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## Global human monkeypox outbreak: atypical presentation demanding urgent public health action



Following confirmation of the first case of monkeypox in the UK by the UK Health Security Agency (UKHSA) on May 7, 2022, events have evolved with dizzying rapidity—as of May 21, 2022, 92 laboratory confirmed cases and 28 suspected cases of monkeypox have been reported in 12 non-endemic countries across three WHO regions.<sup>1</sup> Monkeypox is a rare viral illness that is seldom detected outside of Africa. WHO have projected that more cases of monkeypox will be identified as surveillance expands in non-endemic countries.<sup>1</sup>

Although uncertain, some have expressed concerns that this outbreak of monkeypox could become the next global pandemic. Complicating the situation is the fact that most cases have occurred in men aged 20–50 years who identify as gay or bisexual or have sex with men and do not have recent travel history to monkeypox endemic countries.<sup>1</sup> Additionally, there does not appear to be links between these cases. So far, the number of infections detected outside of Africa since May 7, 2022, has already exceeded the number detected outside of the continent from 1970 to the current outbreak.<sup>2</sup> This unprecedented situation raises the possibility of community spread, with sexual contact being suspected as a factor contributing to transmission.

Monkeypox is a re-emerging zoonotic disease caused by a DNA virus that belongs to the orthopoxvirus genus of the Poxviridae family. Since the first human case of monkeypox was diagnosed in the Democratic Republic of the Congo in 1970, the disease has become endemic in several African countries, including Nigeria, Benin, and Liberia.<sup>2</sup> Monkeypox is closely related to the variola virus (smallpox virus) and results in a smallpox-like disease.<sup>3</sup> Two clades of the monkeypox virus exist: the Congo Basin (central African) clade and the west African clade. Mortality varies between clades, with estimated case fatality rates of 10–6% for the Congo Basin clade and 3–6% for the west African clade.<sup>2</sup>

Monkeypox usually spreads among monkeys, Gambian pouched rats, and squirrels,<sup>4</sup> but occasionally jumps to people, causing small outbreaks. In addition to fever, headache, muscle aches, and lymphadenopathy, infection triggers a distinctive rash that often begins on the face and spreads to other parts of the body,

including the genitals.<sup>5</sup> Monkeypox is generally a mild, self-limiting illness and its established modes of transmission are close contact with infected individuals or contaminated clothes, towels, or furniture and respiratory droplets. The monkeypox virus does not transmit from person to person as readily as SARS-CoV-2 does. However, the current outbreak is exposing gaps in our knowledge of monkeypox.

Promisingly, on May 19, 2022, scientists in Portugal reported the first draft genome sequence of monkeypox virus that had been recently detected in Portugal.<sup>6</sup> Preliminary genetic data suggest that the 2022 monkeypox virus belongs to the west African clade, and is most closely related to monkeypox viruses linked to disease spread from Nigeria to the UK, Israel, and Singapore in 2018 and 2019.<sup>5–7</sup> A monkeypox vaccine (Imvamune or Imvanex) developed by a Danish biotechnology firm (Bavarian Nordic) has been approved by US regulators for both monkeypox and smallpox. Evidence from Africa indicates that smallpox vaccination provides 85% protection against monkeypox infection.<sup>8</sup> The decline in population-level immunity since the cessation of smallpox vaccination in the 1980s contributed to the 2017–20 monkeypox outbreaks in Nigeria.<sup>4</sup> On May 19, 2022, tecovirimat (Tpxx) was approved in the USA, Canada, and Europe for the treatment of human smallpox disease.<sup>9</sup> The European Medicines Agency approval for tecovirimat also includes the treatment of monkeypox.<sup>10</sup>

The unique variation in the epidemiology of human monkeypox during this current outbreak underlines several issues. For example, both the absence of prodromal symptoms, such as fever, malaise, and headache, and the presence of herald skin lesions at the point of sexual contact in some patients are strongly suggestive of sexual transmission. Nonetheless, there are concerns that the media's projection of men who have sex with men as the at-risk population for the outbreak might unduly stigmatise this group. Case definitions of monkeypox disease have been updated to account for possible cases that do not have a history of travel to endemic countries. Similarly, new clinical guidelines are being developed by the UKHSA to address

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For case definitions of monkeypox disease see <https://www.gov.uk/guidance/monkeypox-case-definitions>

important questions, including the use of appropriate personal protective equipment in sexual health clinics and the review of standard operating procedures in laboratories. With several cases of monkeypox now identified in 12 countries, the fear of cross-border transmission is real. Robust public health surveillance and control measures are crucial to address this threat.

We declare no competing interests. AO and BE contributed equally to this Comment.

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