



Multinational monkeypox outbreak: what do we know and what should we do?

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Dear Editor,

The novel multinational monkeypox outbreak has jolted the globe in the midst of the coronavirus disease 2019 (COVID-19) pandemic [1]. The causative agent, monkeypox virus (MPXV), is related to the now-extinct human scourge of smallpox (variola virus). MPXV is an enveloped double-stranded DNA virus with a genome size of approximately 190 kb. It belongs to the genus *Orthopoxvirus* in the family *Poxviridae*. The genus *Orthopoxvirus* comprises several species that infect humans, such as variola virus, MPXV, vaccinia virus, and cowpox virus [2].

The name “monkeypox” dates back to 1958, following an outbreak of the virus in laboratory macaque monkeys in an animal facility in Copenhagen, Denmark. While monkeys do not appear to be the natural host, rodents including rats, mice, and squirrels are the primary carriers [3]. The first human case of MPXV infection was discovered in the Democratic Republic of the Congo (Former Zaire) in 1970 when the country had maximized its efforts to expunge smallpox [4]. Cases outside of Africa have historically been seldom encountered and typically associated with international travel or imported animals. In 2003, the epidemic potential of the disease was shown during the outbreak in the USA, where MPXV hitched a ride with a shipment of animals from Ghana to Illinois [5].

In recent days, an abrupt and portentous surge in the number of cases across the Western Hemisphere raises concerns and disquietude among communities. The outbreak seems

to be highly unusual because established patients thus far have no travel links to the endemic territories. Over two dozen countries have logged cases of monkeypox since early May 2022 [6]. Even more flummoxing is that these cases were mainly, but not exclusively, homosexual and bisexual men. The situation is evolving and more confirmed cases are expected to be announced in the coming days as the World Health Organization (WHO) expands surveillance in countries where the disease is not typically found. Although the disease is not generally considered a sexually-transmitted infection, it can be passed on by close contact with afflicted individuals primarily through respiratory droplets, their clothing, or bed sheets [7]. Superspreader events are perhaps the main culprit behind the rise in global cases [8]. Another explanation for enhanced transmission may be attributable to the official cessation of smallpox vaccination campaigns in 1980. Smallpox vaccination had imparted some degree of cross-protective immunity only to the elderly [9].

Fortunately, a lot of the same countermeasures that are beneficial for diminishing the risk of contracting COVID-19 such as mask wearing, social distancing, handwashing, and surface disinfection will also effectively stymie monkeypox transmission [10]. Treatment for MPXV infection is primarily supportive, though two FDA-approved anti-virals (tecovirimat and brincidofovir) and an intravenous form of vaccinia immune globulin originally developed for smallpox may be exploited to manage monkeypox as well [11]. Tecovirimat is an inhibitor of the viral envelope protein p37, blocking the viral egress from infected cells. Brincidofovir, a lipid conjugate of nucleotide analog cidofovir, inhibits viral DNA polymerase, thereby curbing DNA synthesis and viral replication [12]. As for prophylactic vaccination, there are currently two licensed vaccines in the USA to prevent monkeypox and smallpox. One vaccine (JYNNEOS™) is based on a live, attenuated vaccinia virus (Modified Vaccinia Ankara) that is unable to propagate in the body, but capable of eliciting potent immune responses. The other one is a replication-competent live vaccinia virus vaccine

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(ACAM2000®), meaning that the virus in the vaccine can be transmitted from recipients to unvaccinated individuals [13].

Outbreaks of newly emerging and re-emerging diseases pose unprecedented challenges for vaccine development in terms of design, implementation, and safety. Lessons learned from the COVID-19 pandemic underscore the importance of new-fangled approaches to address such issues. The successful development of vaccines is a lengthy and utterly grueling process. Thanks to their versatility, ease of manufacturing process, and the prerequisite of only pathogenic sequence, RNA-based vaccines are being touted as a promising candidate directed against a myriad of communicable diseases [14]. Emphasis should also be laid upon drug repurposing, the process of finding new indications for existing drugs outside the scope of the original medical indication [15]. A large set of viral gene products are vital or have exactly defined functions in the viral replication cycle. Proteins with enzymatic activity including kinases and phosphatases seem to be ideal targets [16]. Another complementing strategy is host-directed therapy that interferes with cellular signaling pathways. This could augment protective immune responses against a viral pathogen, damp down excessive inflammation, and reduce the likelihood of the development of drug resistance [17]. Last but not least, computer-aided drug design within an artificial intelligence-empowered platform will undoubtedly expedite the anti-viral drug discovery and development process [18].

Author contribution Both authors contributed equally for writing and revision of this manuscript.

Declarations

Ethics approval This article does not contain any studies with human participants or animals performed by any of the authors.

Conflict of interest The authors declare no competing interests.

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