

# Human Monkeypox Disease: Insight into Pathophysiology and Management

Dr. Ajith JS<sup>1</sup>, Vivek Gaikwad<sup>2</sup>, Akash Janrao<sup>3</sup>

Department of Pharmacology, Sanjivani College of Pharmaceutical Education and Research, Kopargoan, Maharashtra.423601, India

**Abstract:** Monkey pox is a smallpox like disease that is caused by infection with monkey pox virus. Monkey pox virus belongs to the orthopoxvirus genus in the family Poxviridae. This disease is pre - dominantly found in central and western African rain forest. Human monkey pox is a zoonosis disease that is transmitted from animals to human and has flu - like symptoms fever, malaise, back pain, headache, and a distinctive rash, which are remarkably similar to common kinds of smallpox. Given this clinical spectrum, it's crucial to exclude out smallpox with a different diagnosis. Human monkeypox has no approved treatments; however the smallpox vaccine can provide protection. Monkey pox, thought to be an uncommon and self - limiting disease has received little attention since its discovery in 1958. Concern has recently been expressed regarding its rise, as well as the occasionally severe clinical presentation that resembles with smallpox. Smallpox is a devastating disease that has been eradicated worldwide by vaccination 40 years ago. Back in the day human monkey pox disease captured the attention when 3 individual patients in the UK were diagnosed with a rare disease, scientists were shocked. The number of instances of human monkey pox and their spread across the west and central Africa has grown in recent years. The human monkey pox virus replicates at the inoculation site after entering via any route (oropharynx, nasopharynx, or intradermal). It then spreads to local lymph nodes. Following that, viral spread and seeding of other organs occurs as a result of an initial viremia. This is the incubation period, which usually lasts 7 to 14 days, with a maximum of 21 days. The preferred laboratory test for monkey pox is viral DNA detection via polymerase chain reaction (PCR). The best diagnostic specimens are directly from the rash – skin, fluid or crusts or biopsy where feasible because Antigen and antibody detection methods do not differentiate between orthopoxviruses they may be ineffective. The transmission of this human monkey pox can be prevented by isolating yourself at home and talking to a health professional if you have symptoms, avoiding any face to face, or skin to skin contact including sexual contact with anyone who has symptoms. This review gives a brief idea about pathophysiology of monkey pox, how it spread, which treatment available on it, its affect all over the world and which preventive measure we can take to avoid from such life threatening diseases.

**Keywords:** Monkeypox, orthopoxviruses, Poxviridae, Smallpox

## 1. Introduction

Human monkey pox virus is an Orthopoxvirus that cause a disease that is similar to smallpox but less severe (1), (2). The genetic material of human monkey pox virus is DNA and the family of this virus is poxviridae (3). This is a life - threatening zoonotic infection that mostly found in west and central African countries and can spread in humans (4). The case rate for monkey pox infection in unvaccinated people can be as high as 10%, though case - fertility rates are lower for infection with the west African clade of MPXV than for infection with the central African clade of MPXV (5). The number of cases and geographic spread is increase in recent years.

## 2. History

Monkey pox was first discovered in 1958, when two outbreaks of a pox - like disease occurred in monkeys which kept for research purpose, hence the name given for virus is monkey pox (6). The first human monkey pox case was firstly identified in a 9 - month - old boy in democratic republic of Congo in 1970, in an area where smallpox had been eradicated in 1968. Since then, the majority of cases have been reported from the Congo basin rural, rainforest from all over central and west Africa (7). Between February 1996 and 1997, the largest outbreak of monkey pox was reported from the same, area raising questions about whether smallpox virus sample should be kept for comparative research with related viruses like monkey pox. In 13 villages in Zaire, 71 clinical cases of monkey pox were reported from February to August 1996, with six deaths (10). After that in 2003, when the first cases in the Western Hemisphere were

