



A Full-Scale Narrative Review On Monkey pox

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ABSTRACT

A developing zoonotic orthopoxvirus with a clinical presentation resembling smallpox is the human monkey pox. A double-stranded DNA virus causes monkey pox (MPX), a viral zoonosis. -For the first time, numerous monkey pox cases and clusters have been recorded simultaneously in endemic and non-endemic nations over a wide range of geographical regions. On 23 July 2022, the World Health Organization (WHO) declared the monkey pox outbreak as a Public Health Emergency of International Concern (PHEIC). From May to July 2022, a multi-country outbreak of monkey pox was reported. The recurrence of the disease has caused global panic and a rise in public health concerns. we performed a thorough literature search for MPVX infection PubMed, Google scholar and Elsevier search engines, articles published in the last 3 months and personal collection of the relevant publications were considered in this review. Despite the fact that this condition has been there for more than 50 years, the recent rise in cases and the growing body of knowledge about it have made it necessary for practicing doctors to conduct a focused review. Therefore, in this review we Summarized the previous concepts, exploring the present, and focusing on future prevention of Monkey pox.

Key words: Monkey Pox, Clinical Features, Transmission, Prevention, Public Health Aspect

INTRODUCTION

The history of Monkeypox goes back to 1958, when a pox-like breakout occurred in two colonies of monkeys in Africa. Despite it being named Monkeypox now, the origins were unknown. The first case of Monkeypox in humans was recorded in 1970 in a human in the Democratic Republic of the Congo. After this incident, Monkeypox was reported in humans in other central and western African countries² Later, in 2018, Monkeypox was seen in travelers from Nigeria to Israel and then in the UK.³

The first Monkeypox outbreak in the USA was in 2003 when a shipment of infected animals was transported from Ghana, the infected rodents spread the infection to pet dogs, which infected 47 individuals in the Midwest. In 2021; a strange case of Monkeypox appeared in a US resident who traveled to Nigeria. In 2022, there was an international breakout in Europe, Asia, America, and Australia; cases outside

central and west Africa are due to international travels. On July 23, 2022, WHO (World Health Organization) declared the monkeypox outbreak a Public Health Emergency of International Concern ⁴.

EPIDEMIOLOGY OF MONKEYPOX

Monkeypox is a virus with double-stranded RNA. It belongs to the orthopoxvirus genus of the pox viridae family. There are two clades: Central African (Congo Basin) clade and the West African clade. Both these clades are commonly seen in Cameroon. It is assumed that African rodents and non-human primates are the virus carriers, which can transfer to humans. The current variant is the lesser west African clade.⁵ Incubation time can range from 6 to 21 days. Transmission can happen by intake of improperly cooked meat. A study in the 1900s also proved that wild squirrels are the active reason for the transmission of the infection.

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PATHOGENESIS OF MONKEYPOX

Monkeypox virus has a larger genome of the material needed for viral replication. This is seen in the cell cytoplasm, which is the causative reason for the pathogenicity in the host. The development of the Orthopoxvirus has been suggested as the result of progressive gene loss. This happens mainly at the end of the terminal genome, therefore making the virus fit for survival. Vaccinia Virus Homolog seen in the terminal end of MPXV has involved in immunomodulation which makes the virus survive at its best.

Viral culture and genetic analysis of human and mouse cells show that the virus depletes the host's innate immune system. MPXV bears a suppressor of a full-length N-terminal domain on its E3 monolog. It inhibits the protein kinase R (PKR) and allows the JC-1 dye (a mitochondrial membrane potential) indicator cell to replicate. The E3 protein binds with double-stranded RNA and isolates it from a known pattern, thereby preventing the activation limits protein release from animal cells in response to viral disease.⁶

The histopathology of the skin lesion in MPVX is similar to other viral infections like smallpox, chickenpox, cowpox, varicella zoster, and herpes simplex virus. Also, it has a similar pattern of development and degeneration of keratinocytes, spongiosis, dermal edema, and acute inflammation. The immature virion cells are more prominently seen in the cytoplasm of the infected cells.⁷

