



OUTBREAK OF NOVEL HUMANMONKEY POX VIRUS-A COMPREHENSIVE REVIEW.

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Abstract

Prior to April 2022, cases of the monkeypox virus infecting people outside of Africa's endemic regions were infrequent. Cases are currently happening everywhere. Infection outcomes, risk factors, clinical presentation, and transmission are all poorly understood. Monkeypox cases in humans are uncommon outside of west and central Africa. There are no approved treatments, no information on viral kinetics or the length of viral shedding. Two oral medications, brincidofovir and tecovirimat, have received approval for the treatment of smallpox and have shown effectiveness in animal tests against monkeypox. Our goal was to characterise the longitudinal clinical course of monkeypox in a setting with a high level of income, together with viral dynamics and any negative side effects from innovative antiviral treatments. To stop the spread of the Monkey pox virus infection during outbreaks, community education and training are required.

Keywords: Monkey pox virus, Aventis Pasteur Smallpox Vaccine, Tecovirimat, Brincidofovir, Vaccinia Immune Globulin

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INTRODUCTION

Public health professionals are concerned about whether a new outbreak brought on by the human monkeypox virus offers a new threat while countries around the world continue to battle the coronavirus disease (COVID-19) pandemic. Monkey pox virus (MPV) is not a freshly found virus; the first instance was recorded in Copenhagen in 1958. It was primarily linked to a number of monkeys who had been moved from Singapore to Denmark and were being kept in a facility that specialised in keeping scientific animals (1-2). Although the virus was initially found in monkeys, it can also live naturally in other species, including a dormice, rope squirrels, tree squirrels, Gambian

pouched rats, and rattlesnakes (3). In the Democratic Republic of the Congo, a zoonotic MPV transmission from animals to people was documented in 1970. (DRC) (4). The MPV has double-stranded DNA and is a member of the Orthopoxvirus genus in the Poxviridae family. The orthopoxvirus genus includes the viruses that cause cowpox, vaccinia (a research tool used to develop the smallpox vaccine), and variola (smallpox). It has been established that MPVs have a 200–400 nm-sized oval or brick-shaped structure (5). Many cases of the present outbreak have been linked to a sexual transmission, especially in guys who are openly gay, bisexual, or who only have intercourse with other males. The usage of shared towels,



bedding, and garments as well as direct contact with infected sores, scabs, or bodily fluids are other important vectors for the spread of the virus. The signs and symptoms include a characteristic rash that is preceded by mild prodromal symptoms such as lymphadenopathy, fever, and flu-like symptoms; these symptoms are similar to, but frequently less severe than, those of smallpox. The characteristic rash has not spread past the vaginal and perineal areas where it first manifested, making the current pandemic distinct. Swabs taken from vesicles or ulcer crusts are used to look for the virus in order to identify active cases of monkeypox. As of the time of this study, the CDC reports that supportive care is often all that is required for persons with monkeypox virus infection and that no specific drugs are now available. However, treatments for this include the use of smallpox immunizations, antiviral medications, and vaccines against vaccinia immune globulin (VIG). Until proven otherwise, all confirmed cases of orthopoxvirus should be treated like monkeypox infections. MPV prophylaxis and treatment are the same as those for other orthopoxvirus infections. As another virus pandemic has just emerged, anxieties about them have risen sharply. The so-called endemic phase of COVID-19 is under way. Even though COVID-19's repercussions on the world economy and healthcare have been felt for more than two years, a second new viral outbreak is predicted to appear soon. The "monkeypox virus" is another potential contributing factor MPV (6).

