

## **A REVIEW FOR MEDICAL AND DENTAL PROFESSIONALS CONCERNING THE NEW MONKEY POX WARNING**

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**Abstract** MPXV, or monkeypox virus, is a member of the Poxviridae family and the Orthopoxvirus genus. Only two different species of wild animals—a rope squirrel in the Democratic Republic of the Congo and a sooty mangabey in Ivory Coast—have had a virus isolated from them. Protection against monkeypox infection after receiving the smallpox vaccine was calculated to be around 85%. Since smallpox was finally eradicated in 1980, widespread vaccination campaigns have tapered down. That opened the door for monkeypox to be considered as a bioterror threat.

**Keywords :** Monkeypox, Diagnosis, Africa, and the United States

### **Introduction**

Monkeypox virus (MPXV), a member of the Orthopoxvirus genus in the Poxviridae family, is the causative agent of this newly recognized zoonotic illness. MPXV is one of four species of

Orthopoxvirus that may cause disease in humans; the others being variola virus (which caused smallpox but has since been wiped from the natural world), cowpox virus, and vaccinia virus. The true host of monkeypox has not been identified, despite the fact that it can infect a broad variety of mammals. To date, the virus has only been isolated twice from wild animals, once from a rope squirrel in the Democratic Republic of the Congo (DRC) and once from a sooty mangabey in Ivory Coast. It is hypothesized that transmission takes place by contact with lesion exudate or crust material, or through saliva/respiratory excretions. Exposure to viruses may also occur through feces. In terms of symptoms, monkeypox is very similar to smallpox, with the exception of an early onset of fever and lymph node enlargement that sets MPX apart from smallpox. Rash symptoms, including fever, lymphadenopathy, and the development of lesions, typically begin 1-3 days after the onset of systemic symptoms. Their typical pattern of spread is at the periphery, but in extreme cases they may spread everywhere. It may take up to four weeks for the lesion to desquamate once the infection has cleared. Secondary bacterial infections, respiratory distress, bronchopneumonia, gastrointestinal involvement, dehydration, sepsis, encephalitis, and corneal infection leading to vision loss are all possible consequences. Supportive care and symptomatic treatment are used to manage people with monkeypox virus infections because there is presently no cure.<sup>1</sup> Case ascertainment bias can cause a significant amount of variation in reported death rates. Outbreaks in the Congo Basin have had documented case fatality rates between 1 and 10 percent, and the viral lineage that is circulating in this area is thought to be more dangerous than others. Recent outbreaks in Nigeria have been traced to the west African lineage, which is associated with a persistently lower overall fatality rate of less than 3%.<sup>6,8</sup> Most of the recorded deaths up to this point have been of children under the age of five and people living with HIV.<sup>2</sup> There has been an increase in the number of confirmed and suspected cases of monkeypox infection in a few countries across North America and Europe over the past few weeks. Among these are the continents of Canada, the United States, the United Kingdom, Italy, Germany, Portugal, Belgium, France, Sweden, and even Australia. Immunization efforts in the past have shown that the smallpox vaccine is about 85% effective in preventing monkeypox. The reduction in routine vaccination programs that followed the 1980 eradication of smallpox allowed monkeypox to re-emerge as a potential hazard.<sup>3</sup> While brincidofovir and tecovirimat, both of which treat smallpox, are not yet allowed for use in humans, they have been approved in the United States in case of a bioterrorist attack. Both medications have shown efficacy against various orthopoxviruses (including monkeypox) in animal models, but human efficacy trials have not yet been conducted. A number of cases of tecovirimat being used for compassionate purposes to treat severe cases of vaccinia and cowpox have been reported, and so far there have been no reported adverse effects. Because of the prevalence of monkeypox in the Central African Republic, a tecovirimat extended access programme is now being developed.<sup>2</sup>

## Historical Background <sup>4</sup>

A case of monkeypox (MPX) contracted by a traveler from Nigeria was confirmed in the United Kingdom (UK) on **May 7, 2022**. The patient reported becoming ill with a rash-like condition on **April 29, 2022**, and then traveling from Lagos to London on May 3 and 4. The Rare and Imported Pathogens Laboratory of the United Kingdom Health Security Agency (UKHSA) verified the diagnosis on May 6 using monkeypox virus (MPXV) PCR on a vesicular swab.

