**Mpox (Monkeypox) – A Comprehensive Overview**

**Abstract**

Monkeypox is a zoonotic viral disease caused by the Monkeypox virus (MPXV), a member of the *Orthopoxvirus* genus. Initially identified in 1958 in research monkeys andthe first human case was identified in 1970 in the Democratic Republic of Congo (DRC). Monkeypox primarily impact Central and West African regions but has emerged globally as a public health concern, with outbreaks occurring in non-endemic nations.The disease manifest with influenzae-like symptoms, fever, lymphadenopathy, and a distinctive rash that evolves from macules to papules, vesicles, and pustules. Transmission occurs through close contact with infected individuals, body fluids, respiratory droplets, or contaminated surfaces. Zoonotic transmission originates from interaction with diseased animals, especially rats, considered to be the principal reservoirs. The 2022 multi-country outbreak highlighted the risk of human-to-human transmission in highly populated areas and among susceptible groups, including immunocompromised adults and children. The management of monkeypox is supportive, emphasising symptom alleviation and prevention of subsequent infections. Vaccines, including Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN)) and ACAM2000, are effective against susceptible high-risk populations. Antiviral agents like tecovirimat have also shown promising results in severe cases. Containment strategies emphasize surveillance, public awareness, and vaccination campaigns targeting at-risk groups. The emergence of monkeypox underscores the necessity for improved monitoring of zoonotic diseases and international collaboration in tackling neglected tropical diseases.

**Keywords**: Monkeypox, zoonotic virus, *Orthopoxvirus*, vaccination, anti-virals

**Introduction**

Mpox (Monkeypox) is a zoonotic viral disease caused by the Monkeypox virus (MPXV), a member of the genus *Orthopoxvirus*, family *Poxviridae*. It exhibits structural and genetic similarities with the Variola virus, the causal agent of smallpox, leading to some overlapping clinical features. The disease was initially identified in laboratory monkeys in 1958 and was first documented in people in the year 1970 at Democratic Republic of Congo (DRC). The population that is immunologically naïve to orthopoxviruses has markedly risen due to the discontinuation of major smallpox vaccination programs [1,2] Since then, it has remained endemic in Central and West Africa, with periodic outbreaks globally.

The population that is immunologically naïve to orthopoxviruses has markedly risen due to the discontinuation of major smallpox vaccination programs. As of September 01, 2024, 15 African countries have reported 3,900 confirmed cases of the disease. [3] The Democratic Republic of the Congo, Burundi, and Nigeria are the three countries with the highest case counts this year. Since the World Health Organization's declaration of a Public Health Emergency of International Concern (PHEIC) in 2022, India has reported 30 cases of Mpox. This declaration underscores the seriousness of the problem and advocates for comprehension of the disease's virology, transmission, clinical characteristics, and management approaches.

**Virology**

***Morphology and Genome:***

Monkeypox virus (MPXV) is an enveloped double-stranded DNA virus that belongs to

the *Orthopoxvirus* genus of the *Poxviridae* family. Two clades of MPXV are recognized [4]:

* **Clade I (Central African clade)**: More virulent, with higher case fatality rates.
* **Clade II (West African clade)**: Less severe disease and lower transmissibility rates

The Congo Basin clade has historically caused more severe disease and was believed to be more contagious. The geographical division between the two clades has so far been in Cameroon- the only country where both virus clades have been found. Outbreaks occurring outside endemic regions are frequently associated with foreign travel or the importation of animals.

***Replication:***

Natural reservoir is still unknown. However, certain rodents (including rope squirrels, tree

squirrels, Gambian pouched rats, dormice) and non-human primates are known to be naturally

susceptible to monkeypox virus. The virus replicates within the host cytoplasm, utilising its DNA-dependent RNA polymerase, so circumventing the necessity for nuclear transcriptional machinery.[5,6]

**Recent Outbreaks**

* 2022-2023 global outbreak: Characterized by human-to-human transmission, with the majority of cases reported among men who have sex with men (MSM) networks.
* Surveillance and genomic sequencing revealed that these cases were predominantly caused by Clade IIb variants.

