

**Review article****Monkeypox Virus the whole story**

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**ABSTRACT**

Monkeypox is caused by a Monkeypox virus that is closely linked to the smallpox virus and spreads through close contact between humans and animals. Monkeypox is only protected by smallpox immunization. Until this year, when more than 16,000 cases have been recorded from nonendemic nations, the global scientific community ignored the gradual rise in Monkeypox cases in Africa over the previous few decades. The WHO declared Monkeypox to be a public health emergency of global significance. The disease poses a greater hazard to the general population. The condition is distinguished by a brief febrile illness with lymphadenopathy followed by a rash that develops in phases of macules, papules, vesicles, and pustules before spreading centrifugally. Most cases recover within 2-4 weeks. Children, pregnant women, and immunocompromised people are more likely to experience complications. For high-risk groups, healthcare professionals, and close connections, vaccination with smallpox vaccines currently on the market is advised. Tecorivimat is an effective antiviral medication. A multifaceted approach is required to contain the monkeypox outbreak, including increased surveillance, early diagnosis, isolation of infected patients, and immunization.

**Keywords:** *Monkeypox, Immunization, Smallpox.*

**Introduction****1. Monkeypox virus and its structure**

A smallpox-like illness is caused by monkeypox disease, which is closely linked to the variola virus (smallpox virus). The monkeypox virus, is a member of the Orthopoxvirus genus, *Chordopoxvirinae* subfamily, and Poxviridae family. It is currently uncommon zoonotic illness. The incubation period for monkeypox in humans is comparable to that of human pox (smallpox) and it is about 10–14 days (Bunge et al., 2022).

Monkeypox was initially detected in 1958 when two outbreaks occurred in monkeys housed for study and developed a pox-like illness. The illness was first identified in humans in 1970 when a kid in the Democratic Republic of Congo was suspected of having smallpox. In 2003, the first monkeypox epidemic outside Africa was

recorded in the United States of America (Yang et al., 2022). An epidemic of monkeypox (MPX) was also detected in the United Kingdom on May 6, 2022, and it was traced back to a British citizen who had visited Nigeria. As of May 21, 2022, 13 countries where the monkeypox virus (MPXV) is not endemic has reported 92 confirmed cases globally. Thus far, incidents that have been reported have mostly, but not completely, involved homosexual and bisexual males in their 20s to 50s (Hraib et al., 2022).

Monkeypox virus is endemic to Central and West Africa. Transmission occurs through direct, close contact with a person during their infectious stage through droplets, contact with infectious fluids, or via fomites, it is less common to be airborne transmission. Fever, rash, and swollen lymph nodes are frequently symptoms of monkeypox disease. The monkeypox virus (MPXV) is spread from infected people or animals to humans through close contact (Yadouleton et al., 2022). A wide range of complications may occur as a result of monkeypox viral infection that involves; bacterial superinfection of skin, permanent skin scarring, hyperpigmentation or hypopigmentation, permanent corneal scarring (that may lead to vision loss), pneumonia, sepsis, acute myocarditis, encephalitis and death (Reynolds et al., 2017).

Poxviruses are large, linear, double-stranded DNA viruses that reproduce in the cytoplasm of vertebrate or invertebrate cells. Their genome size ranges from 130 to 360 kbp (Kaler et al., 2022). Several orthopoxviruses have similar genetic and antigenic characteristics. If you get infected with any of these viruses, this may offer significant protection for you against other viruses in the orthopoxvirus genus (Petersen et al., 2019).

Poxviruses contain the biggest DNA genome of any animal virus. The core, lateral bodies, outer membrane, and the outer lipoprotein envelope are the virion's four main components, as illustrated in figure 1. The viral dsDNA and core fibrils are located in the central core. The major genomic section of the monkeypox virus, which has a genome size of 197 kb, is 101 kb long (Huang et al., 2022). Genes responsible for viral replication, transcription, assembly, and release are conservatively located in the genome's central region, as they are in all orthopoxviruses. Most of the genes expressing virulence are found at both ends of the genome. These terminal genes play a role in the immune evasion by interfering with signalling, presentation, and recognition of antigens and apoptosis (Huang et al., 2022).