CLINICAL FEATURES

Skin: Monkeypox is a rare disease caused by the monkeypox virus. It has symptoms⁸, including flu-like symptoms such as fever, chills, headache, muscle ache, fatigue, and swollen lymph nodes. These are the symptoms seen before the rash formation. Development of the rashes starts as flat, red bumps, which later turn into blisters filled with pus and discharge. These symptoms can last up to two weeks to four weeks. Other than the rashes on the skin, they can also appear inside the mouth and vagina, penis, or anus. This starts 1 to 3 days before the occurrence of the maculopapular rash. During the 1st week, the patient was considered very infectious and advised to stay in isolation until the PCR swab test returns negative. The diameter of the skin lesion should be 0.5mm to 1mm. The lesion progression is similar to that of smallpox. After 2 to 4 weeks, the lesion gets more considerable secreting pus. The lesion raises as papules, increasing ulceration, necrosis, and epithelial hyperplasia with edema. The development of cleft between cells is appreciated with an apical evaluation of lesion and evident inflammation and necrosis of the dermis, which involves tearing down sebaceous glands and follicles.⁹

Lymph Node: Early to the onset of rashes, lymphadenopathy develops. Here the lymph node is firm and tender. The enlarged lymph node suggests the activi-

ty of the immune system towards the infection, which favors the diagnosis of MPXV.

Eyes: A prominent feature of Monkeypox is scarring of the cornea, which further causes vision loss. Therefore, early identification can help to treat patients with ophthalmic lubrication, vitamin supplementation, and antibiotics to avoid secondary bacterial infection and corneal ulceration.

Systemic Illness: Many studies done on non-human primates proved that the gastrointestinal tract showed ulceration and necrosis, which suggests the involvement of gastrointestinal diseases. During the outbreak in the United States, parental exposure was also observed, linked to systemic immune illness¹⁰.

In 2003, US outbreak of MPXV, patients suffered from anorexia, vomiting, sore throat, nausea, and lymphadenopathy, and resulted in early illness and weight loss. Hyperalbuminemia and low hematocrit seen due to malnutrition among them.¹¹ Another illness found was bronchopneumonia. A non-human primate's study showed lung tissue necrosis, diffused pulmonary consolidation, and edema in the lung region. This is an extraordinarily severe and fatal systemic alteration caused by the infection¹². Not everyone with Monkeypox develops all the symptoms. Most of the cases in the 2022 outbreak do not follow the regular pattern of infection. This shows that a person could be the carrier of the condition without showing any symptoms.

Spread of the Virus: Monkeypox spreads through two routes: animal to person and person to person. There are a few ways where direct transmission happens through blood, body fluids, skin, and mucous lesions, and droplets are transmitted through respiration. In addition, some rare mode of transmission includes contact with clothes or fabrics containing the virus. In pregnant women, placental transmission of virus to fetus.

According to CDC (Centre for Disease Control and Prevention), the transmission of the infection can happen through intimate activities like hugging, kissing, or sex, face-to-face contact, sharing bedding, sex toys, or towels with potential monkeypox virus, and bites or scratches from animals or pets, and eating undercooked meat that might contain the virus.¹³

The fatality of Monkeypox: According to the CDC, approximately 99% of the cases can survive due to infection. But specific individuals including younger children around the age group of 1 to 8 years old, immunosuppressed patients like patients with Lupus or AIDS, pregnant and breastfeeding individuals, and those with eczema are more susceptible to the disease and leads to fatal.¹⁴

DIAGNOSIS

Suppose if a person suspected any close contact with individual infected with Monkeypox. There are two methods to conclude the results of laboratory test. In