EPIDEMIOLOGY

A nine-month-old infant in the DRC received the first MPV diagnosis ever in 1970. MPV outbreaks have become more frequent since 1970, however they have largely only affected Africa. Surprisingly, neither Europe nor North America have had a significant viral outbreak (7). Up to 48 confirmed cases of monkeypox were reported from six African countries between 1970 and 1979. In the more over 400 cases of MPV in humans that had been documented by 1986, mortality rates were

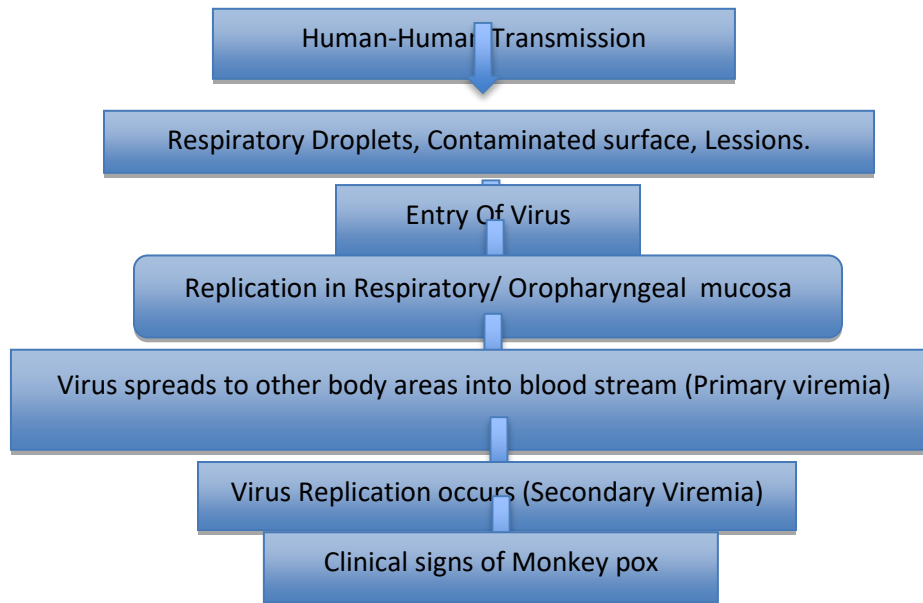
close to 10% (8). The virus returned on May 18, 2022, with 14, 7, and 13 MPV infections recorded in Portugal, Spain, and Canada, respectively (9). On May 19, 2022, the first MPV cases in the globe were officially confirmed in Belgium, Sweden, and Italy. On May 20, Australia reported two events. The initial cases were confirmed in France, Germany, and the Netherlands on May 20. The UK's Health Secretary confirmed eleven more MPV cases on May 20, bringing the total to 71 (10). The initial cases were confirmed in Switzerland and Israel on May 21. The first instance was reported by Spain on May 18, 2022. Spain now has 186 cases, up 20 from the previous count, according to a June 3 report. On May 23, Denmark received a report of the first incident. Quebec, Canada, revealed 15 confirmed cases on May 24, 2022, the same day the Czech Republic made its initial report. At the end of May, the identity of the first victim—a female tourist from West Africa who was 29 years old—was confirmed in the United Arab Emirates. Slovenia also received a first case report that was confirmed. 19 countries have reported MPV cases as of May 24. The cause of the present MPV outbreak, however, remains unknown. It is now thought that the virus may travel between humans and animals due to MPV's dynamic nature. Travelers from an infected region of Africa to non-endemic regions of North America and Europe were the first hosts. 39,434 MPV cases had been reported as of the time of this study in various parts of the world.

PATHOPHYSIOLOGY

The mouth, the nose, and the skin are three locations where MPV can enter a human body. After the inoculation, the virus multiplies there before moving on to neighbouring lymph nodes. The virus spreads to other bodily areas once it has established itself in the bloodstream (viremia). The MPV structure is comparable to other orthopoxvirus. MPVs can be oval or brick-shaped and have an outer membrane made of lipoproteins. Despite being a DNA virus, MPV only replicates in the cytoplasm. Specific proteins are required for viral DNA replication,

transcription, and virion assembly. Congo MPV activates T cells through the T cell receptor

(TCR) pathway (11).