**Incubation Period -** Typically 5–21 days, with an average of 6–13 days.

**Period of communicability**: 1-2 days before the rash to until all the scabs fall off/gets subsided.

**Mode of transmission:**

Human-to-human transmission is known to occur primarily through large respiratory droplets generally requiring a prolonged close contact. Transmission can occur via direct contact with body fluids or lesion material, as well as indirectly through contaminated clothing or linens of an infected individual.[7]

Transmission from animals to humans may occur by bites or scratches from infected animals, such as small mammals (e.g., rodents like rats and squirrels) and non-human primates (e.g., monkeys and apes), or through the preparation of bushmeat.

**Clinical Manifestations**

Monkeypox is usually a self-limited disease with the symptoms lasting from 2 to 4 weeks.

Severe cases occur more commonly among children and are related to the extent of virus

exposure, patient health status and nature of complications.[8] The extent to which asymptomatic infection occurs is unknown. The historical case fatality ratio of monkeypox has varied from 0% to 11% in the general population, with elevated rates observed in young children. Recently, the case fatality ratio has ranged from 3% to 6%.

**Phases of Illness**

Prodrome (0-5 days)

1. Fever
2. Lymphadenopathy

* Usually coincides with fever onset
* Periauricular, axillary, cervical or inguinal
* Unilateral or bilateral

1. Headache, muscle aches, exhaustion
2. Chills and/or sweats
3. Sore throat and cough

Skin involvement (rash) [9]

1. Usually begins within 1-3 days of fever onset, lasting for around 2-4 weeks

Deep-seated, well-circumscribed and often develop umbilication.

1. Lesions are often described as painful until the healing phase when they become

itchy (in the crust stage)

1. Stages of rash (slow evolution)

* Enanthem - first lesions on the tongue and oral cavity
* Macules originating on the face and disseminating to the arms, legs, palms, and soles (centrifugal dispersion) within 24 hours.
* The rash progresses through macular, papular, vesicular, and pustular stages. The classic lesion is vesiculopustular.
* Involvement by area: face (98%), palms and soles (95%), oral mucous membranes (70%), genitalia (28%), conjunctiva (20%). Skin rashes are typically more visible on the limbs and face than on the trunk. The genitalia may be affected, presenting a diagnostic challenge in the sexually transmitted disease population.
* By 3rd day, lesions progress to papules
* By the fourth to fifth day, lesions transform into vesicles that are elevated and filled with fluid.
* By the sixth to seventh day, lesions become pustular, sharply elevated, filled with opaque fluid, hard, and deeply seated.
* May umbilicate or become confluent
* By the end of 2nd week, they dry up and crust
* Scabs remain for a week before falling off
* The lesion heals with hyperpigmented atrophic scars, hypopigmented atrophic scars, patchy alopecia, hypertrophic skin scarring and contracture/deformity of facial muscles following healing of ulcerated facial lesions
* A notable predilection for palm and soles is characteristic of monkey pox

1. The skin manifestation depends on vaccination, age, nutrition,

and associated HIV status. Monkeypox primarily manifests in populations where there is often a high background prevalence of malnutrition, parasitic infections, and other significant heath-compromising conditions, any of which could impact the prognosis of a patient with MPX.

1. The total lesion burden at the apex of rash can be quite high (>500 lesions) or relatively slight (<25).

**Complications**

* Secondary bacterial infections
* Sepsis
* Pneumonia
* Encephalitis
* Corneal infections leading to blindness

**Diagnosis**

For the confirmation of Monkeypox on the suspected clinical specimens:

1. Polymerase Chain Reaction (PCR): Gold standard, for detecting *Orthopoxvirus* genus [Cowpox, Buffalopox, Camelpox, Monkeypox].[10]
2. If a specimen tests positive for Orthopoxvirus, it must be further validated by Monkeypox-specific conventional PCR or real-time PCR for Monkeypox DNA
3. Furthermore, viral isolation and Next Generation Sequencing of clinical samples (Miniseq and Nextseq) are feasible.