Table 1: Asymptomatic and Symptomatic Signs and Symptoms

Asymptomatic	<ul style="list-style-type: none"> Observe signs and symptoms for 21 days post-exposure. 	<ul style="list-style-type: none"> If the symptoms continue, follow the below mentioned
Symptomatic	<p>Rash phase</p> <ul style="list-style-type: none"> The lesion is removed with a scalpel or plastic scrapper and collected. The lesion fluid is collected with an intradermal syringe. The lesion base is removed with a polyester swab and placed in a plain tube. NPS/OPS is collected without any bacterial contamination or VTM. Blood collected in SSGT for about 4 to 5 ml Blood collected in EDTA for about 2 to 3 ml. Urine collected in a sterile container. 	<p>Recovery Phase</p> <ul style="list-style-type: none"> Blood is collected in SSGT. Urine collected in a sterile container.

Note: **EDTA**: Ethylenediaminetetraacetic acid; **SSGT**: They are serum separating tubes. Tubes are coated with a clot activator and gel for serum separation; **Test NPS**: Nasopharyngeal swab; **Test OPS**: Oropharyngeal swabs; **VTM**: Viral transport medium

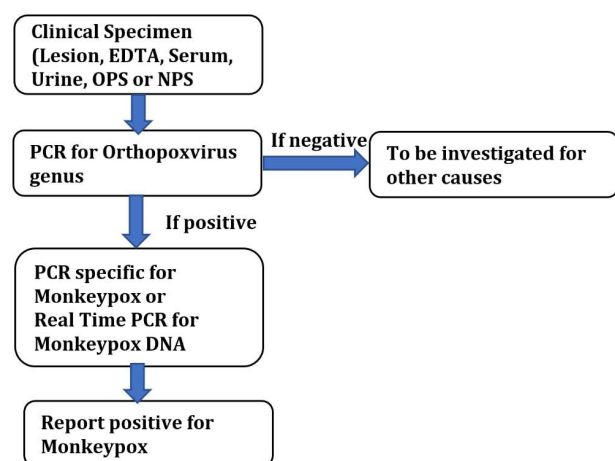


Figure 1: Representing the clinical specimen of MPVX

first method, the fluid will be taken from the boil, in another method dry scabs are taken and then tested using a PCR test (polymerase chain reaction). For biopsy, a small portion of skin is removed to check for the presence of monkeypox virus.¹⁵

Clinical samples are collected from individuals who travelled from outbreak countries and are tested for the infection. The following table stipulates the asymptomatic and symptomatic testing methods.¹⁶

Table 2: Management of MPXV

MPXV management	Symptoms	Management
Protection of compromised skin or mucus membrane.	Skin rashes Genital ulcers Oral ulcers Conjunctivitis	Clean with antiseptics, Mupirocin, Cover the area with minimal dressing, Do not touch or scratch the lesion. Sitz bath Warm saline gargle and oral anti-inflammatory gels. Self-limiting; if the condition persists, consult with an ophthalmologist.
Rehydration and nutritional support	Dehydration due to poor appetite, nausea, vomiting, and diarrhea.	Recommended giving ORS and fluids. Intravenous fluid is indicated and encouraged to consume a nutritious diet.
Symptom alleviation	Fever Itching pruritus Nausea and vomiting Headache or malaise	Tepid sponging and paracetamol. Topical calamine lotion and antihistamines. Anti-emetics Paracetamol and adequate hydration.

PREVENTION AND TREATMENT

To avoid any close skin contact with individuals who are infected with the virus, do not have any intimate contact with infected individuals, and do not share any bedding, utensils, clothes, and towels with infected individuals, and wash your hands often with soap or sanitize them regularly. Follow this especially before eating food; Intake well-cooked meat, use PPE for self-protection, and wear a mask that covers the mouth and nose.

Monkeypox can also be treated with the administration of vaccines such as the Smallpox vaccine, Antiviral medication in animals, Tecovirimat is an antiviral medication used to treat smallpox, Brincidofovir is an antiviral drug used in pediatric smallpox and Cidofovir is used to control viral eye infections caused by cytomegalovirus but has been able to prevent certain monkeypox cases.