Two further MPX cases were reported in the United Kingdom on **May 13, 2022**, both were related to the single imported case from Nigeria that had been reported on May 7. PCR testing on swabs taken from vesicles verified the instances. Thirdly, another family member had a rash before but was completely fine now. No one in this grouping had any relevant travel experience or knew anyone else who did.

Four further PCR-confirmed cases of MPX were reported in the United Kingdom on **May 15th, 2022**. There is no evidence to suggest that the imported case from Nigeria (reported on May 7) or the family cluster are connected to any of these other instances (notified on 13 May). Patients in all four cases presented with a vesicular rash and were classified as men who had sex with men (MSM). Patients in this group were discovered due to their presence at GUM clinics. In the UK, these cases are being handled by specialized clinics for treating infectious infections with potentially devastating outcomes.

As of the **18th of May 2022**, two other cases (both MSM) had been reported, one in London and one in the South-East of the country.

The UK Health Security Agency (UKHSA) confirmed 20 cases of MPX in England as of **May 20**. Eleven more cases were reported on May 20. The MPXV West African clade is responsible for all cases recorded in the United Kingdom.

More confirmed or suspected instances were reported by many EU/EEA Member States beginning on May 18:

On May 18th, **Portugal** announced 14 confirmed cases of MPXV in the Lisbon and Tagus River Valley Area, confirmed by real-time polymerase chain reaction. All patients were male and presented with fever, rash (some ulcerative), muscle weakness, and fatigue. All patients were able to avoid hospitalization. It was reported that there were 23 verified cases as of May 20; nine further cases were confirmed on that day. Two samples were found to belong to the west African clade.

Men accounted for all of the 19 suspected cases and 7 confirmed cases of MPX that were reported in **Spain** on May 19. On May 20th, officials announced 16 more verified cases. Seven additional confirmed cases and 39 additional suspected cases were reported on May 22.

A guy with known ties to Lisbon, Portugal, was proven to have the disease in **Belgium** on May 19. On May 20th, it was discovered that his partner had also been experiencing these symptoms. To date (May 22), four verified cases have been reported.

The first case in **Germany** was confirmed on May 19 in a guy who had previously visited Spain and Portugal. Two additional confirmed instances were announced on May 20.

**France** confirmed its first case on May 20; three other suspected cases are still being investigated.

On May 20th, **Italy** announced that a guy who had recently returned from Spain had contracted MPX and was hospitalized. There were two further confirmed cases that were announced on May 21.

As of May 18th, **Sweden** had confirmed a male case.

One confirmed case, a male with known connections to Belgium, was reported in the **Netherlands** on May 20.

The initial verified case was reported on May 22 in **Austria**.

In nine EU/EEA Member States, 67 confirmed cases and at least 42 probable cases had been recorded as of May 23.

## Epidemiology

**African monkeypox.**<sup>5</sup> Having been spread to humans through close contact with sick monkeys, monkeypox has likely been a problem in sub-Saharan Africa for thousands of years. Nobody knows where MPXV comes from. There is evidence, however, that monkeys are only accidental hosts, much like humans, and that the reservoir is likely to be one of many rodent or squirrel species living in the secondary forest of central Africa. While smallpox had been eradicated from Zaire (present-day Democratic Republic of the Congo [DRC]), the persistence of a disease with similar symptoms in rural regions did not prompt its identification as monkeypox until 1970. Although the global eradication campaign's widespread vaccination in central Africa likely resulted in a temporary decrease in the disease's incidence, the lack of immunity in the generation born since then and the increased dependence on hunting for food in areas devastated by civil war have led to the reemergence of the disease.

**Spread of monkeypox in the United States.**<sup>5</sup> MPXV was discovered to be the culprit for an outbreak of illness in the Midwest of the United States back in the summer of 2003. The appearance of MPXV in the Americas marked its first occurrence in that region. During an outbreak, 37 human cases were confirmed by a laboratory out of a total of 72. Since most of the prairie dogs (*Cynomys* species) in the United States were kept alongside rodents brought from Ghana in western Africa, it was believed that the prairie dogs were the primary source of the outbreak.

