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Opinion Piece

The risk of zooanthroponosis of mpox in South Africa

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Summary

Mpox is a zoonotic disease caused by the monkeypox virus (MPXV). The virus is transmitted from animals to humans in endemic areas in central and western Africa. Although the natural ecology of the MPXV remains to be elucidated, evidence points towards several species of rodents acting as reservoirs and possibly as vectors of the virus. In addition, mpox has been reported in other species, including non-human primates, suggesting a wide host range for this virus. Since 2017, sustained human-to-human transmission via close contact has resulted in the largest mpox outbreaks ever recorded. Cases of mpox have been reported in more than 110 countries since 2022, mostly in countries where the disease has not previously been reported and where zoonotic transmission does not occur. This global emergence of mpox included cases recorded in South Africa in 2022, 2024, and the early months of 2025. Given the proposed wide host range of the MPXV and the increased occurrence of human mpox cases, there are concerns of reverse zoonoses, with the virus being transmitted from infected persons to animals, including rodents, non-human primates, and domestic animals, possibly fuelling new chains of virus transmission. Available evidence points towards a low risk for transmission of MPXV from infected persons to domestic animals. There is, however, not enough evidence to indicate no risk. Several international agencies recommend that persons who have been diagnosed with mpox (and do not require hospitalisation) should self-isolate until they recover, including isolating from their pets. In non-endemic areas where transmission of MPXV is likely to be exclusively human-to-human, outbreak management would benefit from strengthening disease surveillance capacity within human populations and focusing information for the public on the key modes of human-to-human mpox transmission.

Background

Mpox is an infectious disease caused by an orthopoxvirus, *orthopoxvirus monkeypox virus* (MPXV).[1] It was first identified in 1958 in cynomolgus monkeys (*Macaca fascicularis*) kept for research purposes.[2] The natural ecology of MPXV remains elusive because there is no active surveillance in animals and little research that has addressed the topic.[3] A meta-analysis of MPXV infection in animals has shown that findings for fewer than 3 000 subjects have been reported.[4] Despite the relatively small number of subjects, the reports described several species that tested positive for MPXV DNA through PCR testing or for the presence of live virus or indicated prior exposure using serological assays.[4,5] These included species of rodents (*Chinchilla*, *Cricetomys, Cynomys, Funisciurus, Graphiurus, Helioscirurus, Jerbillo, Petrodromus,* and *Oenomys*), non-human primates (*Cercocebus atys*, *Gorilla gorilla*, *Hyobatus lar*, *Saimiri sciureus*, *Cercopithecus hamlyni,* and *Pan troglodytes verus*), and[4-6] a domestic pig (*Sus scrofa*) that tested positive for neutralising antibodies against MPXV.[6] Subject data were obtained under different conditions, including field collections of wildlife, experimental studies involving laboratory animals, and from cases reported in captive animals, either from zoos, laboratories, or the exotic pet trade. Based on this limited data set, it is notable that Clade Ia and Clade IIa MPXV can be considered promiscuous viruses given that they seemingly infect a highly diverse range of species.

Prior to 2022, mpox was considered to be a rare zoonotic disease in humans, with only occasional transmission to persons as reported in West and Central Africa.[7] Zoonotic transmission of the MPXV is presumably through direct contact with skin wounds, scabs, rashes, and infected bodily fluids and secretions. Exposures through bites and ingestion of bush meat have also been associated with cases. It is important to note that the true reservoirs of the virus have not yet been established, and routes of transmission from animals-to-humans therefore remain

uncertain. Human-to-human transmissions are typically restricted to close contacts, often in the household setting.[7] Prior to 2022, reports of mpox in humans outside of endemic countries were limited to persons linked to an outbreak in the United States of America and related to the exotic pet trade industry. People contracted the MPXV primarily through direct contact with prairie dogs, which were co-housed with other rodents imported from Ghana and distributed through exotic pet trade networks in the country.[8] No human-to-human transmissions were noted during this outbreak.[8] Since 2018, a number of cases of mpox have been identified in international travellers returning from Nigeria to several localities.[9] Limited onward transmission to close contacts was recorded among these traveller cases.[9]

From May 2022 through November 2024, more than 100 000 confirmed cases of mpox were reported in more than 110 countries, frequently in individuals with no history of travel to endemic countries.[10] This multi-country mpox outbreak has been marked by ongoing human-to-human transmission, with sexual transmission noted as a frequent mechanism of transmission.[10] Evolutionary pressure from this ongoing human-to-human passage has resulted in the emergence of novel variants of the MPXV, namely Clade Ib and Clade IIb.[11,12] The former emerged from an MPXV outbreak in the Democratic Republic of the Congo, and the latter from the MPXV outbreak in Nigeria.[11,12] The genomic changes identified in Clade Ib and Clade IIb MPXV have been predominantly, but not limited to, APOBEC3 mutations, which may increase the virus's ability to evade host immune responses, although the case fatality rate during the multi-country outbreak does not support the emergence of a more pathogenic virus.[13]