reported, monkey pox was restricted to the rain forests of Central and Western Africa. Multiple people in the midwestern United States developed fever, rash, respiratory symptoms, and lymphadenopathy after being exposed to sick pet prairie dogs (*Cynomys* species) infected with the monkeypox virus in late spring 2003 (8). 71 suspected cases of monkeypox were investigated between May 15 and June 20, 2003, and 37 people in the United States developed laboratory confirmed monkeypox. Human monkeypox had never been documented in the United States or the Western Hemisphere before. The disease was spread from small African animals to other animals, including prairie dogs sold as pets across the Midwest of the United States (9). In last 2 years several cases of monkeypox virus are identified in U. S. resident who recently returned from African countries.

## 3. Pathophysiology

Monkeypox virus:

In view of recent outbreaks of monkeypox in both endemic and non - endemic countries, the WHO R&D Blueprint convened a global research consultation, which brought together over 500 experts and over 2000 participants to discuss knowledge gaps and research priorities for monkeypox.

For two days, researchers and high - level experts from around the world met virtually to review the available evidence on the virus's epidemiology, transmission dynamics, clinical characteristics, One Health research, community engagement, and disease management countermeasures, including clinical care, treatments, and vaccines. They agreed that effective countermeasures should

be made available where the need is more (14).

Monkeypox virus belong to family Poxviridae, genus Orthopoxvirus along with monkeypox virus (MPXV), Variola virus (VARV), cowpox virus (CPXV), and vaccinia virus (VACV) are among the pathogens known to infect humans. The genome of such viruses are approximately 200 kb long, with highly conserved central region coding for replication and assembly machinery and more variable terminal ends containing genes involved in host range determination and pathogenesis (11). Monkeypox virus is divided into two clades: West African and Congo Basin monkeypox virus. The virulence of human and monkey diseases varies between Congo Basin and West African strains, with the former being more dangerous to non-human primates. Human monkeypox has been reported to have clinical symptoms that are similar to smallpox (12). Hairpin loops, tandem repeats, and some open reading frames make up the inverted terminal repeats (ITRs) in the MPXV genome, which is made up of a linear double-stranded DNA (197 kb) covalently joined at its ends by palindromic hairpins (ORF). Despite the fact that MPXV is a DNA virus, it spends its entire life cycle inside infected cells' cytoplasm. The MPXV genome encodes all of the proteins needed for viral DNA replication, transcription, virion assembly, and exit. Housekeeping genes are highly conserved across OPVs and are found in the central region of the genome, whereas virus-host interactions genes are less conserved and found in the terminal region (13). The first complete genome sequence of the current monkeypox virus (MPXV) outbreak (isolate name MPXV USA 2022 MA001) is now available in GenBank, a public database of DNA sequences hosted by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM), with accession ON563414 (15).

#### 4. Transmission

Cases of monkeypox have spread beyond the forests of central Africa, where they were first discovered, to other parts of the world, where they have been imported. This transmission pattern is most likely due to a worldwide decline in orthopoxvirus immunity after smallpox vaccination was discontinued in 1980, when smallpox was declared eradicated. Monkeypox may thus become the most common orthopoxvirus infection in humans (16). The mode of transmission of the monkeypox virus between infected animals and humans is unclear, owing in part to the lack of publication of histopathologic and immune histochemical studies of animals with naturally acquired infection. The prairie dogs in this study had abundant viral antigens and mature poxvirus particles in their tongues and conjunctival lesions; thus, direct contact with saliva or exudates from these lesions could have inoculated monkeypox virus to other hosts' skin or mucous membranes. Furthermore, monkeypox virus replicated abundantly in the bronchi and lung parenchyma, suggesting that transmission to other rodents and humans may have occurred when the infected animal coughed and dispersed infective droplets. Furthermore, the pneumonic process in these prairie dogs implies that rodents get infected through the respiratory system. As a result, the pathologic examination of seriously ill prairie dogs in this outbreak revealed that direct

mucocutaneous contact and respiratory pathways played a role in transmission, as has been hypothesized in human disease outbreaks in Africa (17). But recent discoveries show the mode of transmission MPX is typically spread from active lesions through bodily fluids and close skin-to-skin contact.

