



Monkey Pox, a zoonotic infection in humans: A Review

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Abstract:

Monkeypox is the latest disease to hit the headlines in a troubling trend for emerging diseases. India is 10th country in Asia and 1st country in South Asia to report monkey pox case. Till now in India, there are 23 human reported cases of monkey pox. A zoonotic orthopoxvirus, monkey pox or MPXV can cause disease in humans same as smallpox, but its mortality is low. Although, by eradicating smallpox and lack of its vaccination efforts gave monkey pox to gain relevance clinically. The objective of this review is prevent human to human transmission of monkeypox, to prevent vulnerable humans which are at high risk and to limit the zoonotic transmission of monkeypox infection.

Key words: MPXV, small pox, vaccine

Introduction: The monkey pox virus (MPXV) was identified in a laboratory in 1958, and monkey pox as a disease in humans in 1970.¹ Historically, monkey pox was confined to central and western Africa, largely the Republic of Central Africa and Congo democratic Republic, where it is endemic.¹ In 2003, first report of human monkey pox was in US, as a zoonotic disease originating in imported African rodents. In 2018, UK first case was transmitted from a patient to a healthcare worker and in the same year a case was reported in Israel in an individual who had travelled from Nigeria.^{2,3,4}

MPXV is from family Poxviridae, under the gene Orthopox.⁹ MPXV is an enveloped, double-stranded DNA virus with a diameter of 200 to 250 nanometers.¹ There are two clades (groups) within MPXV: Congo Basin or Clade I and West African or Clade II.^{1,10} Clade I is considered a high-consequence infectious disease in the UK¹⁰ with 1-12% of mortality whereas, Clade II is less virulent with <0.1% of mortality. For Clade I the RO (reproductive number) is between 0.6 and 1.0 and believed to be lower for Clade II.¹ The current monkey pox outbreak is caused by Clade II b. Among other orthopox viruses, the most familiar are smallpox (variola) and cowpox. Since smallpox was eradicated and inoculations against smallpox ceased, the number of cases of monkey pox has increased in areas where the disease is endemic, and it is spreading. It is believed that this may be a consequence of cessation of smallpox inoculations, with increased susceptibility to monkey pox disease.¹¹

WHO (World Health Organization) in July 2022 declared it as International Public Health Emergency.⁵ As of September 1, 2022 there were 52,090 confirmed cases globally, of which less than 500 are in areas where monkey pox historically has occurred.⁶ The first case in the United States was reported on May 15, 2022 and as of September 1, 2022 there were 19,465 confirmed cases of monkeypox.⁷ The largest number of cases has been reported in New York, California, Florida, Texas, and Georgia. The vast majority of cases are in men having sex with men (MSM).⁷ What is believed to be the first death in the United States caused by MPXV was reported on August 30th, in an individual with a severely weakened immune system.⁸ In India, 23 cases of monkeypox with one death reported till date.

Modes of Transmission

People who are living in forested or remote areas and take care of monkeypox infected animals or patients are the risk factors for monkeypox. MPXV is transmitted primarily through direct contact. It can also be transmitted through indirect contact, respiratory secretions, and as a zoonotic disease.^{12,13,14,15,16} It is not known if asymptomatic transmission occurs.¹² Direct human-to-human transmission is the most common mode of transmission, involving close (often intimate) contact with the source individual's rash, scabbed pustules or body fluids (including blood).¹² Transplacental transmission from mother to fetus is possible, as well as from pregnant women to babies during birth.^{17,18} (Figure 1.1) Potential transmission by fecal transplants has been reported, as MPXV has been found in stool samples and rectal swabs.¹⁹ The US (FDA) Food and Drug Administration has now issued the need for additional protections, including screening, exclusion criteria and informed consent on this risk, for investigational use of fecal transplants obtained on or after March 15, 2022.²⁰

MPXV enter the body through respiratory or skin route. In respiratory tract, virus can infect airway epithelial cells such as macrophages and dendritic cells. When inoculated in skin, virus infects fibroblasts and keratinocytes. Skin resident immune cells like macrophages, dendritic cells and Langerhans cells are also affected. There may be direct viral involvement of lymphatics. Lymphadenopathy can occur. After lymphoid tissues involvement, MPXV may target liver and spleen. MPXV antigen detected in Kupffer cells, hepatocytes in non human

primate. It can spread to distant organs like gonads and skin.

