

Monkeypox: A Public Health Challenge due to a Re-emerging Microbe

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Abstract

Monkeypox is a viral zoonotic disease presenting with symptoms like smallpox, which was first identified in 1970 and continued to occur in Africa. With the global eradication of smallpox in 1980 and subsequent cessation of smallpox vaccination, which also provided protection against monkeypox, this has emerged as the most important orthopox virus infection in humans from the perspective of public health.

Recently, since the beginning of the year 2022, cases of monkeypox have been reported from all six regions of the World Health Organization. As the outbreak continued to grow, the WHO declared the situation as a Public Health Emergency of International Concern and issued temporary recommendations in relation to the outbreak. Newer vaccines have been developed of which one has been approved for prevention of monkeypox.

In India, the Ministry of Health and Family Welfare issued guidelines for management of cases as well as public health and prevention measures to contain the disease and end the outbreak. All healthcare facilities should focus on infection prevention and control measures. The community should be made aware regarding the disease, ways of prevention and home management of cases that do not require hospitalization.

Keywords: Monkeypox; Re-emerging microbe; Resurgence; Public health emergency of international concern; Outbreak.

INTRODUCTION

Monkeypox (MPX) is a zoonotic disease caused by a virus that belongs to the Orthopoxvirus

genus of the Poxviridae family. MPX was first discovered in 1958 in colonies of monkeys kept for research, hence the name Monkeypox. Twelve years later, human disease was first identified in 1970 in a 9 month old boy in the Democratic Republic of the Congo, which is a region where smallpox had been eliminated in 1968. Since then most cases have been reported in 11 African countries across Central and West Africa.¹

Resurgence of Human Monkeypox Disease 2022

With the global eradication of smallpox in 1980 and subsequent cessation of smallpox vaccination,

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which also provided protection against monkeypox, this has emerged as the most important orthopox virus infection in humans from the perspective of public health.¹

In 2003, the first MPX outbreak outside Africa was reported in the United States of America which was linked to contact with infected pet prairie dogs that had been housed with Gambian pouched rats and dormice imported into the country from Ghana.²

MPX is currently a disease of global public health importance as it not only affects countries in West and Central Africa, but has started appearing in rest of the world. Since 1st January 2022, cases of monkeypox were reported to the World Health Organization (WHO) from countries across all six WHO regions. A high proportion of these cases were reported since 13th May 2022, from countries without previously documented MPX transmission. This is the first time that cases and sustained chains of transmission have been reported in countries without direct or immediate epidemiological links to areas of West or Central Africa. Confirmation of even one case of MPX, in a country, is considered an outbreak. The unexpected appearance of MPX in several regions in the initial absence of epidemiological links to areas in West and Central Africa, suggests that there may have been undetected transmission for some time.³

As the outbreak continued to grow, with more than 16,000 cases reported from 75 countries and territories, and five deaths, on 23rd July 2022 the situation was declared as a Public Health Emergency of International Concern (PHEIC) by the WHO and temporary recommendations were issued in relation to the outbreak.⁴ As of 13th September 2022, a total of 59,179 laboratory confirmed cases, including 19 deaths, have been reported from 104 countries/areas/territories. Of these, 58,602 cases including nine deaths are from seven locations that have not historically reported MPX while 577 cases including ten deaths are from three locations that have historically reported MPX cases.⁵ WHO has assessed the overall global risk as moderate. WHO Regional risk has been declared as high in European Region; Moderate in African Region, Region of the Americas, Eastern Mediterranean Region, Southeast Asia Region; and Low-Moderate in Western Pacific Region.³

The first case of MPX in WHO South-East Asia Region was reported from India on 14th July 2022, in a 35-year-old man who arrived from the Middle East earlier in the week.⁶ Till 13th September 2022, a total of 18 cases and one death related to it have been reported in South-East Asia Region. Ten of

these cases and the single death are from India.⁵ Even before identification of the first case, Ministry of Health and Family Welfare (MOHFW) has released guidelines for management of the disease in India.²

EPIDEMIOLOGY^{1,7}

Monkeypox virus is a zoonotic double strand DNA virus that belongs to the Orthopoxvirus genus of the Poxviridae family. There are two known clades of MPX, one in West Africa (WA) and one in the Congo Basin (CB) region. The CB clade is considered to be more virulent, with a case fatality rate ranging from 1% to 10%, whilst the WA clade has reported an overall lower case fatality rate of <3%. However, mortality in different settings may be considerably different.¹

The incubation period of MPX is usually 6 to 13 days following exposure but can range from 5 to 21 days. Period of communicability is 1-2 days before the appearance of rash to until all the scabs fall off or subside.⁷ The longest documented chain of transmission in a community has risen in recent years from 6 to 9 successive person-to-person infections. This may reflect declining immunity in all communities due to cessation of smallpox vaccination.¹