While sexual intercourse has been postulated as a possible route of transmission, we think this is the first case of MPX infection with proven sex transmission (18). The first two MPX cases described in Germany follow the pattern of recent MPX cases seen in North America and Europe. The majority of them have not been linked to travel to countries where MPX is an endemic zoonosis. Previously, transmission to humans was primarily through Current cases are primarily, but not exclusively, transmitted between MSM, as evidenced by infected animals. As previously stated, close physical contact appears to be the most important factor in human-to-human transmission. However, our clinical and virological investigations of the first two human MPX cases in Germany have revealed additional findings that may be important for monitoring and assessing the ongoing MPX outbreak (19). Rashes of monkeypox are occasionally found on the genitals and in the mouth, which is likely to contribute to transmission during sexual contact. Where there are skin or mouth lesions, mouth-to-skin contact could result in transmission. Rashes caused by monkeypox can resemble those caused by sexually transmitted diseases such as herpes and syphilis. This could explain why several of the current outbreak's cases have been identified among men seeking care at sexual health clinics. The risk of contracting monkeypox is not limited to sexually active people or men who have sex with men. Anyone who comes into close physical contact with an infectious person is at risk (20). Children are more likely than adolescents and adults to have severe symptoms. The virus can also be transmitted to a fetus or a newborn via birth or early physical contact (21).

#### 5. Sign & Symptoms

Monkeypox symptoms include a fever, severe headache, muscle aches, back pain, fatigue, swollen lymph nodes, and a skin rash or lesions. The rash usually appears one to three days after the fever begins. Lesions can be flat or slightly raised, filled with clear or yellowish fluid, crust, dry, and fall off. A single person can have anywhere from a few to several thousand lesions. The rash usually appears on the face, palms of the hands, and soles of the feet. They are also found on the lips, genitals, and eyes (22). Smallpox antivirals with poxvirus activity, such as cidofovir, brincidofovir, and tecovirimat, have activity against monkeypox, despite the lack of a standard-of-care treatment. The latter two medications have been approved by the US Food and Drug Administration (FDA) for use in smallpox therapy. Such treatments would almost certainly be reserved for severe instances or in immunocompromised people, and would be obtained through a public health department or the CDC (25).

#### 6. Diagnosis & Treatment

Given the current outbreak, doctors should evaluate

monkeypox in patients who have a fresh onset of fever and rash, especially if lymphadenopathy is present. In a centrifugal pattern, the rash usually starts in the lips, then travels to the face, then to the extremities (including the palms and soles). Polymerase chain reaction testing of skin lesions or fluid is used to get a definitive diagnosis. These tests are available at public health laboratories around the state

The bulk of the clinical symptoms of human monkeypox infection (discrete ordinary type or modified type, are similar to those of smallpox. A widespread headache and weariness accompany the early febrile prodrome. Many individuals have maxillary, cervical, or inguinal lymphadenopathy (1–4 cm in diameter) prior to and concurrent with rash development. Lymphoma nodes that have grown in size are hard, sensitive, and occasionally painful.

Smallpox was not associated with lymphadenopathy. The prevalence of lymphadenopathy could indicate that the immune system recognises and responds to the monkeypox virus more effectively than the variola virus, but this idea has to be investigated further (23).

Symptoms of monkeypox frequently resolve on their own without the need for treatment. It is critical to treat the rash by allowing it to dry if possible or covering it with a moist dressing to protect the area if necessary. Avoid touching any mouth or eye sores. As long as Cortisone - containing products are avoided, mouth rinses and eye drops can be used. In severe cases, vaccine immune globulin (VIG) may be recommended. In January 2022, an antiviral developed to treat smallpox (tecovirimat, marketed as TPOXX) was also approved for the treatment of monkeypox (WHO).