**Differential Diagnoses**

* Smallpox
* Chickenpox (Varicella)
* Measles
* Secondary syphilis
* Disseminated herpes zoster
* Disseminated herpes simplex
* Hand foot mouth disease
* Infectious mononucleosis
* Molluscum contagiosum.

**Management**

***Preventive Strategies***

Prevention generally emphasises increasing awareness of risk factors and educating individuals on minimising exposure to the virus.[11],12 Key preventive measures encompass:

* Avoid contact with materials (e.g., bedding, clothing) that have been in contact with infected individuals.
* Isolating infected patients from others.
* Engaging in proper hand hygiene, including washing hands with soap and water or utilising alcohol-based hand sanitisers, particularly following contact with infected animals or individuals.
* Utilising suitable personal protection equipment (PPE) during patient care.
* Correctly managing and disposing of contaminated waste (e.g., dressings) in accordance with Biomedical Waste Management protocols for infectious materials

***Supportive Care***

* Protection of compromised skin and mucous membranes
* Skin rash
  + Disinfect with a basic antiseptic
* Mupironic Acid/Fucidin
* Cover with light dressing if extensive lesion present
* Avoid touching or scratching the lesions
* In case of secondary infections, relevant systematic antibiotics may be considered
* For Genital ulcers sitz bath are beneficial
* Warm saline gargles/ oral topical anti-inflammatory gel to be applied for oral ulcers.
* Conjunctivitis
* Typically, self-limiting
* Consult an ophthalmologist if symptoms persist
* Eye pain/ visual disturbances
* Rehydration therapy and nutritional support
* Symptomatic relief, hydration, and treatment of secondary infections.
* Antipyretics for fever and analgesics for pain relief.
* Topical Calamine lotion and Anti-histaminics for pruritis and itching.

***Antiviral Therapy***

Currently there is no approved medicinal treatment specifically for monkeypox infections. However, some antivirals developed for use in smallpox patients may prove useful against MPX: Tecovirimat or ST-246, Cidofovir, and Brincidofovir.[13,14]

***Vaccination***

* **Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN)** vaccine available in the name - JYNNEOS: Effective pre- and post-exposure prophylaxis.[15]
* **ACAM2000**: A live, replication-competent vaccine that may be administered to select individuals following a personalised evaluation when alternative vaccinations are unavailable.

**Public Health Implications**

***Prevention Strategies***

1. **Vaccination Campaigns**: Target high-risk groups, including healthcare workers and MSM populations.
2. **Surveillance Systems**: Strengthen monitoring in endemic regions.
3. **Public Education**: Enhance awareness on transmission prevention and initial symptoms

***One Health Approach***

The management of Monkeypox under the One Health framework emphasizes the interconnectedness of human, animal, and environmental health to prevent and control outbreaks. Monkeypox, being a zoonotic disease, necessitates concerted efforts to monitor and manage its transmission between animals and people. Surveillance systems must identify cases promptly in both communities, while public education initiatives advocate for hygiene, safe animal handling, and symptom awareness Vaccination and isolation of human cases, alongside monitoring and reducing contact with animal reservoirs like rodents and primates, are key strategies. Environmental initiatives, such as effective waste management,restriction of deforestation andmitigation of spill over risks. By fostering collaboration among healthcare providers, veterinarians, ecologists, and policymakers, the One Health approach ensures a comprehensive and sustainable response to Monkeypox.

**Conclusion**

Monkeypox is a re-emerging zoonotic disease that poses significant public health challenges due to its ability to spread across humans, animals, and environments. Effective management necessitates a multi-faceted approach encompassing surveillance, vaccination, public education, and robust healthcare infrastructure. Addressing the ecological and societal factors driving its resurgence, such as deforestation and wildlife interaction, is equally critical. Implementing a One Health paradigm facilitates interdisciplinary collaboration, uniting human, animal, and environmental health to alleviate outbreaks. Continued research, resource allocation, and global cooperation are essential to control Monkeypox and prevent future zoonotic disease threats, safeguarding public health and biodiversity alike.