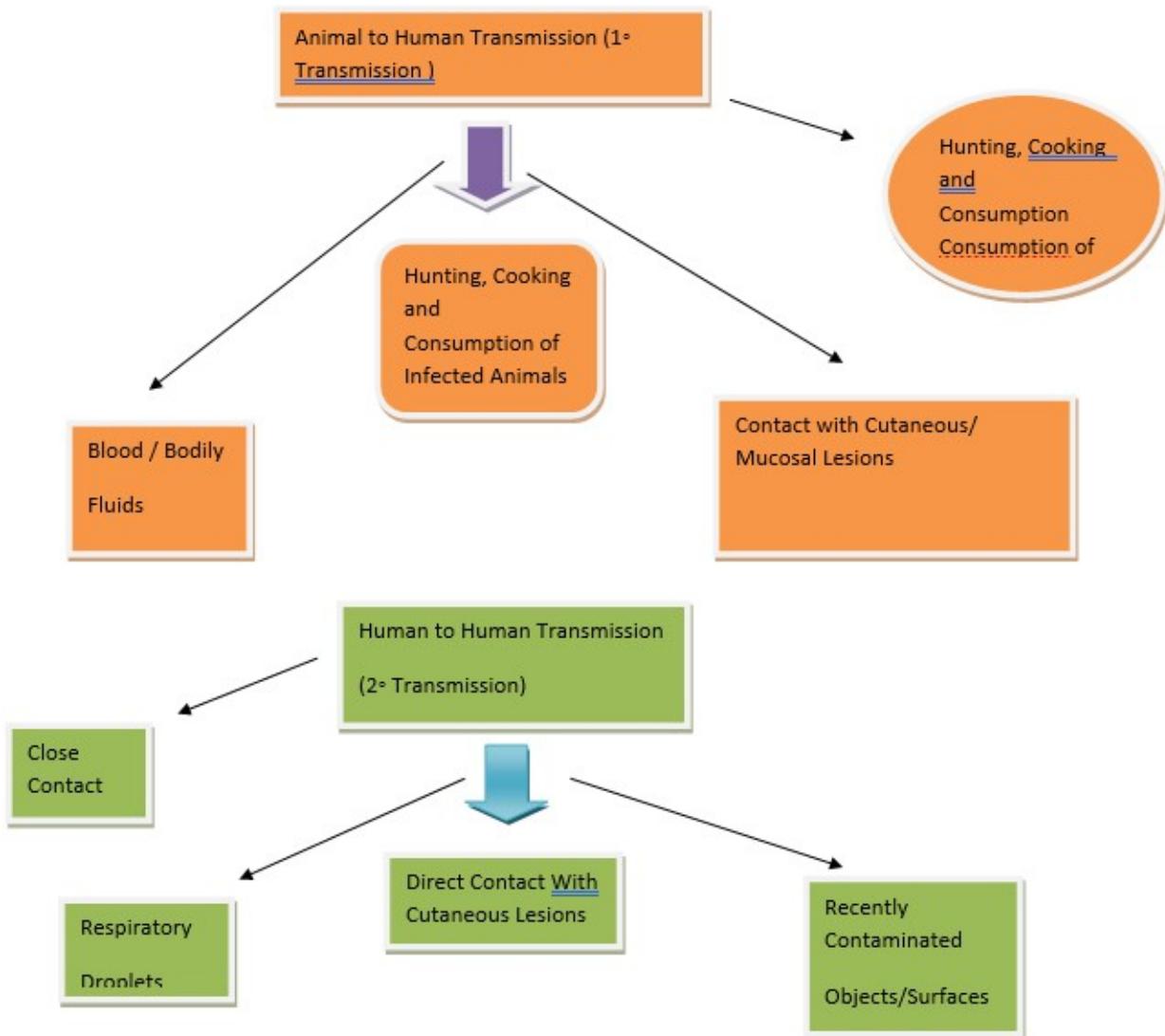
Avoid contact with domesticated prairie dogs as a source of infection. Although it was believed that the virus was spread through contact with an infected prairie dog, two of the patients had direct touch with their sick children through caring for them.

