



Viewpoint

A viewpoint: The 2022 monkeypox outbreak

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1. Introduction

Since early May 2022 an unprecedented outbreak of monkeypox has been documented globally, with the first cases initially described in the United Kingdom and soon after in other countries of Western Europe, as well as North and South America, the Middle East and North Africa and Australia.¹

The monkeypox (MPX) virus is an orthopoxvirus of the Poxviridae family, that causes a viral zoonotic disease, similar to other orthopoxvirus, in particular smallpox, although less severe.² Two clades of this virus exist, the West African and Central African ones, named after their geographic distribution, both causing a similar clinical syndrome but with different degrees of severity, with the Central African variant being associated with an up to three times higher mortality.³

Following the eradication of smallpox there are ongoing outbreaks documented as early as the 1980s, with Nigeria and the Democratic Republic of Congo (DRC) being the countries with the majority of documented cases, and ongoing outbreaks in both.⁴ The first human case was documented in 1970 in the DRC.⁵ Outside of Africa, all diagnosed cases have been directly linked to travel to Africa with the exception of the 2003 outbreak in the USA, whose origin was traced to the import of infected prairie dogs.^{6,7}

Transmission classically happens in the context of close contact with skin/mucosal lesions,⁸ body fluids (blood, urine), respiratory droplets and contaminated materials (clothing, bedding, towels).^{8,9} The incubation period ranges from 5 to 21 days, with the majority of cases developing symptoms 6–13 days after the first contact.⁸ Different potential reservoirs have been identified but the full sylvatic cycle is not yet completely understood.⁹

Monkeypox generally causes a self-limited febrile rash of limited

severity.¹⁰ The current case definition includes the following symptoms seen in association with an unexplained acute rash: headache, acute onset of fever, lymphadenopathy, myalgia, back pain and asthenia.¹¹ Disease progression can be more severe in specific risk groups such as children, pregnant women or persons with immune suppression due to other health conditions.^{12–14} Diagnosis is confirmed by a two-stage testing, initially with a pan-orthopox polymerase chain reaction (PCR) followed by a specific monkeypox PCR test.¹

2. The current outbreak

This is an unprecedented, multi-national outbreak which is affecting non-endemic countries with simultaneous chains of transmission reported without known epidemiological links to West or Central Africa. Phylogenetic analyses of the whole genome sequences from a number of countries during the current outbreak suggest that circulating viruses are closely related to each other and to previous MPX infections described in West Africa, and in travellers from that region.^{1,15} Further ongoing collection and analysis of the full viral genome sequences will be important to understand whether these have originated from multiple introductions or have been circulating but undetected outside of 'endemic' areas.

Another feature that makes this outbreak atypical is the fact that the vast majority of documented cases have been in gay, bisexual or other men that have sex with men (MSM). According to the most recent update, a total 1882 cases have been diagnosed.¹

The clinical spectrum documented so far points towards a milder form of the illness than the one in documented cases in Africa, with a more subtle and variable rash, often involving the ano-genital regions and not always associated with the systemic symptoms classically

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associated with MPX.¹⁵ Deaths have not been reported outside endemic areas.^{7,12}

It is presently unclear why a rare, although emerging pathogen, is currently associated with such an atypical outbreak. The following questions remain unanswered: (i) why now, (ii) how did this new chain of transmission start in Europe, (iii) why are MSM disproportionately affected (iv) and why is the clinical presentation milder?

3. Why now?

It is conceivable that two years of strict lockdowns and enforced social distancing might have induced a generalized lower individual immunity to infectious diseases. A few on-going theories are trying to support this assumption which is nonetheless difficult to prove. Additionally, the role of a waning herd immunity to smallpox may be a major factor in the occurrence of this outbreak. The vast majority of cases described are in men between the ages of 20–59 years.¹⁶ It would not be surprising to see monkeypox filling in the ecological niche left after smallpox eradication in 1980, with the general population becoming increasingly more susceptible to it, with each passing generation that has not been vaccinated.¹⁷

Another more tangible effect that two years of pandemic-related restrictions might have precipitated is that of a heightened need for travelling and social interaction. This would explain, to an extent, why transmission is being seen at this time of the year, when travelling abroad increases and specific international social gatherings take place.¹⁸

4. Why in Europe?

The link between Western Europe and the African countries in which monkeypox is endemic is well known, and the virus at the origin of the current outbreak indeed belongs to the Western African clade.¹ There are reports of previous imported cases into the UK and it is not unreasonable to assume that this outbreak has its origins in a similar situation, but no such link has been established yet. However, whilst Europe might have been the site of introduction(s), established local chains of transmission with no links to Europe have been described in the USA and Canada.¹

5. Why are MSM in the United Kingdom disproportionately affected?

This is perhaps the most important and difficult question to answer, at the risk of stigmatizing an already highly stigmatized group. Although not classically described as a sexually transmissible infection (STI), monkeypox can be transmitted through intimate contact.^{15,19} It is known that there is a viremic period and that the virus can also be detected in semen, although their role in terms of transmission remains unknown.¹⁵ Moreover, it is as yet unknown, whether like some other viruses - e.g, Ebola, Lassa^{20,21} MPX can establish reservoirs in the uro-genital tract with a potential for transmission after the skin and mucosal lesions have healed.

MSM have traditionally been linked with a heightened risk of STI acquisition in the context of a higher number of sexual partners and reduced propensity for safe sex practices in the age of PrEP.²² A number of epidemiological investigations have suggested that individuals engaging in 'high-risk' sexual practices are at risk of virus acquisition.²³

6. Why is the clinical presentation milder?

The MPX causing the current outbreak is the West African clade, which is associated with a lower mortality when compared to the Central African one. Reports from outbreaks in Africa, however, have a higher proportion of cases among more vulnerable populations (children and pregnant women in particular) and other confounding factors

like nutritional state and poorer health care access which might influence presentation and disease progression in these settings.²⁴

The hypothesis of a viral mutation causing increased infectivity at the cost of symptom severity (similarly to what has been seen with SARS-CoV2) seems unlikely as DNA viruses are less error prone in terms of replication and the fact that no new mutations have so far been identified.¹ However, mutation analyses will be crucial for the understanding of the impact of the currently circulating and future strains in terms of their propensity for transmission, clinical disease, response to antiviral treatment and use of vaccine as pre- and post-exposure prophylaxis.²³

7. The future

It is difficult to predict exactly what the outcome of this outbreak will be as there are still too many unanswered questions. However, the fact that it is caused by a pathogen not exceedingly prone to mutations that seemingly requires intimate physical contact for its transmission and the availability of an effective vaccine both point towards the possibility of containing and resolving this outbreak.^{25,26} Careful attention is needed to develop case-finding, contact-tracing, isolation/quarantine to prevent further spread as well as judicious and equitable use of antiviral therapies and vaccination strategies. More importantly as, we move into the 'Summer Festival' season in the northern hemisphere, messaging around creating awareness amongst healthcare professional and communities will be crucial.²⁷ Nonetheless, the risk factors for its recurrence remain and an equitable rollout of smallpox vaccination guidelines would be in order.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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