



Need of Monkeypox animal vaccine and its global distribution: right time to address?

Ranjan K. Mohapatra, PhD^{a,*}, Snehasish Mishra, PhD^b, Lawrence S. Tuglo, PhD^f, Lakshmi V. S. Kutikuppala, MBBS^d, Pranab K. Mohapatra, PhD^c, Venkataramana Kandi, PhD^e, Subrat K. Panda, PhD^b, Dhruv N. Desai, PhD^g

Dear Editor,

The ongoing coronavirus disease 2019 pandemic has been tough on human lives globally in recent times. Most pandemics that affect human life involve microbes of animal origin, and virus has been increasingly responsible for disease transmission. Thus, restricting microbial spillover from animals to humans, as also the reverse, is essential. It is equally vital to meticulously assess the zoonotic microbial flora of animals that coexist with humans. Measures such as vaccination would be increasingly beneficial for microbial transmissions from animals to humans. It would ensure controlling such transmissions and also minimizing the possibilities of microbial multiplication in a susceptible host/carrier thereby reducing its chance of mutation^[1]. From a microbiology perspective, zoonotic viruses have been ever more efficient host adaptation. It is particularly evident from the emerging novel influenza viruses, some causing pandemics. They find a reservoir host and suitable niche, allowing them to remain unnoticed until they spill on to humans^[1]. Viruses like lyssa and rabies could infect domesticated (cats, dogs, ferrets) and wild (bats, monkeys) mammals, thereby posing an increased risk of spillovers and emergences. Other viruses like dengue and chikungunya among others are hosted by arthropod vectors like mosquitoes that ensure their survival and frequently infect humans.

The reported human-to-dog transmission of the human Monkeypox (MPX) virus confirms that infected humans too could infect susceptible animals, and hence it is further

challenging to prevent human-to-animal transmission in pets^[2,3]. The virus has infected nearly 70,696 humans in 107 countries as on October 6, 2022^[4]. Thus, the virus now has a truly global presence. The WHO also declared MPX as a global Public Health Emergency of International Concern^[5]. Although B.1 is responsible for the current 2022 MPX resurgence that could be linked to the earlier West African clade, many virus variants (A, A.1, A.2, and B.1) are identified till date^[6]. The West African clade is reportedly less severe compared to the Central African clade, and its infectivity is debatable due to the large number of cases that has reached to more than 100 countries. Although MPXV is noticed, in general, public it circulates in particular group/community like gay, bisexuals, or men–men sex preference primarily, which means that the regions with high gay or bisexual male population shall have an increasing concern. The WHO advises such groups to limit sexual promiscuity to reduce transmission risk. Further, HIV-infected MPX patients show severe symptoms in such groups. Being immunocompromised, the possibility of the virus mutating in such patients that provide a best-fit favorable situation is high. It is really challenging as the mutated virus may have increased severity and infectivity in future compared to the native strain and most importantly the genetic diversity and evolutionary origin of the MPX virus are not completely understood^[6,7].

Recent data reveal that human–human MPX transmission occurs through direct contact with contagious rashes, scabs, or body fluids. It could also transmit via respiratory secretions or intimate physical contact like kissing, cuddling, or having sex. However, the human-to-animal transmission mechanism is unknown. According to the owners of the infected dog, the dog slept with them in bed. Although infected animals could spread MPX virus to people and to other animals, whether this dog transmitted the infection is unclear/unreported. Moreover, humans and animals may show different clinical signs^[8]. An important precaution is to isolate pets from family members infected with MPX. Investigating secondary transmissions via pets is suggested.

The infected dog had lesions on its skin and mucous membranes, pustules on its abdomen and a thin anal ulceration. There is an array of susceptible animals that need special surveillance. All MPX-infected animals may not exhibit rashes. Wild animals like rodents (squirrel, rat, and dormice) and nonhuman primates (like chimpanzee, African gorilla, marmoset, and monkey) could be MPXV carriers^[9–11]. According to the CDC, squirrels, prairie dogs, marmots, groundhogs, giant-pouched rats, chinchillas, hedgehogs, shrews, monkeys, apes, and dogs could be MPXV infected^[12]. Gerbils, Guinea pigs, hamsters, raccoons, mice, rats, domestic rabbits, cats, cattle, camels, skunks, voles, badgers, coyotes, and foxes can be infected with other orthopoxviruses, although whether these can be MPXV infected is still

^aDepartment of Chemistry, Government College of Engineering, Keonjhar, ^bSchool of Biotechnology, Campus-11, KIIT Deemed-to-be-University, ^cDepartment of Chemistry, CV Raman Global University, Bhubaneswar, Odisha, ^dDepartment of General Surgery, Dr NTR University of Health Sciences, Vijayawada, Andhra Pradesh, ^eDepartment of Microbiology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India, ^fDepartment of Nutrition and Dietetics, School of Allied Health Sciences, University of Health and Allied Sciences, Ho, Ghana and ^gSchool of Veterinary Medicine, Ryan Veterinary Hospital, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Government College of Engineering, Keonjhar 758002, Odisha, India. E-mail address: ranjank_mohapatra@yahoo.com (R.K. Mohapatra).

Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

International Journal of Surgery (2024) 110:8164–8166

Received 19 October 2022; Accepted 16 November 2022

Published online 29 March 2023

<http://dx.doi.org/10.1097/JS9.000000000000100>

unknown^[12]. Orthopoxvirus infection in other animals like goats, sheep, and pigs is also unknown, so also in reptiles, amphibians, and birds. Understandings of the complete array of susceptible animals need to be deciphered.

Although MPX continues to spread globally and its human-to-animal transmission is confirmed, its manifestation is different than severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Investigating the cases and circumstances of infection is important that will be very helpful to contain it. Understanding how MPX spreads from humans to animals could help figure out why and how the disease has spread so rapidly in nonendemic regions recently. How the various species transmit the MPXV and by what route need to be investigated. Understanding the animal reservoir, including domestic pets, is critical. Although humans to pet transmission do not seem to be occurring widely, and perhaps there could be unreported cases, remaining alert is needed.

During the incubation period, neither the humans nor the animals are symptomatic. As symptoms arise after incubation, the symptoms differ in humans and animals^[13]. Skin lesions appear initially in MPX-infected pets. Consulting a veterinarian is recommended if lesions suddenly appear. The most common symptoms later are fever, swollen lymph nodes along with lethargy, cough, runny nose, red eyes, and loss of appetite, and also skin rashes as disease progresses. Frequent hand-washing with soap or using an alcohol-based sanitizer and using personnel protective equipment like eye protection, mask, gloves, and a long-sleeved gown are recommended when caressing sick animals^[14]. Self-monitoring and avoiding animal contact particularly in MPX-reported localities are also suggested^[14]. Following isolation protocols as prescribed by the WHO and medical agencies to minimize the transmission is also recommended.

Although numerous animal vaccines against SARS-CoV-2 and its variants that infect pets and wild animals exist, currently, no vaccines for pets and wild animals exist to protect them from MPXV^[13,15]. The available MPX vaccines have only been approved for humans, and also these are still not globally available, particularly in lower and lower-middle-income countries. The time seems right and urgent to develop MPX animal vaccine and its distribution to particularly the affected countries. Due to human–animal and animal–human transmission of MPXV, it will be an effective way to prevent the future emergence of MPX variants. Effective surveillance of MPXV in high-risk group animals is recommended.

Nearly 50 people were infected with MPXV after contacting infected pet prairie dogs during the 2003 MPX outbreak^[12,13], suggesting possible pet-to-human transmission in households. Although whether cats can contract MPX is unknown, a cat might catch MPX, as per the American Veterinary Medical Association^[13]. As the disease becomes more prevalent in future, the understanding may be better. Currently, it is probably not possible to vaccinate the exposed pets. It is important to get oneself vaccinated if exposed to the MPX infected, which shall also ensure pet protection. The instances of zoonotic life-threatening disease outbreaks like the coronavirus disease 2019 and MPX through virus spillage from animals to humans are likely to spread worldwide ever more rapidly and frequently. Arguably, a significant reason for such disruptive events is the altered land-use pattern, particularly in areas that were once dominated by wildlife, thereby destroying the biodiversity. It forced

wild animals to shelter and search for food elsewhere, often closer to human habitation.

Historically, most pandemic-causing viruses originate from animals at some point. Declared as a global health concern by WHO, which has warned to check MPX spread, it could only be possible by vaccinating humans as well as animals in view of the intense human–animal contacts. Vaccines for wildlife should be next-generation, one-shot and effectively of long-term mRNA, subunit, and vector based that would be easy to administer. Antibody against SARS-CoV-2 was detected in wild deer which indicates that the wild animal was infected by SARS-CoV-2 at some point of time^[16]. Thus, spillover of MPX to wild animals from humans could be a possibility due to human–animal proximity. Thus, the time is ripe to have the next-generation MPX vaccine for the animal as well.