TRANSMISSION

Rats in Africa are thought to be a major source of the MPV virus. Contact with skin lesions, body fluids, or respiratory droplets from infected animals are the most frequent ways that MPV is spread. The virus can enter the body through the lungs, cuts on the skin, or mucous membranes, as was previously indicated (oropharynx, nasopharynx, or intradermal routes) (12) Transmission from animals to people may occur through scratches, bites, the preparation of bush meat, direct or indirect contact with bodily fluids, or by material from lesions. Sneezing, coughing, and other large respiratory droplets can transfer an infection from one person to another (13). Since respiratory droplets only travel a short distance, transmission requires prolonged, close, and sustained face-to-face contact. Other ways that people might transmit viruses to one another include sexual contact, direct contact with bodily fluids or viral lesions, and indirect contact with contaminated items like clothing or linens. Congenital monkeypox is a disease when the virus is transferred from mother to kid after

delivery via the placenta. Monkey pox cannot be transmitted by sexual activity, even though physical contact is necessary for its propagation. It is necessary to conduct additional research investigations using carefully monitored animal models to learn more about the virus and determine whether it may be transmitted sexually (14). In order to stop the virus from spreading, it is crucial to identify sick persons and isolate the person who may be affected for a long period of time, such as up to three weeks (15).

CLINICAL MANIFESTATIONS

An MPV infection is characterised by symptoms that are more mildly similar to smallpox (16). Smallpox does not produce lymphadenopathy; instead, MPV infection does. An MPV infection begins with a fever, chills, headache, aches in the muscles and back, and lethargy that eventually results in exhaustion. Monkeypox normally takes 7 to 14 days to develop, but it can take up to 21 days. Fever is followed by a facial rash, and the illness subsequently spreads to other parts of the body. Oropharyngeal lesions are the first to appear, then lesions in

other parts of the body (17). The onset of serum antibodies occurs 14 days following exposure. The MPV strain's clade and the availability of modern healthcare can affect the fatality rate, which can range from 1% to 10%. (18).

DIAGNOSIS

A combination of the patient's medical history, physical examination, and laboratory tests may be used to identify MPV infection. The diagnosis is made using techniques such as polymerase chain reaction (PCR), enzyme-linked immunosorbent assay (ELISA), western blotting, and immunohistochemistry. To rule out other contagious diseases like smallpox, a firm diagnosis is necessary (19). Swabs of lesion exudate or crust are used to isolate viral nucleic acids for testing. Viral DNA is required as an input for the MPV genome-specific real-time polymerase chain reaction (RT-PCR) assay. As an alternative, monkey pox virus infection can be verified by western blot analysis on MPV proteins. The World Health Organization states that the best test for identifying monkey poxvirus during an acute infection is an RT-PCR. (20).

PREVENTION

The research that is currently available suggests that smallpox vaccination prior to monkey pox infection may lessen its clinical symptoms. The three smallpox vaccines currently in the US Strategic National Stockpile are ACAM2000®, JYNNEOSTM (also known as IMVAMUNE, IMVANEX, and MVA-BN), and the Aventis Pasteur Smallpox Vaccine (APSV), which may be used for smallpox under an investigational new drug (IND) programme. The US Food and Drug Administration (FDA) gave the vaccine the all-clear in September 2019 for use in people age 18 and older who are at a high risk of contracting smallpox or monkey pox (21). The vaccinia virus vaccine, which is also used to treat smallpox, has an efficacy rate against monkey pox of roughly 85%, according to historical records. In the United Kingdom, the IMVANEX® vaccine, which is approved in Europe, has been used off-label to treat monkey pox. ACAM2000® also has live vaccinia

virus in it. It is recommended that those who are at a high risk of contracting the illness receive the ACAM2000® active immunisation against smallpox infection. ACAM2000® may be used in outbreaks of non-variola orthopoxvirus diseases under the CDC's emergency access IND methodology (such as monkey pox) (18, 21). It has been proven that some people who get replication-competent vaccinia vaccines like ACAM2000® may experience unregulated viral reproduction and develop progressive vaccinia and eczema vaccinatum. Myopericarditis (estimated to occur in 5.7 per 1,000 main ACAM2000® vaccinations) and post-vaccination encephalitis are two additional severe side events that are more frequent with ACAM2000® than with JYNNEOSTM. An investigational new drug (IND) or emergency use authorization (EUA) of the Aventis Pasteur Smallpox Vaccine can prevent smallpox if available or effective licenced vaccines are ineffective or unavailable (APSV).