The authors of an epidemiological modeling study found that the R<sub>0</sub> value of monkeypox, also known as the reproduction ratio or the degree of transmissibility of the disease, ranges from 1.10 to 2.40 in nations with low levels of exposure to Orthopoxvirus species. When applied to hypothetical scenarios including imported human or animal cases, this value strongly predicts that an epidemic of monkeypox is impending. As was indicated before, the observed R<sub>0</sub> indicates that each infected person can potentially infect one to two others. The contagious nature of the virus makes it critical for an infected person to isolate and avoid contact with others. There have been 5,783 confirmed cases of monkeypox as of July 1, 2022, in 52 nations, according to the Centers for Disease Control and Prevention (CDC). At present, Europe and other parts of the western hemisphere are seeing a disproportionate share of monkeypox cases. According to recent data, the United Kingdom has the highest prevalence rate among European countries. Many of the currently confirmed cases of monkeypox are found in people under the age of 40, with the median age being just 31. Because this group was born after the smallpox vaccination program ended, they have no cross-protective immunity. In addition, males are more likely to contract monkeypox than females, though the reason for this disparity is unclear.<sup>6</sup>

### **Etiology<sup>7</sup>**

The Monkeypox virus belongs to the genus Orthopoxvirus and the species Monkeypox virus. The monkeypox virus is visible as a relatively big particle in electron micrographs (200-250 nanometers). Poxviruses have a lipoprotein sheath around their brick-shaped, double-stranded DNA genome. Poxviruses have all of the proteins necessary for replication, transcription, assembly, and egress encoded in their genome, albeit they must use host ribosomes for mRNA translation.

## Transmission Routes



## Differential Diagnosis<sup>7</sup>

- Smallpox

Worldwide Immunization Program

- Zoster disseminatus

- Chickenpox

Herpes simplex dermatitis

Spreading herpes simplex virus

- Syphilis
- Yaws
- Scabies
- Rickettsialpox
- Measles
- Skin diseases caused by bacteria

The Drug-Induced Eruption

### **Prognosis<sup>7</sup>**

The monkeypox virus can be divided into two groups known as clades. With a case fatality rate of less than 1%, the West African clade has a better outlook. A case fatality rate of up to 11% in unvaccinated youngsters has been reported for the Central Basin clade (Central African clade), which is more dangerous. Patients usually make a full recovery within four weeks of symptom onset, with the exception of permanent scarring and skin discoloration.

### **Western and Central Europe of Monkeypox<sup>8</sup>**

The monkeypox viruses in West Africa and those in Central Africa belong to separate phylogenetic clades. Evidence from the West African clade epidemic in the United States in 2003 revealed that illness severity also varied across clades. Liberia, Sierra Leone, Nigeria, and Côte d'Ivoire each reported less than ten cases of West African monkeypox between 1970 and 2005, and the United States experienced an outbreak with 47 confirmed cases. The severity of symptoms in humans and nonhuman primates infected with West African monkeypox is often lower than in other regions of the world. There were a lot of hospitalizations and serious illness in the US outbreak, but no deaths. A list of potential genes that may be involved in the distinguishing clade pathogenicity was uncovered by comparing the genomes of West and Central African strains. These ORFs are thought to play a role in virulence, host range expansion, immune system evasion, or other viral adaptations. Human cells obtained from monkeypox patients are resistant to T-cell receptor-mediated T-cell activation and the subsequent generation of inflammatory cytokines. These findings point to the possibility that monkeypox can result in antagonistic modulator of host T-cell responses. Central African monkeypox virus has been found to have multiple potential mechanisms of immune evasion. A major immune modifying component contributing to the enhanced virulence of Central African strains has been linked to the presence of a gene that inhibits complement enzymes in the monkeypox virus but is missing in West African strains. Furthermore, Central African monkeypox strains selectively down regulate host responses, including apoptosis in the host, in comparison to West African viruses. The observed pathogenicity variations may involve many loci. In addition, studies of transcription have revealed that Central African monkeypox appears

to selectively repress transcription of genes implicated in host immunity during infection. It will need a complex effort to learn the full scope of these viruses' potential consequences.