Figure 1.1
Modes of transmission



Indirect contact transmission occurs via contaminated inanimate objects (fomites), such as cups, tables, bedsheets, and towels.¹² Contamination of surfaces in the healthcare setting has been confirmed.²¹ In one study, swabs were obtained from high-touch areas in isolation rooms containing patients with monkey pox and from personal protective equipment (PPE) worn by personnel. Wide-spread contamination of surfaces was found, with 66 of 73 samples testing positive for MPXV. Positive results were also obtained for PPE used while seeing patients or changing bed linen.²¹

Respiratory secretions in exhaled large droplets can spread MPXV at short distance from the source individual. It is believed that MPXV does not linger in the air.²² Aerosolized transmission has not been reported.²³ However, aerosolized transmission in experimental studies in monkeys has occurred.²⁴ In the UK, MPXV is included under airborne transmission.¹⁰ In a study in which air samples were taken before and while changing bed linen in the isolation unit in a hospital setting, 5 of 15 samples showed contamination with MPXV and three of four taken while bed linen was being changed.²¹

Zoonotic transmission occurs as a result of direct contact with an infected animal (touch, scratches or bites) and preparing/eating infected meat.^{1,4} Rope squirrels, giant pouched rats and dormice imported to the US in 2003 were infected, the disease was transmitted to prairie dogs, and in turn humans and a rabbit.^{1,25} Affected animals in Africa includes monkeys, chimpanzees and orangutans,¹ and MPXV antibodies have been found in several other species. This does not, however, determine potential transmission to humans. The primary reservoir remains

unknown.²⁶ (Figure 1.1)

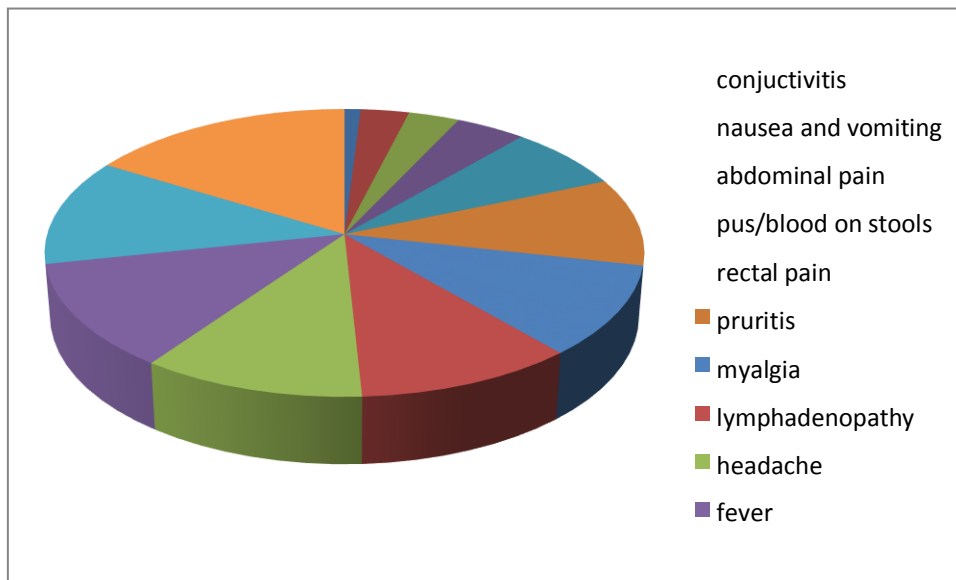


Figure 1.2. Signs and symptoms of monkey pox (% of infected individuals affected)