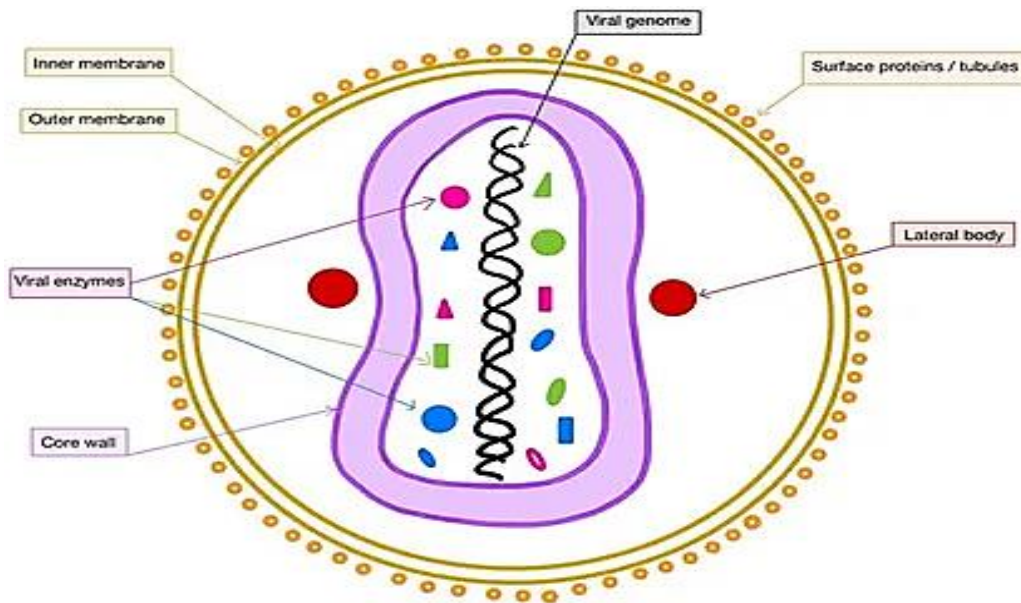


Figure (1): Structure of monkeypox. Lu et al. (2022).

## 2. Mode of transmission

Monkeypox viral infection is transmitted from human to human by direct, close contact, oral/respiratory secretions, droplets, skin lesions or through contaminated fomites. Sexual contact especially between homosexual partner plays an important role in monkeypox viral transmission as reported by Iñigo et al., (2022). Infected animal can transfer infection to human. Also, the mother can transfer infection to her foetus via placenta, this is called congenital monkeypox that may result in an anomaly of the foetus. Airborne transmission is considered to be less common (Nalca *et al.*, 2005). Congenital monkeypox infection has been described in one case series from the Democratic Republic of the Congo. It causes stillbirth which is a tragically common outcome (Mbala *et al.*, 2017). Three of the four infections described in this case series occurred after maternal infection in the first and second trimester, and resulted in foetal demise (Kisalu *et al.*, 2017). Vertical transmission was confirmed in one foetus, presenting with elevated viral loads in foetal tissues, disseminated cutaneous lesions, hepatomegaly and hydrops fetalis (Mbala *et al.*, 2017).