## **Diagnosis<sup>9</sup>**

The ongoing 2022 outbreak highlights the importance of maintaining a high index of suspicion for monkeypox infection and being mindful of the frequently atypical presentations of the infection. Clinicians who suspect monkeypox should inquire about recent travel, sexual activity, and close contacts with other patients who may have been exposed to the virus. Sleeping together, sharing utensils while eating or drinking, sharing a home, etc. are all examples of intimate contact behaviors. A lack of a travel history or a specific known close contact with a rash or with a suspected or confirmed monkeypox infection should not rule out the possibility of this diagnosis. The skin should also be examined carefully. Extraction of a lesion sample for molecular testing by PCR is the best method for diagnosing a patient with a suspected active monkeypox infection. Lesions should be unroofed to appropriately capture virus-containing fluids, and ideally more than one specimen should be acquired from two independent lesions on different areas of the body. While some labs are equipped to provide direct PCR testing for MPXV, others only test for OPXV, which then needs to be confirmed by testing for MPXV at a reference lab. It is reasonable to assume that a positive OPXV test indicates monkeypox infection in the context of the current outbreak, even before findings from confirmatory testing are available. It is preferable to coordinate testing plans with public health officials before collecting specimens.

Virus strains for further characterization can be grown in cells, however this can only be done in approved biosafety level 3 reference laboratories. Serological testing has the potential to aid in epidemiological studies, the retrospective diagnosis of prior infections, and the diagnosis of late clinical symptoms such as encephalitis. Although people who have already been vaccinated against smallpox may have an adverse reaction to MPXV serology, this is not a problem for those who have not been immunized.

## **Clinical Management<sup>9</sup>**

Clinical management of a typical monkeypox illness focuses on providing comfort and relief. Maintaining a healthy fluid balance is an important part of providing comfort care (because of the possibility of increased insensible fluid losses from the skin, decreased oral intake, and vomiting or diarrhea). In some cases, it could be necessary to resort to measures such as hemodynamic support, supplementary oxygen, or other respiratory assistance, or to treat bacterial superinfections of skin lesions. Ocular infection/complication management, including corneal scarring and/or vision loss, has also been described in the context of earlier OPXV infections as part of supportive care. Topical lubricants, topical antibiotics, and possibly topical antivirals like trifluridine are all viable options to investigate here.

There are currently no treatments for monkeypox that have been authorized by the US Food and Drug Administration (FDA). However, cidofovir, brincidofovir (a lipid-conjugate prodrug of cidofovir), and tecovirimat are all effective antiviral medicines against MPXV. Vaccinia immune

globulin intravenous (VIGIV) is a drug that the FDA has previously green-lighted for use in treating vaccinia vaccination side effects such progressive vaccinia and severe generalized vaccinia. The CDC maintains Expanded Access Investigational New Drug (EA-IND) protocols for the treatment of OPXV infections from the Strategic National Stockpile with the drugs tecovirimat, cidofovir, and VIGIV. The Centers for Disease Control and Prevention (CDC) processes requests from state and territorial health agencies in the United States for access to these drugs.

### **Immunization<sup>9</sup>**

OPXV infection has been shown to provide cross-protection against other orthomyxoviruses. Unfortunately, there are currently no vaccines available to prevent monkeypox. The vaccinations against MPXV that are currently under consideration (vaccines based on the Vaccinia virus) were originally designed to combat smallpox.