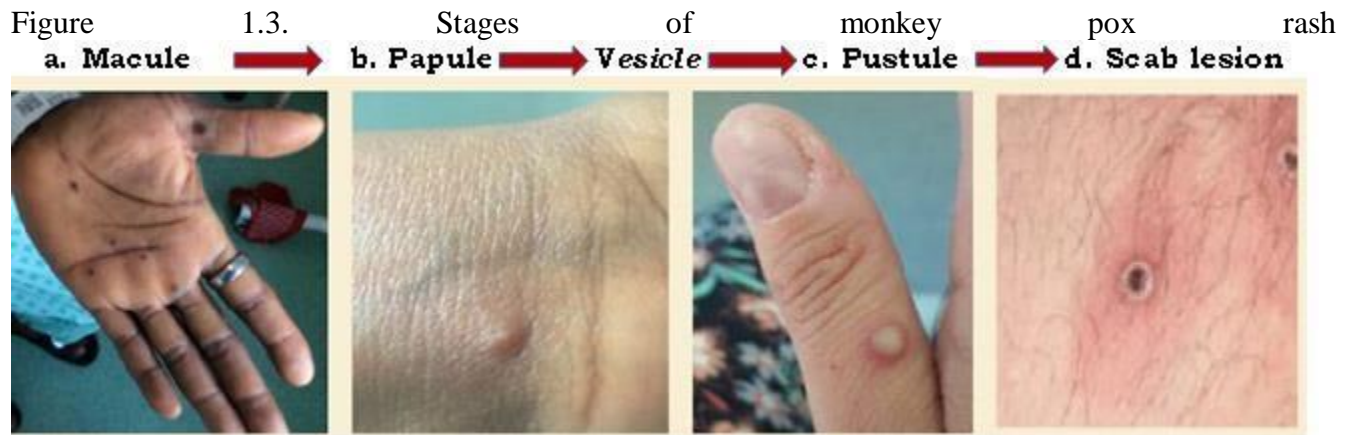
Signs and Symptoms of Monkeypox Disease

Signs and symptoms include a rash, malaise, fever, chills, lymphadenopathy, headaches, and myalgia. An estimated 98.6% of individuals with MPVX experience a rash, considered part of the definitive diagnosis.²⁷ As shown in Figure 1.2, in general, for other signs and symptoms the percentage of individuals experiencing a given sign/symptom ranges from 6% to 72.7%.

Individuals are considered infectious from the onset of symptoms until the rash has resolved and skin has formed over the area. Generally, this takes 2 to 4 weeks after onset of symptoms.²⁸ One percent of individuals do not experience a rash and, while multiple lesions are typical, individuals with just one lesion have been diagnosed with monkey pox. Monkeypox incubation period is 12 days to 3 weeks.²⁸ Fever, fatigue, lymphadenopathy, headache, and backache occur during the prodromal phase, lasting up to 4 days.¹ The fever subsides prior to the onset of a rash. In contrast to chickenpox, a monkey pox rash consists of lesions at various stages of development and resolution. Oral lesions are often the first signs, developing prior to skin and other potential mucosal lesions (including ocular).

Skin lesions in the facial region typically occur first before spreading out, and lesions can

develop over the whole body. The lesions are typically between 2 and 5 mm in diameter, but may reach 1 cm.^{1,29} After presenting as macules the lesions progress after 1 to 2 days through the stages of papules (1 to 2 days duration), vesicles containing clear fluid (1 to 2 days duration), and pustules containing opaque fluid (5 to 7 days duration).³⁰ Lesions then crust over, and the scabs later fall off. (Figure 1.3) Areas of hypo- and hyper-pigmentation may be evident after monkey pox lesions have healed.³⁰ Monkeypox lesions are distinct, well defined and umbilicated.



Source: a-c CDC; NHS England and High Consequence Infectious Diseases Network; d CDC; UK Health Security Agency

Figure 1.4. Lymphadenopathy



Source: CDC/Brian W.J. Mahy, BSc, MA, PhD, ScD, DSc

Most of the signs and symptoms are common to smallpox and to chickenpox

(varicella).^{1,9} Lymphadenopathy is a key feature for monkey pox and does not occur with chickenpox or smallpox.^{25,29} (Figure 1.4) Most of the cases are currently presenting without typical early signs and symptoms (fever, headache, exhaustion, muscle aches and lymphadenopathy). Further, instead of widespread distribution of a rash, cases are presenting with fewer lesions and confined to specific areas of the body.³¹

Potential complications of severe disease include corneal scarring with permanent loss of vision, secondary infections, pneumonitis, and encephalitis.^{1,29} Very rarely, infection during pregnancy has led to miscarriage and stillbirth.¹⁷ In previous outbreaks in Africa, fatalities ranged from 1% to 10%,⁴ influenced by MPXV clade, immunosuppression status, general health, and availability of care. In the current global outbreak, population who are in direct contact with monkeypox infected individuals are at risk for MPXV.

Oral and Oropharyngeal Manifestations

An estimated 70% of individuals with monkey pox are reported to experience intraoral lesions.³² However, in a recent retrospective cohort case series a different presentation was found for 197 individuals with monkeypox.³³ All were men and, all but one identified as MSM, oral lesions were seen in less number of patients. Oral lesions can present as ulcerations or erythematous areas, on any area of oral mucosa. In one case study, a patient presented with a tan-grey ulcerated lesion 1 cm across on the tip of the tongue and smaller cluster lesions presenting as vesicles on the anterior ventral (inferior) area.³⁴ Skin lesions developed later. A second patient presented with an ulcerated nodule 1 cm across on the tip of the tongue. Perioral lesions may also be present. In some cases, lesions have a similar appearance to herpes lesions (cold sores), trauma or hand, foot and mouth disease.³⁵ Oropharyngeal manifestations are much less common. In the retrospective case series described above, 13.7% of participants presented with oropharyngeal lesions, and 4.6% presented with redness, swelling, pustules or abscesses in the tonsillar region.³²