Studies using the above medications have successfully treated Tecovirimat in non-human specimens. Whereas in humans, they are effective with minimal side effects.

The ACAM2000 vaccine and JYNNEOS vaccine. It is also approved to help protect against smallpox and Monkeypox.

Table 3: On-going analysis and literature review

Country	Study Period	Sample Size	Age/Sex	Sexual Exposures	Small pox vaccination status	Clinical presentation	Treatment	Diagnosis	Deaths
Italy ¹⁸	17-22 May 2022	4	30/M	4 (Sexual encounters during festivals and gathering events in 3 cases, sex work in 1 case)	1	Fever, asthenia and fatigue, myalgia, anogenital lesions, inguinal lymphadenopathy, lesions affecting the pubic area, anterior and posterior thorax, calf, back, head, legs and foot sole, arms and hands	Oral ciprofloxacin, acyclovir, a single dose of benzyl penicillin anti-inflammatory and anti-histaminic drugs (1)	Real-time PCR from various samples (skin, anogenital lesions, serum, plasma, semen, feces, and nasopharynx), viral quantification cycle (Cq), and DNA sequencing	0
Czech Republic ¹⁹	May 2022	1	34/M	1 (Sexual encounters during a festival/gathering event)		Tonsil ulceration, fever, chills, lymphadenopathy, anal and forehead lesions	Cephalosporins	Vesicle fluid electron microscopy, PCR	0
UK ²⁰	End of April-May 2022	2		2		Perioral white spots, perianal blistering lesions, anogenital and pubic lesions, lymphadenopathy, fever, headache, diarrhea	High-dose antiviral and antibacterial medications, including intravenous ceftriaxone	RT-PCR from respiratory, serum, lesion, and urine samples	0
Australia ²¹	May 2022	1	30/M	1		Fever, malaise, genital lesions, trunk, and to a less extent face and limbs	Oral doxycycline, intramuscular ceftriaxone, oral and intravenous cephalixin, oral analgesia	Real-time PCR from skin, nose throat swabs, DNA sequencing, viral isolation and visualization through thin-section electron microscopy	0
Portugal ²²	29 April-23 May 2022	27	(22-51)/M	14/16 (7 Cases in saunas and other venues)	1 (A middle-aged individual)	Fever, asthenia and fatigue, myalgia, headache, anogenital ulcers and vesicles, exanthema, inguinal, cervical, and axillary lymphadenopathy	NR	Real-time PCR from skin lesions (surface, exudate, and crusts) and oral mucosa, and DNA sequencing	0

Other treatments focus on managing the symptoms of the monkeypox infection, such as analgesics, oral antihistamine, and topical creams. Complications can include individuals more susceptible to secondary infections like pneumonia, sepsis, and encephalitis. In some individuals, corneal infections can lead to vision loss. It is advised to take proper medications, isolate yourself if infected, cover single lesions, and avoid contact with pets, especially rodents. Visit a doctor if you have difficulty in breathing, a stiff chest, difficulty in speaking or moving, loss of consciousness, loss of appetite, and occurrence of seizures.¹⁷

MANAGEMENT OF MPXV

Table 2 shows management protocol for monkey pox.

RESEARCH DEVELOPMENTS

WHO is suggesting that the Member States make all steps to use existing or new vaccines against monkeypox within a framework of collective clinical efficacy studies, using standardized methods and data display tools for clinical and outcome data. To improve the evidence on efficacy and safety rapidly, data are collected on the effectiveness of the drug (e.g., such as comparison of one or two dose vaccine regimens), and to perform vaccine efficacy studies.²³

CONCLUSION

Monkeypox is a self-limiting condition. In recent times due to more frequent infection of communicable diseases, it is important that both central and state government should encourage capacity building activities at various level on knowledge of medicine and practice, education, research, and to increase enormous funding for future prevention of communicable diseases. Early identification and screening, along with the known means of disease management, will be useful in preventing communicable disease. Differences in the provision of healthcare facilities must be managed to permit better primordial deterrence of the disease.

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