## 7. Prevention

You can reduce your risk by avoiding contact with people who have monkeypox, whether suspected or confirmed. If you must come into contact with someone who has monkeypox because you are a health worker or live together, encourage the infected person to isolate themselves and cover any skin lesions if possible (e. g., by wearing clothing over the rash). They should wear a medical mask when you are physically close to them, especially if they are coughing or have lesions in their mouth. You should also wear one. When possible, avoid skin-to-skin contact and wear disposable gloves if you have direct contact with lesions. Wear a mask when handling clothing or bedding if the person is unable to do so themselves. Regularly wash your hands with soap and water or an alcohol-based hand rub, especially after contact with the infected person, their clothes, bed sheets, towels, and other items or surfaces they have touched or that may have come into contact with their rash or respiratory secretions (e. g., utensils, dishes). Warm water and detergent should be used to wash the individual's clothes, towels, bed sheets, and eating utensils.

The public health response in the world has focused on: Clean and disinfect any contaminated surfaces, and dispose of contaminated waste (e. g., dressings) properly (ii) avoiding further spread by isolating cases and tracing

identifiable contacts; (iii) providing smallpox immunization to high-risk households and identified close contacts up to 14 days after exposure (Imvanex, Bavarian Nordic, Kvistgd, Denmark). (iv) international notifications to the World Health Organization and the European Union on 07 and 16 May 2022 for Incident 1, 13 May 2022 for Incident 2, and 15 May 2022 for Incident 3, including posts on the European surveillance site for infectious illnesses (EpiPulse) (26).

## 8. Conclusion

The current monkey pox outbreak should prioritise preventing further spread and protecting frontline health-care workers and those most vulnerable globally. The unprecedented multiplication of monkeypox cases seen in the last three weeks outside of Africa emphasises the importance of developing effective capacity at the source for effective global public health preparedness and surveillance for zoonotic threats to global health security.

1, 2 Rapid accumulation of financial and political resources to fuel reassurance, support for this is required. rather than fear and stigma. The quality and accessibility of care for neglected tropical diseases is recognised as a key performance indicator for countries working toward disease eradication.

This goal should also apply to diseases like monkeypox, which, while not specifically mentioned, targeted for eradication, affects almost entirely people without access to sophisticated technology or specialised medical care. Developing evidence-based case management strategies is also essential. a component of epidemic preparedness, as defined by the Integrated Disease Surveillance and Response Plan 2010 Technical Guidelines. Data from observational studies and animal experiments can help inform how to improve patient outcomes, but more clinic-based research is needed to ensure that approaches to care are optimised for both positive outcomes and efficient utilisation.

## References

- [1] Reemergence of human monkeypox in Nigeria, 2017 DOI: <https://doi.org/10.3201/eid2406180017>.
- [2] oc EK, Sg BM Lor YN Hoo UB, Bee YC, Job S1, tu Multiple el 1556 laghly pathogenic avian influenza vives, South Korea 2016 Infest et al.2015121 - 3.
- [3] [https://wwwnc.cdc.gov/travel/destinations/traveler/none/nigeria?s\\_cid%2](https://wwwnc.cdc.gov/travel/destinations/traveler/none/nigeria?s_cid%2).
- [4] Likos AM, Sammons SA, Olson VA, Frace AM, Li Y, Olsen - Rasmussen M, et al. A tale of two clades: monkeypox viruses. *J Gen Virol*.2005; 86: 2661 - 72.10.1099/vir.0.81215 - 0 [PubMed] [CrossRef] [Google Scholar] [Ref list].
- [5] <https://www.cdc.gov/poxvirus/monkeypox/index.html>.
- [6] <https://www.who.int/news-room/questions-and-answers/item/monkeypox>.
- [7] Reed KD, Melski JW, Graham MB, Regnery RL, Sotir MJ, Wegner MV, et al. The detection of monkeypox in humans in the Western Hemisphere. *N Engl J Med*.2004 Jan 22.350 (4): 342 - 50. [QxMD