Greek Symbols and Special Characters -None

Equations and Mathematical Ex Publisherions -None

Patient Consent NA

Ethical issues -None

**List of Abbreviations**

1. MPXV – Monkeypox virus
2. DRC - Democratic Republic of the Congo
3. PCR - Polymerase Chain Reaction
4. MVA-BN- Modified Vaccinia Ankara-Bavarian Nordic
5. PHEIC - [Public health emergency of international concern](https://en.wikipedia.org/wiki/Public_health_emergency_of_international_concern)
6. MSM- Men sex with men
7. STD- Sexually transmitted diseases
8. HIV -Human Immunodeficiency Virus
9. PPE - Personal Protective Equipment
10. CDC – Centre for Disease Control

References -Enclosed with main text

Figure/Illustrations -None

Chemical Structures -None

Tables -None

Supportive/Supplementary Material –None

Disclaimer

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

**References**

1. 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 Feb 11;16(2):e0010141.
2. Rimoin, A.W., Mulembakani, P.M., Johnston, S.C., Lloyd Smith, J.O., Kisalu, N.K., Kinkela, T.L., Blumberg, S., Thomassen, H.A., Pike, B.L., Fair, J.N. and Wolfe, N.D., 2010. Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo. *Proceedings of the National Academy of Sciences*, *107*(37), pp.16262-16267.
3. Mpox(Monkeypox) Outbreak: Global Trends202246 [https://worldhealthorg.shinyapps.io/mpx\_global /#5\_Genomic\_epidemiology](https://worldhealthorg.shinyapps.io/mpx_global%20/#5_Genomic_epidemiology)
4. Likos AM, Sammons SA, Olson VA, Frace AM, Li Y, Olsen-Rasmussen M, Davidson W, Galloway R, Khristova ML, Reynolds MG, Zhao H. A tale of two clades: monkeypox viruses. Journal of General Virology. 2005 Oct;86(10):2661-72.
5. Petersen BW, Karem KL, Damon IK. Orthopoxviruses: Variola, vaccinia, cowpox, and monkeypox. Viral infections of humans: Epidemiology and control. 2014:501-17.
6. Shchelkunov SN. Orthopoxvirus genes that mediate disease virulence and host tropism. Advances in Virology. 2012;2012(1):524743.
7. Fine PE, Jezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. International journal of epidemiology. 1988 Sep 1;17(3):643-50.
8. Adler H, Gould S, Hine P, Snell LB, Wong W, Houlihan CF, Osborne JC, Rampling T, Beadsworth MB, Duncan CJ, Dunning J. Clinical features and management of human monkeypox: a retrospective observational study in the UK. The Lancet Infectious Diseases. 2022 Aug 1;22(8):1153-62.
9. Wang X, Lun W. Skin manifestation of human monkeypox. Journal of Clinical Medicine. 2023 Jan 24;12(3):914.
10. da Silva SJ, Kohl A, Pena L, Pardee K. Clinical and laboratory diagnosis of monkeypox (mpox): Current status and future directions. Iscience. 2023 Jun 16;26(6).
11. Lepelletier D, Pozzetto B, Chauvin F, Chidiac C. Management of patients with monkeypox virus infection and contacts in the community and in healthcare settings: a French position paper. Clinical Microbiology and Infection. 2022 Dec 1;28(12):1572-7.
12. Johri N, Kumar D, Nagar P, Maurya A, Vengat M, Jain P. Clinical manifestations of human monkeypox infection and implications for outbreak strategy. Health Sciences Review. 2022 Dec 1;5:100055.
13. de la Calle-Prieto F, Muñoz ME, Ramírez G, Díaz-Menéndez M, Velasco M, Galparsoro HA, Lletí MS, Forte TM, Blanco JL, Mora-Rillo M, Arsuaga M. Treatment and prevention of monkeypox. Enfermedades infecciosas y microbiologia clinica (English ed.). 2023 Dec 1;41(10):629-34.
14. Parker S, Handley L, Buller RM. Therapeutic and prophylactic drugs to treat orthopoxvirus infections. Future Virology. 2008 Nov 1;3(6):595-612.
15. Poland GA, Kennedy RB, Tosh PK. Prevention of monkeypox with vaccines: a rapid review. The Lancet Infectious Diseases. 2022 Dec 1;22(12):e349-58.