TREATMENT

Most people with monkey pox have very moderate symptoms and recover without treatment. The CDC advises that there is no specific treatment for monkey pox virus infections at this time. But antiviral medications already approved to treat smallpox may also be effective against monkey pox.

Supportive Care:

Most people infected with monkey pox get well without any therapy at all. Those experiencing gastrointestinal issues (vomiting, diarrhoea) should be prescribed oral/intravenous rehydration to help prevent dehydration (22).

Antivirals:

Animal studies suggest that certain antivirals, originally developed for the treatment of smallpox, may also be useful against monkey pox. Although human dose-finding trials have been done, the medicines' effectiveness remains unclear.

Tecovirimat

The first antiviral recommended for the treatment of smallpox in adults and paediatric patients weighing at least 3 kg, tecovirimat (also

known as TPOXX or ST-246) is the therapy of choice.^[44] In extremely ill individuals, a combination of tecovirimat and brincidofovir may be administered. Patients suffering side effects from the smallpox vaccination, such eczema vaccinatum and progressive vaccinia, have been treated with tecovirimat and vaccinia immune globulin (VIG) in small trials. Use of tecovirimat for non-variola orthopoxvirus infections, such monkey pox, is approved under the CDC's Emergency Access Investigational New Protocol. For children weighing less than 13 kg, the protocol allows the oral capsule to be opened and the contents mixed with liquid or soft food. The Strategic National Stockpile provides two different forms of tecovirimat, one in capsule form for oral administration and another in intravenous vial form.(22, 23).

Cidofovir and Brincidofovir

In the United States, brincidofovir has been used to treat smallpox since June 2021. Because it is structurally similar to the intravenous medication cidofovir, brincidofovir (oral) may have a better safety profile than cidofovir, namely less renal toxicity. It is not known if

cidofovir is effective against monkey pox in humans, although it has been shown to be active in vitro and to prevent fatal Monkeypox virus infections in animals (24). Cidofovir must be administered with intravenous normal saline and probenecid treatment. Brincidofovir may raise serum transaminases and serum bilirubin, thus it's important to monitor liver function before and throughout therapy. A EUA or IND is required to access these treatments (25).

Vaccinia Immune Globulin (VIG)

Hyperimmune globulin (VIG) is approved by the FDA to treat vaccinia vaccine side effects. Eczema vaccinatum, progressive vaccinia, severe generalised vaccinia, vaccinia infections in people with skin problems, and aberrant infections generated by vaccinia virus (apart from isolated keratitis, for example ocular infections) are all examples. Patients with severe immunodeficiency in T-cell function should not get vaccinia virus vaccine, but they may receive VIG instead if they have a history of exposure (26). An Investigational New Drug (IND) application is necessary for VIG treatment.

Treatment

Drug	Tecovirimat	Brincidofovir	Cidofovir
Dose	Adults: 600 mg BID for 14 days; Paediatrics, if 13 kg to less than 25 kg: 200 mg BID for 14 days, if 25 kg to less than 40 kg: 400 mg BID for 14 days, if 40 kg or more: 600 mg BID for 14 days	Adults weighing ≥ 48 kg: 200 mg once in a week for two doses; adults and paediatric patients weighing ≥10 kg to less than 48 kg: 4 mg/kg of the oral suspension once in a week for two doses; Paediatrics weighing less than 10 kg, the dose is 6 mg/kg of the oral suspension once in a week for 2 doses.	5 mg/kg once in a week for 2 weeks, followed by 5 mg/kg IV once every other week.
Mechanism of action	Orthopoxvirus VP37 envelope wrapping protein inhibitors.	Phosphorylated to active metabolite, cidofovir diphosphate, that selectively inhibits orthopoxviral DNA polymerase-mediated viral DNA synthesis.	Undergoes cellular phosphorylation, then selectively inhibits orthopoxviral DNA polymerase-mediated viral DNA synthesis.



