



## MPOX VIRUS INFECTION IN HUMANS: A REVIEW

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**ABSTRACT** Zoonotic Mpox (formerly Monkeypox) infection has been noted in endemic areas such as Central and West Africa. In recent times, known cases were found in non-endemic areas and WHO declared the Mpox outbreak as a Public Health Emergency of International Concern. In this review we focused on the details of Mpox infection, its diagnosis and treatment.

**KEYWORDS :**

Mpox formerly known as Monkey pox is a zoonotic viral disease caused by the Monkeypox Virus (MPXV), a brick shaped, double-stranded DNA virus belonging to the *Orthopoxvirus* genus of the *Poxviridae* family. Other members of this genus include Variola virus (VPXV), Cowpox virus (CPXV) and Camelpox virus (CMLV) [1]. MPXV has two distinct clades: I (with subclades Ia and Ib) and II (with subclades IIa and IIb). These clades were formerly known as the "Congo Basin" and the "West African" clades respectively.

The virus, like other members of the *Orthopoxvirus* genus, has a central conserved core region and variable regions at the left and right ends. Species and strain specific characters for Orthopoxviruses are found in the variable region. The Mpox virus strains isolated in 2022 have exhibited a higher number of Single Nucleotide Polymorphisms (SNPs) when compared to those isolated in 2017 and 2018 [1].

**EPIDEMIOLOGY**

The virus was first identified among laboratory monkeys in Denmark in 1958. The first human case was reported from the Democratic republic of Congo (DRC) in a 9-month-old boy in 1970. Since then, the virus has been an endemic in the countries of Benin, Cameroon, the Central African Republic, the DRC, Gabon, Ivory Coast, Liberia, Nigeria, the Republic of the Congo, Sierra Leone, and South Sudan [2]. The 2003 Mpox outbreak in the United States marked the first occurrence in a non-endemic region. It was caused by a shipment of infected mammals from Ghana and was particularly severe in pediatric patients, with one-fifth experiencing serious complications.[1]

In the endemic region, the DRC has reported yearly cases of Mpox, with the tropical region of the country being responsible for 98.7% of global cases before 2022. Between 2017 and 2022, Nigeria reported a total of 830 Mpox cases [2].

In the non-epidemic region, 11 travel related Mpox cases were reported in the US, UK, Israel and Singapore between 2018 and 2021. These cases were determined to have been originated in Nigeria and confirmed to be Clade II [2].

In July 2022, the WHO declared Mpox to be a Public Health Emergency of International Concern (PHEIC) after an outbreak of Mpox was seen in countries with no history of sustained transmission. Of the 82807 confirmed cases between January 1, 2022 and January 29, 2023, majority were Clade IIb (lineage B.1). 96.4% of the cases were reported among men and 86.9% of these were identified in Men having Sex with Men (MSM), with the most common route of transmission being sexual contact (68.7%). Hospitalization rates were noted to be at 7.3% but higher risks were observed in children, adults over the age of 65 and immunocompromised individuals [3]. As of August 2, 2023, there were a total of 152 deaths in the 88600 laboratory confirmed cases (case-fatality rate of 0.17%) across 113 countries [2]. Owing to significant progress in controlling the outbreak globally, the

WHO Director General on recommendation of the IHR committee removed Mpox's PHEIC status in May 2023. However, after a rise in Mpox cases in the DRC and neighboring countries, the WHO, for a second time in two years, declared Mpox to be a PHEIC in August 2024. The virus affecting the DRC and its neighboring countries is Clade Ib, which has been determined to be "High Risk" by the WHO. A total of 8- countries have reported 19823 cases with 73 Mpox deaths in 2024. As of October 2024, the number of monthly reported new cases has decreased by 11.4%, compared to the previous month [4].

India has reported 30 cases of Mpox since WHO's 2022 PHEIC declaration and has since been taking proactive measures against the viral disease, with involvement of experts from National Centre for Disease Control (NCDC), Indian Council of Medical Research (ICMR), Director General of Health Services (DGHS) and various central and state government hospitals among others [5].

**CLINICAL FEATURES OF MPOX**

MPXV, due to its highly evolving nature, is characterized by varied manifestations impacting multiple organ systems. The disease is transmitted through direct contact with saliva and respiratory droplets from infected individuals. There is a significant risk of contact transmission via clothing, bedding, and fabric used by the affected patient. Vertical transmission from a pregnant woman to the fetus is possible during pregnancy and childbirth. Sexual contact is the primary mode of transmission in the most recent outbreak with 68.7% of the reported cases. Most number of cases were reported among men who have sex with men (MSM) [1]. MPXV has an incubation period of 7-14 days, post which clinical symptoms are manifested. Patients experience fever, chills, headache, myalgia and lymphadenopathy along with skin lesions, often presented as rashes, pustules, scars [1]. The clinical manifestations of Mpox in different organ systems are as listed below.