Finding solutions to avoid imminent catastrophe is important. Along with humans, animal vaccines with wildlife vaccination strategies could help. Raccoons are vaccinated against rabies in North America by dropping vaccines in the form of edible baits using helicopters^[13]. To ensure long-term benefits of immunity, vaccinating a susceptible species with a longer life span may be suggested^[17]. Vaccinating a susceptible species that has a shorter life span could be by increasing the frequency wherever practicable. Another prudent strategy could be to develop vaccines that provide immunity not just horizontally (in a generation) but vertically (through generations). Also a suggestible better way is to find ways for herd immunity in wildlife that moves through animals instead of directly vaccinating each. The animal directly vaccinated with transferable and self-disseminating vaccine on the skin or fur returns to trigger the effect in the herd. The vaccine manifests its action there through herd immunity. Yet, a self-disseminating vaccine consisting of an attenuated (weakened) virus that is designed to alleviate the disease risk within a population through herd immunity is quite complex. In view of ‘One Health Approach,’ urgent global alliance towards developing and distributing such animal vaccines is highly recommended.

Ethical approval

This article does not require any human/animal subjects to acquire such approval.

Sources of funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author contribution

R.K.M. contributed to the conceptualized, writing, reviewing and editing of the paper. L.V.S.K., P.K.M., S.K.P. made the initial draft. V.K., L.S.T. updated the manuscript. S.M., D.N.D. writing, reviewing and editing of the paper. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

Conflicts of interest disclosure

The authors declare that there is no conflict of interest regarding the publication of this paper.

Research registration unique identifying number (UIN)

None.

Guarantor

All authors.

Data statement

Data not available/not applicable.

References

- [1] Sudhan SS, Sharma P. Human viruses: emergence and evolution. *Emerg Reemerg Viral Pathog* 2020;53–68. doi:10.1016/B978-0-12-819400-3.00004-1
- [2] Seang S, Burrell S, Todesco E, *et al.* Evidence of human-to-dog transmission of monkeypox virus. *Lancet* 2022;400:P658–9.
- [3] Mohapatra RK, Mishra S, Kandi V, *et al.* Monkeypox plays similar like SARS-CoV-2; intensive animal screening is crucial after the first human-to-dog transmission report. *Int J Surg* 2022;106:106925.
- [4] CDC. 2022. Accessed September 20, 2022. <https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html>
- [5] WHO. WHO Director-General declares the ongoing monkeypox outbreak a Public Health Emergency of International Concern. July 23, 2022. Accessed September 20, 2022. <https://www.who.int/europe/news/item/23-07-2022-who-director-general-declares-the-ongoing-monkeypox-outbreak-a-public-health-event-of-international-concern>.
- [6] Chakraborty C, Bhattacharya M, Sharma AR, *et al.* Evolution, epidemiology, geographical distribution, and mutational landscape of newly emerging monkeypox virus. *GeroScience* 2022.
- [7] Desingu PA, Nagarajan K. Genomic regions insertion and deletion in Monkeypox virus causing multi-country outbreak-2022. *bioRxiv* 2022. <https://doi.org/10.1101/2022.06.28.497936>
- [8] Shepherd W, Beard PM, Brookes SM, *et al.* The risk of reverse zoonotic transmission to pet animals during the current global monkeypox outbreak, United Kingdom, June to mid-September 2022. *Euro Surveill* 2022;27:2200758.
- [9] Khodakevich L, Jezek Z, Kinzanzka K. Isolation of monkeypox virus from wild squirrel infected in nature. *Lancet* 1986;1:98–9.
- [10] Falendysz EA, Lopera JG, Doty JB, *et al.* Characterization of Monkeypox virus infection in African rope squirrels (*Funisciurus* spp.). *PLoS Negl Trop Dis* 2017;11:e0005809.
- [11] Beer EM, Rao VB. A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. *PLoS Negl Trop Dis* 2019;13:e0007791.
- [12] CDC. Monkeypox in Animals. August 17, 2022. Accessed September 9, 2022. <https://www.cdc.gov/poxvirus/monkeypox/veterinarian/monkeypox-in-animals.html>
- [13] AVMA. Monkeypox. American Veterinary Medical Association (avma.org). 2022. Accessed September 20, 2022. <https://www.avma.org/resources-tools/one-health/veterinarians-and-public-health/monkeypox>.
- [14] Africa CDC. Multi-country monkeypox outbreak declared a global Public Health Emergency of International Concern. July 25, 2022. <https://africacdc.org/news-item/multi-country-monkeypox-outbreak-declared-a-global-public-health-emergency-of-international-concern-2/#:~:text=Addis%20Ababa%2C%2025th%20July,health%20emergency%20of%20international%20concern%20>
- [15] WHO. (2022). Multi-country monkeypox outbreak: situation update. 17 June 2022. Accessed September 25, 2022. <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON393>
- [16] Willgert K, Didelot X, Surendran-Nair M, *et al.* Transmission history of SARS-CoV-2 in humans and white-tailed deer. *Sci Rep* 2022; 12:1–9.
- [17] Saied AA. Besides human booster doses: could vaccinating highly susceptible animals to SARS-CoV-2 be the needed urgent strategic step? *Int J Surg* 2022;104:106761.