Adverse effects	Headache, nausea, abdominal pain, vomiting. Infusion-site reactions in case of IV administration.	Diarrhea, nausea, vomiting, and abdominal pain.	Decreased serum bicarbonate, proteinuria, neutropenia, infection, hypotony of eye, iritis, uveitis, nephrotoxicity, Pyrexia.
Contraindications	None	None	Hypersensitivity to cidofovir or any component of the formulation; history of clinically-severe hypersensitivity to probenecid or other sulpha-containing medications; serum creatinine > 1.5 mg/dL; CrCl ≤ 55 mL/minute; urine protein ≥ 100 mg/dL (≥ 2+ proteinuria); use with or within 7 days of nephrotoxic agents; direct intraocular injection
Major Drug-Drug interactions	Repaglinide, Midazolam,	OATP1B1 and 1B3 inhibitors increase Brincidofovir exposure which inturn may increase Brincidofovir - associated adverse reactions.	Probenecid
Use in Special populations	Should not be administered to patients with severe renal impairment.	Not recommended in pregnant and lactating women.	Dose adjustment based on renal function is required.

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CONCLUSION AND OUTLOOK:

The World Health Organization has issued a warning that the world may be in for another major challenge in the form of the monkey pox pandemic amid the awful Ukraine-Russian conflict. A total of 39,434 cases had been confirmed worldwide as of August 17 of 2022. As a result, the MPV epidemic is spreading to other countries. Epidemiologists, doctors, scientists, and decision-makers have all been monitoring the monkey pox outbreak. The

health agency of the British government has advised those who have monkey pox to quarantine themselves. Belgium has mandated a three-week quarantine for anyone with monkey pox, becoming the first country to do so. Monkeypox is an illness caused by the Monkeypox virus. The Monkeypox virus is the infection that causes monkeypox. It can spread from animals to people since it is a viral zoonotic infection. Additionally, it is transferrable between people and the



environment, as well as between humans. Although there have been some fatalities related to the global monkeypox outbreak, the fatality rate is lower than anticipated based on past data, and experts are cautiously relieved. At least 22 persons have passed away out of the more than 57,000 cases of monkeypox that have been confirmed, which equates to a mortality rate of roughly 0.04%. Compared to the 1-3% that have been reported during epidemics brought on by a comparable virus strain in West Africa over the past two decades, that number is noticeably lower. Global economic growth is under urgent threat from the recent outbreak of monkey pox. If this Monkeypox epidemic is not contained soon, it will exacerbate existing economic difficulties. Children, the elderly, and pregnant women are particularly vulnerable and should get extra care.

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REFERENCES

1. John P. Thornhill, M.D., Ph.D., SaphaBarkati, M.D., Sharon Walmsley, M.D., Juergen Rockstroh, M.D., Andrea Antinori, M.D., Luke B. Harrison, M.D., Ph.D., Romain Palich, M.D., Ph.D., Achyuta Nori, M.D., Iain Reeves, M.D., Maximillian S. Habibi, M.D., Ph.D., Vanessa Apea, M.D., M.P.H., Christoph Boesecke, M.D., et al., Monkeypox Virus Infection in Humans across 16 Countries, *N Engl J Med* 2022; **387**:679-691.
2. Patel A, Bilinska J, Tam JCH, et al Clinical features and novel presentations of human monkeypox in a central London centre during

the 2022 outbreak: descriptive case series. *BMJ*.2022; **8**:679-691.

3. [Boghuma K Titanji](#), [Bryan Tegomoh](#), [Saman Nematollahi](#), [Michael Konomos](#), [Prathit A Kulkarni](#), Monkeypox: A Contemporary Review for Healthcare Professionals, *OFID*. 2022.

4. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, Steffen R. The changing epidemiology of human monkeypox— A potential threat? A systematic review. *PLoS neglected tropical diseases*. 2022; 16; 2.

5. Food and Drug Administration. FDA approves first live, non-replicating vaccine to prevent smallpox and monkeypox. <https://www.fda.gov/news-events/press-announcements/fda-approves-first-live-non-replicating-vaccine-prevent-smallpox-and-monkeypox>.

