The
28 study showed that the greatest amount of MPXV DNA is found in skin lesion swabs,
29 followed by rectal swabs, whole blood, oropharyngeal swabs, and semen samples.
30 The median durations of detectable MPXV DNA varied across the compartments
31 sampled, from just five days for blood to 25 days for skin lesions.

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33 While DNA detected by PCR can be useful in studying viral shedding, the authors
34 also performed virus isolation on selected samples, which is a better proxy for
35 infectious virus. Virus could not be isolated from any sample-type collected beyond
36 day 15 of illness and only 2% of semen samples had MPXV DNA loads in the range
37 where virus isolation is likely to be successful. While exposure to virus in semen is a
38 potential route of transmission, direct contact with skin or mucosal mpox lesions is a
39 more likely route of transmission during sex.⁵

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41 Some public health agencies recommend a period of self-isolation or avoiding
42 prolonged close contact to reduce onward transmission, and using condoms during
43 and following illness, so average viral shedding data like these will help inform
44 guidance. However, the results from this study are from specific populations infected

with clade IIb MPXV and, therefore, may not be generalisable to all outbreaks or all populations affected by mpox. Severely immunosuppressed patients are one example where infection and infectiousness may be prolonged,⁶ and such patients were rare in this study. Evidence of resolution of mpox signs and symptoms combined with a minimum period since onset (e.g., 15 days) may be an appropriate, practical indicator for ending isolation or resuming contact with others, at least for typical community patients with non-severe clade IIb mpox.

Suñer and colleagues commenced their study while a window of opportunity existed, recruiting sufficient participants before the number of new cases thankfully decreased in the second half of 2022. This epitomises a good outbreak research response and suggests the scientific community is applying lessons learned after 'missing the boat' with previous emerging infection outbreaks.⁷

The greatest burden of mpox, both previously and going forward, is likely to be in African countries with zoonotic reservoirs; several of these countries also experience significant human-to-human transmission during outbreaks.^{2,8} The greatest number of reported cases in 2022 have occurred in non-African countries, but it is likely that many cases of mpox go undetected in parts of West and Central Africa, for multiple reasons.⁹ Therefore, besides providing equitable and fair access to vaccines, treatments, and diagnostics for mpox in Africa, there should be equal opportunities

for people living in African countries to participate in, and benefit from, mpox research.

The 2022 clade IIb outbreaks demonstrate that MPXV can spread globally via international travel, and that it can exploit a transmission niche – such as a socio-sexual network – when it finds one. Meanwhile, outbreaks of clade I and clade II infections continue in Africa. While different mpox outbreaks may be connected, the groups affected, the patterns of disease, the modes of transmission, and the impact on health and wellbeing often vary between countries. This means that research questions may differ between countries, outbreaks, and affected populations, and this needs to be reflected in study designs and research priorities.¹⁰

Future morbidity and mortality from mpox is difficult to predict, but as the virus infects an increasing number of people and enters new populations, future outbreaks of mpox may look different from the outbreaks we see today. Despite the challenges involved and the many competing priorities, it is vital that research efforts continue and intensify, particularly in African countries with recurring outbreaks. A failure of the global community to enable a truly global response to mpox, including research efforts in all affected regions, may prove self-defeating.

[749 words]

Contributors

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102 1. Durski KN, McCollum AM, Nakazawa Y, et al. Emergence of Monkeypox - West
103 and Central Africa, 1970-2017. *MMWR Morb Mortal Wkly Rep* 2018; 67(10): 306-10.

104 2. Yinka-Ogunleye A, Aruna O, Dalhat M, et al. Outbreak of human monkeypox
105 in Nigeria in 2017-18: a clinical and epidemiological report. *The Lancet Infectious*
106 *diseases* 2019.

107 3. Pittman PR, Martin JW, Kingebeni PM, et al. Clinical characterization of human
108 monkeypox infections in the Democratic Republic of the Congo. *medRxiv* 2022:
109 2022.05.26.22273379.

- 110 4. Suñer C UM, Tarin-Vicente EJ, et al. Viral dynamics in patients with monkeypox
111 infection: a prospective cohort study in Spain. *The Lancet Infectious diseases* 2022; In
112 Press.
- 113 5. Tarin-Vicente EJ, Alemany A, Agud-Dios M, et al. Clinical presentation and
114 virological assessment of confirmed human monkeypox virus cases in Spain: a
115 prospective observational cohort study. *Lancet* 2022; 400(10353): 661-9.
- 116 6. Miller MJ, Cash-Goldwasser S, Marx GE, et al. Severe Monkeypox in
117 Hospitalized Patients - United States, August 10-October 10, 2022. *MMWR Morb*
118 *Mortal Wkly Rep* 2022; 71(44): 1412-7.
- 119 7. Sigfrid L, Maskell K, Bannister PG, et al. Addressing challenges for clinical
120 research responses to emerging epidemics and pandemics: a scoping review. *BMC*
121 *medicine* 2020; 18(1): 190.
- 122 8. Beer EM, Rao VB. A systematic review of the epidemiology of human
123 monkeypox outbreaks and implications for outbreak strategy. *PLoS Negl Trop Dis*
124 2019; 13(10): e0007791.
- 125 9. Nakoune E, Olliaro P. Waking up to monkeypox. *Bmj* 2022; 377: o1321.
- 126 10. Rojek A, Dunning J, Olliaro P. Monkeypox: how will we know if the treatments
127 work? *The Lancet Infectious diseases* 2022; 22(9): 1269-70.

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