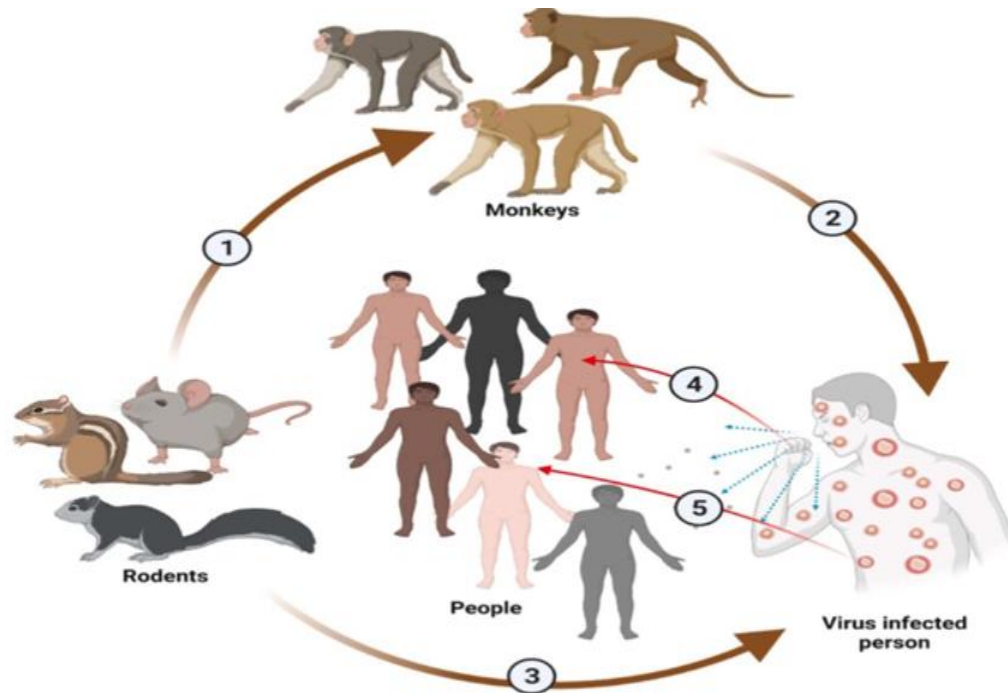


Figure (2): Mode of transmission of Monkeypox virus (Kumar et al., 2022).

### 3. Clinical manifestations of Monkeypox

#### 3.1 Skin manifestation

Monkeypox has an average incubation period of 8.5 days. The invasion stage lasts between 0 and 5 days and involves; fever, severe headache, chills, exhaustion, asthenia, lymphadenopathy (swelling of the lymph nodes), back pain, and myalgia. The skin eruption period often starts one to three days after the onset of a fever (Yinka-Ogunleye et al., 2022; Miura et al., 2022). The rash frequently starts on the face and quickly spreads over the body. The typical Monkeypox rash on humans starts as 2–5 mm-diameter maculopapular lesions. The face makes up for 95% of all cases of the rash, followed by the palms of the hands and soles of the feet in 75% of cases, oral mucous membranes in 70% of cases, genitalia in 30% of cases, conjunctivae in 20% of cases, and cornea in 20% of cases (Jezek et al., 1987; Luo and Han et al., 2022).

Sometimes, patients get a spherical rash resembling that of chickenpox. The subsequent phases of Monkeypox lesions range from blister-like lesions to scabs and last for 1-2 days each. The number of lesions varies from a few to several thousand. The rash develops sequentially from macules to papules, vesicles, pustules, and crusts that dry up and fall off (Breman and Henderson, 2004; Hobson et al., 2021).

The person is no longer contagious once the scabs on their lesion peel off to reveal healthy tissue underneath, which typically takes 2-4 weeks after the symptom first appears. Because Monkeypox causes a rash, it must be differentiated from other illnesses that also generate a rash (Petersen et al., 2022).



Figure (3): Skin manifestation of leg and face (Wang et al., 2023)

### 3.2. Respiratory symptoms

Monkeypox can spread by airborne droplets. To shield sick patients from airborne transmission channels, it is advised that they wear personal protective equipment close to infected patients. Patients with monkeypox infection have been reported to experience respiratory symptoms such as coughing, dyspnea, and nasal congestion (Orviz et al., 2022). However, secondary bacterial infections by *Streptococcus pneumonia* and *Mycoplasma pneumonia*, have been linked to pharyngeal inflammation and bronchopneumonia, which can cause respiratory distress and make breathing difficult. Consequently, (Damon, 2011; Petersen et al., 2019).

### 3.3 Backache and Myalgia

Patients have described other typical physical symptoms that typically appear together with the development of a fever, such as weariness, headache, and myalgia (muscle discomfort). Before the

cutaneous rash appears, infected patients may be misdiagnosed with flu-like symptoms since these symptoms are not disease-specific (Petersen et al., 2019; Kumar et al., 2022).