6. Guarner J, Del Rio C, Malani PN. Monkeypox —what clinicians need to know. *Jama* 2022; **2**:139-40.

7. Velavan TP, Meyer CG. Monkeypox outbreak: an update. *Tropical Medicine & International Health* 2022.

8. Centers for Disease Control and Prevention (CDC). Monkeypox virus infection in the United States and other non-endemic countries 2022.

9. UK Health Security Agency. Monkeypox cases confirmed in England—latest updates 2022.

10. Food and Drug Administration. FDA approves first live, non-replicating vaccine to prevent smallpox and Monkeypox 2019.

11. Kumar N, Acharya A, Gendelman HE, Byrareddy SN. The outbreak and the pathobiology of the monkeypox virus. *Journal of Autoimmunity* 2022.

12. Minhaj FS, Ogale YP, Whitehill F, Schultz J, Foote M, Davidson W, Hughes CM, Wilkins K, Bachmann L, Chatelain R, Donnelly MA.; Monkeypox outbreak—nine states. Morbidity and Mortality *Weekly Report* 2022; **6**: 764.

13. Food and Drug Administration. FDA approves first live, non-replicating vaccine to prevent smallpox and Monkeypox. 2022.

14. Adalja A, Inglesby T, A novel international monkeypox outbreak. *Ann Intern Med* 2022; **175**:1175–1176.



15. UK Health Security Agency. Monkeypox cases confirmed in England—latest updates.

16. Centers for Disease Control and Prevention (CDC). Monkeypox virus infection in the United States and other non-endemic countries 2022.

17. Eltvedt AK, Christiansen M, Poulsen A. A case report of monkeypox in a 4-year-old boy from the DR Congo: challenges of diagnosis and management. *Case Reports in Pediatrics* 2020; 1-5

18. Hugh Adler, Susan Gould, Paul Hine, Luke B Snell, Waison Wong, Catherine F Houlihan, Jane C Osborne, Tommy Rampling, Mike BJ Beadsworth, Christopher JA Duncan, Jake Dunning, Tom E Fletcher, Nicholas M Price Clinical features and management of human monkeypox: a retrospective observational study in the UK, *Lancet Infect Dis* 2022; **22**:1153-1162.

19. Hobson G, Adamson J, Adler H, Firth R, Gould S, Houlihan C, Johnson C, Porter D, Rampling T, Ratcliffe L, Russell K, Shankar AG, Wingfield T Family cluster of three cases of Monkeypox imported from Nigeria to the United Kingdom, *Euro Surveill* 2021; **26**:32.

20. Peiró-Mestres A, Fuertes I, Camprubí-Ferrer D, Marcos MÁ, Vilella A, Navarro M, Rodríguez-Elena L, Riera J, Català A, Martínez MJ, Blanco JL: Hospital Clinic de Barcelona Monkeypox Study Group. Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients. *Euro Surveill* 2022; **27**.

21. Costello V, Sowash M, Gaur A, Cardis M, Pasieka H, Wortmann G, Ramdeen S: Imported Monkeypox from International Traveller, Maryland, USA. *Emerg Infect Dis* 2022; **28**:5.

22. Velavan TP, Meyer CG. Monkeypox 2022 outbreak: An update: *Trop Med Int Health* 2022; **27**:604-605.

23. Rizk JG, Lippi G, Henry BM, Forthal DN, Rizk Y: Prevention and Treatment of Monkeypox. *Drugs* 2022; **82**:957-963.

24. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox Virus in Nigeria, Infection Biology, Epidemiology, and Evolution. *Viruses* 2020; **05**; 12.

25. Vivek P. Chavda, Lalitkumar K. Vora & Vasso Apostolopoulos, Monkey pox: a new face of

outbreak: *Expert Review of Vaccines* 2022; **21**:11; 1537-1540.

26. Benatti SV, Venturelli S, Comi N, et al. Ophthalmic manifestation of monkey pox infection: *Lancet Infect Dis* 2022; **22**:1397.