### **Discussion**

Thirty years after smallpox vaccination efforts end in the Democratic Republic of the Congo, **Rimoin A W et al. (2010)**<sup>10</sup> found a dramatic increase in the prevalence of human monkeypox. Cumulative Active surveillance data from the same locations between 1981 and 1986 was compared to incidence (per 10,000 population) and significant drivers of infection. Laboratory confirmation of 760 cases of human monkeypox was obtained in the health zones that participated between 2005 and 2007. The overall cumulative incidence rate each year was 5.53 per 10,000 (2.18–14.42). Living in a wooded region, being male, being under the age of 15, and having never been vaccinated against smallpox all enhanced the likelihood of contracting the disease. The probability of getting monkey pox was reduced by 5.2-fold among vaccinated individuals compared to those who hadn't been (0.78 vs. 4.05 per 10,000). Analyzing 1980s active surveillance data from the same health zone (0.72 A comparison of the human monkey pox incidence rates in 1996-97 (0.00 per 10,000) and 2006-07 (14.42 per 10,000) implies a 20-fold rise. Human monkey pox has reemerged in rural DRC 30 years after large immunization operations against small pox were abandoned. Epidemiological and surveillance improvements in order to assess the public health burden and devise methods to lessen the likelihood of further infection, research is required.

Outside of the endemic areas in Africa, it was first documented in **2022 by Thornhill J.P. et al.**<sup>11</sup> There are currently cases happening all across the world. Almost every aspect of this sickness is unknown to us: how it is spread, what causes it, how it manifests in the body, and what happens to those who contract it. This case series shows that there is a wide range of dermatological and systemic manifestations of monkeypox. The need for quick case identification and diagnosis is highlighted by the simultaneous discovery of cases outside of locations where monkeypox has traditionally been endemic.

For the year **2022, Sherwat A., et al.**<sup>12</sup> The current situation presents the same dilemma: how to manage compassionate access to a drug whose safety and efficacy in humans have not been established, in this case tecovirimat, available for clinical use under an expanded-access protocol

that may theoretically speed resolution of monkey pox illness and improve outcomes. Since both smallpox and monkeypox are caused by the same genus of viruses, it is important to understand the basis for tecovirimat's approval by the U.S. Food and Drug Administration (FDA) for the treatment of smallpox and the knowledge gaps that remain in order to determine what role it might play in our response to the monkeypox outbreak. The antiviral medication tecovirimat under a rule commonly referred to as the "Animal Rule," which was authorized for use in the treatment of smallpox. When human efficacy studies are not possible or ethical, and field trials cannot be conducted to test a drug or biologic product's efficacy, this route can be used to approve the drug for use in treating serious or life-threatening conditions. The Animal Rule requires that research in animal models be both sufficient and well-controlled in order to prove efficacy. sickness or condition in humans; proper human safety testing is required. Animal experiments with closely similar orthopoxviruses (to smallpox) demonstrated tecovirimat's efficacy, and the medicine was eventually licensed for use in humans. animals that aren't humans, such monkeys infected with the monkeypox virus or rabbits infected with the rabbit pox virus. In these experiments, animals given tecovirimat had a far higher survival rate than those given a placebo between the participants who were given a placebo and the others. Adverse reactions in healthy volunteers who were given tecovirimat were investigated to determine the drug's human safety. Dosing for the treatment of smallpox in humans with tecovirimat was determined by comparing plasma concentrations of doses proved to be fully effective against monkeypox and rabbitpox in animal models and test it on healthy humans. Findings from research in animals and healthy people were also used to determine the optimal therapy duration for humans.

## Conclusion

MPXV, or monkeypox virus, is a member of the Poxviridae family and the Orthopoxvirus genus. The rope squirrel and the sooty mangabey are the only two wild animals to have their virus isolated. Protection against monkeypox infection after receiving the smallpox vaccine was calculated to be around 85%. Since smallpox was eradicated in 1980, systematic vaccination programs have decreased, allowing monkeypox to reappear as a disease that could pose a concern. Two instances in the United Kingdom have been linked to the West African lineage of MPXV. As of May 23rd, 2022, nine EU/EEA Member States had reported a total of 67 confirmed cases, with an additional 42 instances being investigated as possible cases. The reproduction ratio ( $R_0$ ) for monkeypox is 1.10-2.40. The viral transmission rate,  $R_0$ , measures how easily the virus can be spread. This raises concerns that an imported human or animal case could quickly spread into a full-blown epidemic.

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