### **3.4 Digestive system symptoms**

Another uncommon viral infection consequence that typically happens in the second week of infection is GIT manifestation that involves diarrhea and vomiting, which causes dehydration and deteriorates general health (Damon, 2011; Petersen et al., 2019).

### **3.5 Corneal ulcers**

Several individuals also experienced corneal ulcers and keratitis, which led to vision loss and opacity. Fortunately, the symptoms disappear quickly when antimicrobials are used (Adler et al., 2022; Damon, 2011).

## **4. The virulence of Monkeypox virus**

Monkeypox virus replicates in the host cell's cytoplasm. A unique feature of poxviruses is that they produce two types of infectious particles: extracellular virions (EVs) and mature virions (MVs). Both viral particles have different viral surface epitopes (Huang et al., 2022).

Despite not being able to identify specific receptors for poxviruses, several glycosaminoglycans, such as laminin, heparin sulphates, and chondroitin, help the virus attach to cells. Virion binding to the membrane and fusion with the host cell occurs after viral attachment, resulting in the release of the virion's core into the cytoplasm of the cell. Transcription-starting enzymes and factors are present in the virion core (Huang et al., 2022).

## **5. Diagnosis of Monkeypox virus**

An individual with the mentioned symptoms may have monkeypox, especially if he has travelled to endemic area or had contact with people who have the disease. The gold standard for diagnosis of monkeypox virus is the polymerase chain reaction (PCR) test, which should be carried out first. PCR can confirm a suspected case of monkeypox. If monkeypox infection is still suspected after a negative PCR test, additional confirmatory tests can be performed (Table 1). If a monkeypox PCR test results is a positive result, it is important to track down and test anybody who has come into contact with the patient, and if at all possible, vaccinate them (Cheema et al., 2022).

Table (1): Diagnostic tests for Monkeypox (Cheema et al., 2022)

Tests	description	Sample used
PCR	Real-time PCR is the gold standard.	Lesion fluid
Viral culture	The virus is grown and isolated from a patient sample	Lesion fluid
Electron microscope	Is used to morphologically identify pox virus	Biopsy specimen, Vesicular fluid
Immunohistochemistry	Detect the specific virus antigen	Biopsy specimen
IgG and IgM tests	To asses recent or remote exposure to the virus	Blood specimen

## 6. Complications of Monkeypox

A potential complication of the monkeypox virus is acute myocarditis which was reported in one case. Days following the onset of skin lesions, a 31-year-old male patient with a confirmed monkeypox infection developed acute myocarditis. Myocardial inflammation was confirmed by a cardiac magnetic resonance examination. That patient received supportive treatment and fully recovered clinically (Pinho et al., 2022).

Another serious complication of monkeypox on the eye is the development of ocular monkeypox. It results in conjunctivitis, blepharitis, keratitis, and vision loss (Cash-Goldwasser et al., 2022).

Regarding the foetal effect of monkeypox, a study that was performed on four pregnant participants who took part in an observational study performed by Mbala et al., (2017). He reported that one female delivered a healthy baby, two experienced first-trimester miscarriages, and one gave birth to a macerated stillborn who had diffused cutaneous maculopapular skin lesions covering his head, trunk, and extremities, including the palms of his hands and the soles of his feet.

## 7. Disease Spectrum in Children and the peripartum period

In patients who are immunosuppressed and/or children, problems can happen. There have been past reports of neurological symptoms such as encephalitis, convulsions, disorientation, discomfort, exhaustion, visual changes, photophobia, headaches, and myalgia. Either an immune-mediated mechanism or a viral invasion of the central nervous system can cause encephalitis (Puccioni-Sohler et al., 2022).