Mode of Transmission is as follows:⁷

- Human-to-human transmission is known to occur through large respiratory droplets or secretions from skin lesions, generally requiring a prolonged close contact. It can also be transmitted through direct and indirect contact with body fluids or lesion material of an infected person. Transmission can also occur via the placenta from mother to fetus (which can lead to congenital monkeypox) or during close contact during and after birth.
- Animal-to-human transmission may occur by bite or scratch of infected animals like small mammals including rodents (rats, squirrels) and non-human primates (monkeys, apes) or through eating inadequately cooked meat and other animal products of infected animals. The natural reservoir of monkeypox has not yet been identified, though rodents are the most likely ones. People living in or near forested areas may have indirect or low level exposure to infected animals.

CLINICAL FEATURES^{1,7}

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. Underlying immune deficiencies may lead to worse outcomes. Persons younger than 40 to 50 years of age may be more susceptible to MPX due to cessation of smallpox vaccination campaigns globally after eradication of the disease. Complications can include secondary infections, bronchopneumonia, sepsis, encephalitis, and corneal infection with ensuing loss of vision. The extent to which asymptomatic infection may occur is unknown.¹

MPX presents with symptoms like smallpox, but of less clinical severity. The disease can cause a range of clinical signs and symptoms and goes through several phases.⁷

- Initial phase of clinical illness typically lasts for 1 to 5 days, during which time patients may experience fever, headache, back pain, muscle aches, lack of energy and lymphadenopathy, the latter being a distinctive feature of this disease.
- This is followed by appearance of rash 1 to 3 days after fever subsides. MPX rashes present in sequential stages – macules, papules, vesicles, pustules, umbilication before crusting over and desquamating over a period of 2 to 3 weeks. The lesions range in size from 0.5 to 1 cm in diameter and from a few to several thousand in number. The eruption tends to be centrifugal, starting on the face and extending towards the palms and soles of the hands and feet, and can involve the oral mucous membranes, conjunctiva, cornea and/or genitalia.
- Severe and life-threatening complications, though uncommon, may occur like serious skin lesions including cellulitis, abscesses, necrotizing soft tissue infections; severe pneumonia and respiratory distress; corneal infection which may lead to loss of vision; loss

of appetite, vomiting and diarrhoea leading to severe dehydration, electrolyte abnormalities and shock; cervical lymphadenopathy which may further lead to retropharyngeal abscess or respiratory compromise; and life threatening conditions like sepsis, septic shock, encephalitis and death.

Blood picture shows leucocytosis, elevated transaminases, low blood urea nitrogen and hypoalbuminaemia, lymphocytosis and thrombocytopenia.⁷

Differential Diagnosis includes Varicella (Chicken pox), disseminated herpes zoster, disseminated herpes simplex, measles, chancroid, secondary syphilis, hand foot mouth disease, infectious mononucleosis, molluscum contagiosum.⁷

Although most people recover within weeks, severe complications and sequelae have been reported to be more common among those who are unvaccinated for smallpox compared with those vaccinated. To date, the current MPX outbreak is mostly among men who have sex with men (MSM) and those who have reported recent sex with one or multiple partners. Cases have been identified mainly amongst men seeking health services in primary healthcare facilities and sexual health clinics with symptoms similar to other sexually transmitted infections. Most reported deaths have occurred in young children and immunocompromised individuals, such as those with poorly controlled HIV.⁷

DIAGNOSIS & MANAGEMENT^{2,8}

Guidelines for diagnosis and management have been released by the MOHFW, India, which include case definitions, sample collection and supportive management.

MPX case definitions for surveillance have been outlined for identifying the diseases, which are shown in Table 1.⁸

Table 1: Case definitions for Monkeypox

Type of case	Purpose	Criteria
Suspect case	Screening	A person of any age presenting with: An unexplained acute rash* anywhere over the body <i>One or more of the following signs or symptoms:</i> a. Swollen lymph nodes b. Fever c. Headache d. Body aches e. Profound weakness (*Presence of acute onset ano-genital lesions may specifically be ascertained)

Probable case	Sample collection, testing and isolation	A person meeting the suspected case definition and has an epidemiological link with a confirmed case (Direct physical contact with skin or skin lesions or body fluids or sexual contact; Face-to-face exposure, Health care workers without appropriate personal protective equipment (PPE); Contact with contaminated materials such as clothing, bedding or utensils).
		or
Confirmed case	Management	A clinically compatible case. A case which is laboratory confirmed for monkeypox virus (by detection of unique sequences of viral DNA either by polymerase chain reaction (PCR) and/or sequencing).

Source: (8)

Clinical samples from travellers from outbreak/endemic region or community transmission should be collected from the cases as per the criteria mentioned in Table 2.²

Table 2: Clinical samples from travellers from outbreak/endemic region or community transmission.

