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OPINION

Monkeypox 2022 outbreak: An update

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The recent outbreak of monkeypox virus (MPXV) has now occurred in several countries on almost on continents. Unlike sporadic cases associated with travel to endemic countries, no source of infection has been confirmed to date. As of 13:00 h on 21 May, 92 laboratory-confirmed cases and 28 suspected cases with ongoing investigations have been reported to WHO from three WHO regions (Australia, North America and Europe) with no deaths [1]. Most cases occurred in young men, many of whom identified themselves as men who have sex with men (MSM), with genital lesions suggesting that transmission most likely occurred through close physical contact [2]. The disease background and transmission are puzzling due to the unusually high frequency of human-to-human transmission observed in this outbreak. We must find out and confirm that the virus has not been modified in any way.

MPXV is a double-stranded DNA virus belonging to the genus Orthopoxviruses in the family Poxviridae. It is a sylvatic zoonotic virus transmitted by droplet exposure via exhaled large droplets and by direct contact with infected skin lesions and/or with contagious materials, and it has an incubation period of 6-13 days (range 5-21 days). The natural animal reservoir remains unknown, although it is found among rodents in Africa. Additional known zoonotic reservoirs for MPXV are the Gambian marsupial, tree squirrel, rope squirrel and sooty mangabey monkey, and possibly others [3]. The disease has a similar clinical presentation as smallpox, with maculopapular rash, frequently on the palms and soles [4, 5]. A new specific treatment for monkeypox with Tecovirimat, a VP37 assembly protein inhibitor, has been approved by the European Medical Association (EMA) 2022 and a newer vaccine based on a Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) platform was approved

in 2019 for the prevention of monkeypox. Also, crossimmunity with smallpox vaccination has been shown to be about 85% effective in preventing monkeypox in several observational studies [6]. Given that smallpox was eradicated through concerted vaccination efforts in the late 1970s and vaccines have been phased out over the past four decades [7], the resurgence of monkeypox in Europe and elsewhere may intensify the burden in the world population. The immune-naïve population is also likely to add to the increase of monkeypox incidences due to more sustained person-to-person transmission and novel transmission routes.

The first recognised case of human infection with MPXV was in 1970 in a 9-month-old child admitted to Basankusu Hospital in Equatorial Province, Democratic Republic of the Congo, with suspected smallpox [8, 9]. MPXV genomes (198 kb size) sequenced thus far confirm the existence of two distinct MPXV clades, namely the West and Central African clades, with case fatality rates of 3.6% and 10.6%, respectively [10]. Monkeypox is endemic in both Central Africa (Democratic Republic of Congo, Central African Republic, Republic of Congo, Gabon and Cameroon) and West Africa (Nigeria, Benin, Côte d'Ivoire, Liberia and in Sierra Leone) [1].

The index case of the current outbreak of monkeypox in 2022 was confirmed in a UK resident on 6 May 2022 and was associated with travel to Nigeria. Sequencing of the first isolate from the patient in Portugal [11], collected on 4 May 2022, suggests that MPXV isolates are homologous to those imported into the United Kingdom in 2018–2019 and are genetically related to the Nigerian MPXV genome [12], belonging to the West African clade of monkeypox virus [11]. Other available MPXV genomes from patient isolates

in the United States (Nucleotide sequence NCBI: ON563414) and Belgium [13] also show closer genetic relatedness to West African MPXV isolates, as well as to isolates of Nigerian origin imported into the United Kingdom in 2018–2019, according to currently available genomic data [13]. Gene losses, usually caused by nonsense or frameshift mutations leading to loss of protein-coding genes and equally to loss of non-coding genes or regulatory regions, have already been observed in endemic regions of Central Africa. These losses are thought to be associated with human-to-human transmission. It is highly likely that this 2022 outbreak of monkeypox affecting multiple countries has a single origin, with early signs of microevolution within the outbreak clusters [14, 15].

WHO reported 1315 cumulative cases of monkeypox in endemic countries between 15 December 2021 and 1 May 2022, with the Democratic Republic of Congo reporting 1238 cases (1 January to 1 May 2022), followed by Nigeria with 46 cases (1 January to 30 April 2022), Cameroon with 26 cases (15 December to 22 February 2022) and the Central African Republic with 6 cases (4 March to 10 April 2022) [1]. Between 1 January and 8 May 2022, Nigeria reported 111 suspected cases of MPXV (with a sudden onset of fever followed by a vesiculo-pustular rash appearing mainly on the face, palms and soles) to the WHO Regional Office for Africa. Urbanisation driven by population growth in West Africa, particularly in Nigeria, may increase the risk of MPXV infection in humans [16], and monitoring of potential animal reservoirs, such as rodents and others, but also of novel transmission routes, must be considered.

Because this is the largest and most widespread outbreak of monkeypox ever seen in Europe, there is concern that infections in Europe could accelerate as the population gathers for parties and festivals during the summer months. One possible avenue is to administer smallpox vaccine to health care workers and people who may have been exposed to monkeypox. If cases can be well isolated through contact tracing, it is unlikely that this outbreak will last long. The world population will continue to be at risk from such outbreaks, and timely international coordination is essential to contain the global spread.

In summary, heightened awareness, active disease surveillance, early diagnosis, and rapid communication of data for health systems to implement any public intervention measures are crucial components of controlling the spread of a MPXV that exhibits epidemic potential.

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