Poxvirus genomes are generally adaptable, and genetic changes result from/occur through point mutations, inverted terminal repeat expansion or contraction, homologous and non-homologous recombination, gene duplications and loss, and the acquisition of genes through horizontal transfer.[14] Not all genetic alterations/modifications translate into phenotypic changes, but it is important to elucidate those genetic changes that may result in increased fitness, virulence and/or pathogenicity in hosts, and to monitor for such changes through genomic sequencing of the circulating virus.[15] The question therefore arises as to whether Clade Ib and Clade IIb viruses have retained their ability to productively infect a broad host range as is observed for Clade Ia and Clade IIa viruses.

Surveillance for mpox in companion animals of confirmed human mpox cases during the multi-country outbreak provides some insights. Two studies in the United States and the United Kingdom did not identify any cases of transmission from infected pet owners to their companion animals.[16,17] A single report from France involving mpox in a domestic dog with contact with its owners who were diagnosed with mpox has been refuted.[18,19] Experimental studies on this topic are still greatly lacking. However, an experimental study has demonstrated Clade IIb MPXV to be less virulent and less transmissible in laboratory mouse animal models when compared to Clade Ia and Clade IIa MPXV.[20] On the other hand, Clade IIb MPXV challenge in a non-human primate model resulted in clinical progression similar to observations in human patients.[21]

Discussion

The emergence of mpox since 2022 shows altered epidemiology characterised by sustained human-to-human transmission, resulting in cases almost worldwide. In 2022, during the peak of the Clade IIb multi-country outbreak, five unlinked cases of mpox were diagnosed in South Africa. From May to September 2024, a further 25 mpox cases were confirmed in-country, and these were also linked to the ongoing Clade IIb multi-country outbreak. There were no travel histories or epidemiological links recognised for 24 of the cases despite being diagnosed with infection of the same sub-lineage of MPXV. One case, identified in 2024, reported a travel history to Peru prior to developing mpox. In February 2025, three linked cases of mpox associated with Clade Ib were confirmed in South Africa, with the index case reporting a travel history to Uganda prior to the onset of illness. As the multi-country outbreak continues, South Africa, where mpox is a category 1 notifiable medical condition, remains vulnerable to the introduction of mpox via travellers.

The unprecedented global outbreak of mpox raises a concern about the risk of reversal of MPXV transmission from humans to animal hosts, particularly companion animals. Several international agencies recognise the potential risk for reverse zoonoses of mpox from confirmed human mpox cases to their companion animals. [22–25] This concern goes to the wide host range and increased circulation of the virus. Evidence of several species being susceptible to MPXV infection raises the possibility of new chains of virus transmission. There is currently a paucity of information concerning the susceptibility and ability to sustain productive MPXV infection in different animal species. Likewise, surveillance data to date have involved few subjects, and the findings do not distinguish animals that are merely susceptible to infection as opposed to those that may support productive infection, resulting in onward virus transmission. Therefore, the natural reservoir(s) of the virus is yet to be determined. Active surveillance for mpox in companion animals has similarly been very limited. However, reports from the United States and United Kingdom have not identified any such cases during the multi-country outbreak—this at a time when large numbers of mpox cases in humans were being confirmed.

Conclusion

Available evidence points towards a low risk for transmission of MPXV from infected persons to rodents, non-human primates, and domestic animals. There is, however, not enough evidence to indicate no risk, so a cautious approach remains valid.

Recommendations

- Where transmission of mpox is likely to be exclusively human-to-human, outbreak management would benefit from national and sub-national strengthening of disease surveillance capacity within human populations, such as the Notifiable Medical Conditions Surveillance System. Rapid case identification allows for treatment and contact tracing, reducing the risk of onward spread.
- Where transmission of mpox is likely to be exclusively human-to-human, local health authorities should conduct sustained awareness campaigns that inform the public of key modes of mpox transmission focussed primarily on human-to-human transmission routes, e.g., close or intimate contact, and not those that may be important in areas where mpox is endemic, e.g., undercooked bush meat consumption.

- As several international agencies recognise the potential risk for reverse zoonoses of mpox from confirmed human mpox cases to their companion animals, we recommend that persons who have been diagnosed with mpox should self-isolate at home until they recover, as well as isolate from their pets to prevent possible transfer of the virus.[22–25]
- Research into the host range specificity of newly emerging variants of MPXV is required to assist in determining the risk and designing interventions for potential reversal of MPXV from infected humans to animals.

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Conflict of interest

The authors declare no conflict of interest.

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