- MEDLINE Link].
- [8] Monkeypox in the United States: an occupational health look at the first cases. Bruce E Cunha AAOHN Journal: Official Journal of the American Association of Occupational Health Nurses 2004, 52 (4): 164 - 8.
- [9] Cohen J. Exotic Diseases: Is an old virus up to new tricks? Science.1997; 277: 312- 313. [PubMed] [Google Scholar] [Ref list].
- [10] Kugelman JR, Johnston SC, Mulembakani PM, Kisalu N, Lee MS, Koroleva G, McCarthy SE, Gestole MC, Wolfe ND, Fair JN, Schneider BS, Wright LL, Huggins J, Whitehouse CA, Wemakoy EO, Muyembe Tamfum JJ, Hensley LE, Palacios GF, Rimoin AW. Genomic variability of monkeypox virus among humans, Democratic Republic of the Congo. Emerg Infect Dis.2014 Feb; 20 (2): 232 - 9. [PMC free article] [PubMed]
- [11] Virulence and pathophysiology of the congo basin and west African strains of monkeypox virus in non - human primates DOI: 10.1099/vir.0.010207 - 0.
- [12] Monkeypox virus in Nigeria: infection biology, epidemiology and evolution <https://doi.org/10.3390/v12111257>.
- [13] <https://www.cdc.gov/poxvirus/monkeypox/outbreak/us-outbreaks.html>. 15) <https://www.google.com/amp/s/ncbiinsights.ncbi.nlm.nih.gov/2022/05/26/monkeypox-virus-genome/amp/>.
- [14] <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2022.27.22.2200422?crawler=true>.
- [15] Monkeypox transmission and pathogenesis in prairie dogs: jeannette guarner, bill j johnson and the veterinary monkeypox virus working group.
- [16] Transmission of monkeypox virus through sexual contact – a novel route of infection DOI: <https://doi.org/10.1016/j.jinf.2022.05.028>.
- [17] Clinical and virological features of first human monkeypox cases in Germany <http://coi.org/10.21203/r3-1725831/v1>.
- [18] <https://www.who.int/news-room/questions-and-answers/item/monkeypox>.
- [19] Clinical feature and management of human monkeypox: retrospective observational study in the UK. [https://doi.org/10.1016/S1473-3099\(22\)00228-6](https://doi.org/10.1016/S1473-3099(22)00228-6).
- [20] epidemiological trends and clinical features of the ongoing monkeypox epidemic: a preliminary pooled data analysis and literature review Nicola Luigi Bragazzi, Jude Dzevela Kong<sup>1</sup>, Naim Mahroum<sup>2</sup>, Christina Tsigalou, Rola Khamisy - Farah, Manlio Converti<sup>1</sup>, Jianhong Wu<sup>1</sup> 'Laboratory for Industrial and Applied Mathematics (LIAM). Department of Mathematics and Statistics. York University, Toronto, ON, Canada.
- [21] A novel international monkeypox outbreak <https://doi.org/10.7326/M22-1581>.
- [22] Human monkeypox: andrea M. McCollum, inger K. Damon. <https://doi.org/10.1093/cid/cit703>.
- [23] Centers for Disease Control and Prevention. Clinical Recognition. Accessed at [www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html](http://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html) on 19 May 2022.
- [24] UK Health Security Agency (UKHSA). Monkeypox contact tracing guidance: classification of contacts and advice for vaccination and follow up. London: UKHSA; Published: 20 May 2022. [Accessed 26 May 2022]. Available from: [http://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/107732/9/20220520\\_monkeypox\\_contact\\_tracing\\_classification\\_and\\_vaccination\\_matrix.pdf](http://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/107732/9/20220520_monkeypox_contact_tracing_classification_and_vaccination_matrix.pdf).