1) Cutaneous manifestations: Skin lesions are a universal manifestation of Mpox, presenting in various forms, including pustules, papules, macules, and ulcers. Pustules are the most common lesions, as seen in 46% of cases; followed by papular lesions in 33%, vesicular lesions in 27% and ulcerative lesions in 13%. The lesions which initially start out as vesicular eruptions, later progress into papules and finally form ulcerating lesions on the skin. Before 2022, Mpox associated skin lesions were moderate in severity, whereas post-2022 cases have exhibited milder lesions. Complications of skin lesions have been reported to cause ocular lesions, bacterial infections, hemorrhagic pustules and necrotic lesions. While facial lesions were the most prominent skin lesions before 2022, genital lesions have become more common in the recent outbreak. Perianal and rectal lesions have also been observed in the recent outbreaks which were previously absent. Angiogenital lesions on the penis with painful lymphadenopathies have been seen in sexually transmitted cases. Location of genital rashes are often related to the site of sexual contact. [11]

2) Neurological manifestations: Headache is the most frequently reported neurological symptom of Mpox, with more prevalence in the previous outbreaks. Symptoms like myalgia, fatigue and malaise are commonly observed. Complications of neurological symptoms include seizures, confusion and encephalitis. Photophobia and visual defects, although less common, have been reported in a few patients [11].

3) Oral manifestations: Sore throat is a usual manifestation, associated with mouth sores, tonsillitis and rashes. Complications could lead to oral ulcers and dysphagia. In cases prior to 2022, facial lesions were observed to appear before the development of oral lesions. [7]

4) Ocular manifestations: Most common ophthalmic manifestations of Mpox are conjunctivitis and eye lesions, with more prevalence in prior outbreaks. Eye lesions could vary from lesions on the eye lids to corneal and conjunctival lesions. Photophobia has been reported in a few cases. Complications could lead to keratitis, corneal ulceration, unilateral blindness and impaired vision.

5) Respiratory manifestations: Cough was a common symptom reported in nearly one-half of the cases prior to 2022. Other respiratory symptoms like nasal congestion and dyspnea have also been documented, although there has been a decreasing trend in the respiratory symptoms since 2022. Only 7% of patients have been presented with cough during the 2022 outbreak [8].

6) GIT: Anorexia and decreased appetite have been observed. Nausea and vomiting maybe occasionally seen. Rectal/anal pain combined with bleeding has been prevalent in the 2022 outbreak.

7) Cardiovascular manifestations: Myocarditis is a common manifestation of Mpox. It is often associated with symptoms like chest pain and dyspnea.

8) Mpox complications in pregnancy: A study has reported that nearly one half of the pregnant women affected by Mpox have experienced fetal deaths. No maternal deaths have been reported so far. Fetal loss and miscarriages have been high in early trimesters of pregnancy [9].

## DIAGNOSIS OF MPOX

Identifying symptoms and diagnosing the disease early are crucial for effective management. Administering post-exposure prophylaxis promptly after early detection can lead to a more favorable prognosis. The real time quantitative Polymerase Chain Reaction (qPCR) remains the cornerstone for MPXV testing but other techniques like Loop Mediated Isothermal Amplification (LAMP) based assays are also in the process of development. Studies suggest that while PCR testing of skin lesions has the highest yield (clinical sensitivity between 91-100%), high sensitivity has also been reported for testing of rectal swabs (78-97%) and upper respiratory specimens (69-100%) [10]. Numerous rapid antigen and antibody tests have been developed for different types of specimens. Recently, CRISPR-based assays have been developed for point-of-care testing (POCT) due to their rapid detection capability and high specificity. A portable CRISPR-Cas12a based assay has been developed for the detection of MPXV [11]. These assays have proven to be more efficient than qPCR; however, they have not yet been commercialized for large-scale use.

## TREATMENT

Treatment is suggested for the patients who are suffering with severe infections, are immunocompromised or have aberrant infections. Although no specific treatment is recommended, drugs like brincidofovir, tecovirimat, and cidofovir are known to be effective against the virus [12]. Tecovirimat has been used as an effective antiviral Mpox drug during the 2022 outbreak [13]. Although no clinical evidence has been reported for the use of cidofovir against the Mpox infection, CDC recommends the outbreak of Orthopoxviruses including Mpox can be effectively treated with this drug [14].

## VACCINATION

There exists no vaccine specifically for Mpox. Studies reported that the first-generation live vaccinia vaccines provided protection against the infection due to cross reactive antibodies [15]. The second-generation vaccine, CAM2000, is a live attenuated vaccinia vaccine and was found to be protective when challenged against aerosolized Mpox virus in cynomolgus macaques [16]. A smallpox vaccine, JYNNEOS known to be effective against Mpox is the only FDA approved vaccine at present [17].

## CONCLUSION

Mpox has been declared as a public health emergency of international concern and people should know about the important pathways of pathogenesis, spread and manifestations of the infection. Countries all over the world must develop and enhance their diagnostic capabilities to deal with the widespread infection while also focusing on its clinical management, prevention and control.

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