Even though monkeypox frequently has a substantial impact on children, there is little research on the paediatric (Huhn et al., 2005; Damaso, 2022). Children typically contract monkeypox at home or after having close contact with diseased animals (Nolen et al., 2015). Cohabitation in the same bed, room or the sharing of tools with an infected individual are two specific risk factors. In 2022, more and more kids have been exposed in households as the sickness has spread. Children under the age of 10 currently make up a significant share of deaths attributable to monkeypox, accounting for 100% of recorded fatalities from 1970 to 1999 to 37.5% from 2000 to 2019 (Bunge et al., 2022). Children who present with oropharyngeal monkeypox lesions and nausea or vomiting may need to stay in the hospital for a longer period of time. pneumonia, corneal ulceration, encephalitis, multi-organ failure, and (rarely) hepatosplenic infiltration are just a few of the severe signs that have been documented in newborns and young children and have the potential to be fatal or result in long-term damage (Sejvar et al., 2004). Clinical symptoms could resemble varicella zoster virus (VZV) infection (MacNeil et al., 2009). Also, co infection with VZV is a well-known condition (Hoff et al., 2017; Hughes et al., 2020).

## **8. Prevention of Monkeypox virus**

Using personal protective equipment suitable for MPX and instructions are important steps in the primary prevention of MPX of infection in Health Care Workers (Rimoin and Graham, 2011). Secondary methods of prevention involve the administration of smallpox vaccine. Research conducted before and right after smallpox eradication showed that smallpox vaccination could also provide protection against MPXV infections. The smallpox vaccine may cause adverse effects, like eczema vaccinatum and progressive vaccinia. The latter is an adverse effect in which uncontrolled vaccinia virus replication and results in death (Rimoin and Graham, 2011). Another example is the uncertain prevalence of human immunodeficiency virus (HIV) infection or other types of immunosuppression in monkeypox endemic



areas. Other significant issues include the possibility of foetal vaccinia, contact transmission of vaccination virus, and the presence of dermatological risk factors (Reed et al., 2012).

Persons infected with HIV and persons who have atopic dermatitis have been tested against third-generation vaccines (e.g., IMVAMUNE) produced using modern good manufacturing practices. Clinical trials have demonstrated the safety and immunogenicity of IMVAMUNE as well as the protection against monkeypox as was demonstrated in several animal model studies (Walsh et al., 2013).

## **9. Treatment of Monkeypox virus**

### **9.1 Supportive Care**

The majority of monkeypox patients heal without any medical assistance. To reduce gastrointestinal fluid losses, those with gastrointestinal symptoms such as vomiting or diarrhoea need oral or intravenous rehydration treatment. Rash shouldn't be touched or scratched and a local anaesthetic gel may be used. If the rash is itchy, an oral antihistamine or a topical anti-itch cream may be applied (Reynolds et al., 2017).

### **9.2 Antiviral drugs**

#### **a- Tecovirimat (TPOXX)**

Tecovirimat (ST-246) was approved for the treatment of smallpox. It is active only against orthopoxviruses. It is given either orally or intravenously. Orthopoxvirus inhibits the envelope wrapping protein (Reynolds., et al., 2017). The most common side effects after a dose of 600 mg for two weeks were weariness, headaches, and nausea (Siegrist and Sassine, 2022).

#### **b- Brincidofovir (tembexa)**

Since 2021, brincidofovir has been administrated for the treatment of smallpox in the US. The mechanism of action is by the inhibition of viral DNA polymerase. It has severe side effects like a decreased serum bicarbonate, proteinuria, neutropenia, hypotony of eye, iritis, uveitis, nephrotoxicity and fever (Chittick et al., 2017).

### **9.3 Vaccinia Immune Globulin (VIG)**

In principle, antibodies from human plasma of individuals immunized with the smallpox vaccine is injected to patient to provide passive immunity (Wittek, 2006). The use of VIG for monkeypox or smallpox has not been tested in humans, despite the fact that it is a potential treatment. Data on the effectiveness of VIG against monkeypox and smallpox are largely lacking.

## Conclusion

The monkeypox virus causes multi-system disorders. People should avoid direct skin contact with infected people and should avoid handling contaminated materials. Tecovirimat is the best treatment for the monkeypox virus. It prevents the progression to severe illness. Smallpox vaccines are important in stopping the spread of monkeypox. Although several researches have been published about the virus, we still need more research to save humanity from this illness.

## Disclosure

The authors have no conflicts of interest to declare

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