Type of case	Clinical samples to be collected	
Asymptomatic	- Observe the person for development of any signs and symptoms for 21 days' post exposure - If signs and symptoms develop, collect specimens as per the duration of illness as mentioned below	
Symptomatic	Rash phase	Recovery phase
	- Lesion roof - with scalpel or plastic scrapper collected in plain tube - Lesion fluid - with intradermal syringe - Lesion base - scrapings with sterile polyester swab collected in plain tube - Lesion crust - in plain tube - NPS/OPS - in dry plain tube [without any bacterial medium or VTM] - Blood - collected in SSGT (4-5 ml) - Blood - collected in EDTA (2-3ml) - Urine - in sterile urine container (3-5ml)	- Blood collected in SSGT (4-5 ml) - Urine in sterile urine container (3-5ml)

* The specimens from lesion should be collected from multiple sites

Source: (2)

Confirmation of diagnosis done at National Institute of Virology (NIV), Pune under Indian Council for Medical Research (ICMR) in the following manner:²

- PCR for Orthopoxvirusgenus (Cowpox, Buffalopox, Camelpox, Monkeypox).
- Monkeypox specific conventional PCR or real time PCR for Monkeypox DNA, if specimen is positive for the Orthopoxvirus.
- Virus isolation and the Next Generation Sequencing of clinical samples (Miniseq and Nextseq) for characterization of the positive

clinical specimens.

All the clinical specimens should be transported to the Apex laboratory of ICMR-NIV Pune routed through the Integrated Disease Surveillance Programme (IDSP) network of the respective district/state.

Principles of management include protection of compromised skin and mucous membranes; Rehydration therapy and Nutritional support; Symptom alleviation; Monitoring and treatment of complications. Supportive management is shown in Table 3.²

Table 3: Supportive management of Monkeypox

Management components	Symptoms/ signs	Management measures
Protection of compromised skin and mucous membranes	Skin rash	• Clean with simple antiseptic • Mupiroic Acid/Fucidin • Cover with light dressing if extensive lesion present • Do not touch/ scratch the lesions • In case of secondary infection relevant systematic antibiotics may be considered
	Genital ulcers	• Sitz bath
	Oral ulcers	• Warm saline gargles/ oral topical anti-inflammatory gel
	Conjunctivitis	• Usually, self-limiting • Consult Ophthalmologist if symptoms persist or there are pain/ visual disturbances
	Dehydration due to poor appetite, nausea, vomiting, diarrhoea	• Encourage ORS or oral fluids • Intravenous fluids if indicated • Encourage nutritious and adequate diet
Symptom alleviation	Fever	• Tepid sponging • Paracetamol as required
	Itching/pruritus	• Topical Calamine lotion • Antihistaminics
	Nausea/vomiting	• Consider anti-emetics
	Headache/ malaise	• Paracetamol and adequate hydration

Source: (2)

PUBLIC HEALTH & PREVENTIVE MEASURES²

Prevention of transmission of infection involves several measures viz. isolation of suspect and confirmed cases; infection prevention and control at healthcare facility as well as at home; tracing and monitoring of contacts; and risk communication to community.

Isolation of Suspect and Confirmed Cases

All suspect and confirmed cases should be isolated and isolation precautions should be continued until all lesions have resolved and a fresh layer of skin has formed. Affected individuals should avoid close contact with immunocompromised persons and pregnant women until all crusts are gone.

Infection Prevention and Control at Healthcare Facility

Standard, contact, droplet and airborne precautions should be undertaken in all healthcare settings having patients with fever and vesicular/pustular rash. Early identification and immediate isolation of patient to be done as measure of source control. Surgical mask should be applied if tolerable to the patient and exposed skin lesions should be covered with a sheet or gown. All individuals, including family members, visitors and HCWs should apply

standard, contact and droplet precautions. While transporting a patient, the personnel accompanying the patient should wear PPE and disposable linen should be used in the ambulance if available. The ambulance should be cleaned and disinfected with a freshly prepared 1% hypochlorite solution or equivalent before using for other patients.

Healthcare workers should use PPE for all patient contact i.e. disposable gown, gloves, N95 mask, eye goggles, which should be donned before entering the patient's room and disposed of prior to leaving the isolation room where the patient is admitted. Hand hygiene should be maintained following standard steps of hand hygiene, after all contact with an infected patient and/or their environment during care. All masks and any waste contaminated with crusts, secretions, serum or body fluids should be disposed of in yellow bag for infectious waste, in accordance with Biomedical Waste Management Rules 2016.

Infection Prevention and Control at Home

Patients who do not require hospitalization may be managed at home taking proper preventive measures. Patients should be isolated in a room or area separate from other family members. Healthy household members should limit contact with the patient. Patients should not leave the home except for medical care and no visitors should be allowed

at home. Pets and domestic animals should be excluded from the patient's environment.

Patients should wear a surgical mask. If this is not feasible, other household members should wear a surgical mask in presence of the patient. Disposable gloves should be worn for direct contact with lesions and disposed of after use. Skin lesions should be covered to the best extent possible to minimize risk of contact with others.

Contaminated waste such as dressings and bandages should be contained and disposed of in biomedical waste disposable bag. Proper hand washing with soap and water or by using an alcohol based hand rub should be performed by the patient and other household members after touching lesion material, clothing, linens, or environmental surfaces that may have had contact with lesion material.

Laundry e.g. bedding, towels, clothing may be washed with warm water and detergent. Dishes and other eating utensils should not be shared. Soiled dishes and eating utensils should be washed with warm water and dish washing soap. Contaminated surfaces should be cleaned and disinfected. Standard household cleaning/disinfectants may be used in accordance with the manufacturer's instructions.

Contact Tracing and Monitoring

A contact is defined as a person who, in the period beginning with the onset of the source case's first symptoms, and ending when all scabs have fallen off, has had one or more of the following exposures with a probable or confirmed case of monkey pox:

- Face-to-face exposure (including health care workers without appropriate PPE)
- Direct physical contact, including sexual contact
- Contact with contaminated materials such as clothing or bedding

Cases can be prompted to identify contacts across household, workplace, school/nursery, sexual contacts, healthcare, houses of worship, transportation, sports, social gatherings, and any other recalled interactions.

Contacts should be monitored at least daily for the onset of signs/symptoms for a period of 21 days from the last contact with a patient or their contaminated materials during the infectious period. In case of occurrence of fever, clinical/laboratory evaluation should be undertaken. Asymptomatic contacts should not donate blood, cells, tissue, organs or semen while they are under

surveillance. Pre-school children may be excluded from day care, nursery, or other group settings. Health workers who have unprotected exposures to patients with monkeypox or possibly contaminated materials do not need to be excluded from work duty if asymptomatic, but should undergo active surveillance for symptoms for 21 days.

Risk Communication and Preventive Measures

Raising awareness of risk factors and educating people about the measures they can take to reduce exposure to the virus is the main prevention strategy for monkeypox. This includes providing public health advice through the channels that target audiences use, on how the disease transmits, its symptoms, preventive measures and what to do in case of suspect or confirmed infection. This should be combined with targeting community engagement to the population groups who are most at risk, working closely with health care providers, including STD clinics, and civil society organizations.

The key points to prevent infection with monkeypox virus that should be in focus for awareness generation activities are as follows:

- Isolate infected patients from others who could be at risk for infection.
- Avoid contact with any materials, such as bedding, that has been in contact with a patient of monkeypox.
- Practice good hand hygiene after contact with infected persons by washing hands with soap and water or using an alcohol-based hand sanitizer.
- Use masks and gloves when caring for patients.

Vaccination

Vaccination against smallpox was demonstrated through several observational studies to be about 85% effective in preventing monkeypox. Thus, prior smallpox vaccination may result in milder illness. Evidence of prior vaccination against smallpox can usually be found as a scar on the upper arm. At the present time, the original (first generation) smallpox vaccines are no longer available to the general public. Some laboratory personnel or health workers may have received a more recent smallpox vaccine to protect them in the event of exposure to orthopoxviruses in the workplace. A still newer vaccine based on a modified attenuated vaccinia virus (Ankara strain) was approved for

the prevention of monkeypox in 2019. This is a two dose vaccine for which availability remains limited. Smallpox and monkeypox vaccines are developed in formulations based on the vaccinia virus due to cross-protection afforded for the immune response to orthopoxviruses.¹

Reducing Risk of Zoonotic Transmission¹

Unprotected contact with wild animals, especially those that are sick or dead, including their meat, blood and other parts must be avoided. All foods containing animal meat or parts must be thoroughly cooked before eating.

Some countries have imposed regulations restricting importation of rodents and non-human primates. Captive animals that are potentially infected with monkeypox should be isolated from other animals and placed into immediate quarantine. Any animals that might have come into contact with an infected animal should be quarantined, handled with standard precautions and observed for monkeypox symptoms for 30 days.

CONCLUSION

Monkeypox is a viral zoonotic disease presenting with symptoms like smallpox, which has recently seen a resurgence following eradication of smallpox and subsequent cessation of vaccination. The disease in humans was first discovered in 1970 and continued to occur in Africa. Recently, since the beginning of the year 2022, cases of monkeypox have been reported from all six regions of the World Health Organization. As the outbreak continued to grow, the WHO declared the situation as a Public Health Emergency of International Concern and issued temporary recommendations in relation to the outbreak.

In India, the Ministry of Health and Family Welfare has issued guidelines for diagnosis and management of cases as well as public health and prevention measures to contain the disease and end

the outbreak.

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