Role of Dental Professionals

Healthcare professionals have been “urged to be alert for patients who have rash illnesses consistent with monkeypox”.³¹ As dental professionals, there is an opportunity to review updated medical history forms and look out for signs and symptoms that suggest monkeypox.³² This includes oral, oropharyngeal, and peri-oral lesions, as well as skin rashes, lymphadenopathy of the submandibular and cervical areas can be detected. If monkey pox is suspected, the patient needs to be referred immediately for medical investigation, testing and a definitive diagnosis. If confirmed, the patient needs to isolate and receive care. Early identification can help to prevent spread through earlier diagnosis and isolation of infected individuals. Testing and Treatment

Non-variola orthopox/MPXV testing is available and recommended for individuals with a rash or lesions consistent with monkeypox.³⁶ Swabs are taken from more than one lesion, with results in a few days. Polymerase chain reaction testing is performed for confirmation.³⁶ If exposed to MPXV or at high risk, vaccination against monkey pox is recommended and preventive measures.³⁷ For the treatment of monkey pox, EA-IND (Expanded Access Investigational New Drug) protocol is use of antiviral agents, including TPOXX.³⁷

Antiviral drug Tecovirimat does not affect the intracellular mature form of virus, although it target MPXV VP37 membrane protein to prevent envelop virion formation which are capable of cell egress, so disrupts the spread of virus. Brincidofovir (FDA approved) inhibits orthopoxvirus DNA polymerase mediated DNA synthesis but its adverse effect is elevated liver enzyme. Cidofovir is active drug type of Brincidofovir and has antipox virus activity but it is nephrotoxic.

Vaccines against monkey pox

2 S/C (sub cutaneous) injections of FDA-approved vaccine JYNNEOS, at one stat and second after 28 days against monkey pox and smallpox, were administered in age 18 years and above.³⁸ After second dose of vaccine, peak immunity was attained after 14 days. The vaccine is contraindicated during pregnancy and while breastfeeding. It is also in short supply and is now being used in the US at a 20% dose and given intra-dermally. The alternative is the ACAM2000

vaccine, which is effective against smallpox. Vaccines against smallpox provide cross-immunity for monkey pox, however there is no efficacy data available in the current outbreak.³⁸ ACAM2000 is available against monkey pox under an EA-IND application.³⁹ ACAM2000 should not administered in people who are pregnant or have a weakened immune system or skin conditions such as eczema. More information can be found on the CDC website, including contraindications and potential adverse events.

Infection Control

It is essential to follow infection control protocols to minimize the risk of transmission for all diseases. As part of general infection control guidance, standard precautions are required to prevent the transmission of microorganisms and disease.⁴⁰ For patient care, this includes appropriate hand hygiene, and PPE consisting of clinical attire, single-use disposable gloves, a face shield that wraps around the face or goggles, and a mask. Transmission-based and stepped-up precautions have additional requirements, including wearing an N95 respirator (or equivalent in other locations).

Patients with confirmed monkey pox or already suspected should be isolating (and as such not visiting a dental office). Patients should be screened prior to any appointment for signs and symptoms suggesting monkey pox infection, and for contacts/potential exposure. In addition, during patient appointments, dental professionals should be alert for signs and symptoms of monkey pox and a history suggesting exposure. It has been noted that aerosol-generating procedures can put dental healthcare personnel at risk of contracting monkey pox when treating patients with suspected or confirmed monkeypox.³²

It is in general recommended for healthcare professionals to wear an N95 respirator (FFP3 or equivalent in other countries) when treating a patient with suspected (or confirmed) monkeypox.⁴¹

Considerations for pets and animals

The CDC has advised that ‘veterinarians should consider all mammals susceptible to monkeypox’.⁴² The CDC also advises individuals with monkey pox to avoid contact with pets,

domestic animals, and wildlife to prevent transmission.⁴³ If an infected individual did not have direct contact with pets prior to the onset of symptoms, it is recommended that someone else in another home should look after the pet until the individual has recovered. If it is impossible to avoid caring for pets, the infected individual must avoid direct contact with pets and make sure that they cannot come into contact with contaminated inanimate objects. Advice includes wearing long sleeves and long pants to cover any rash, performing hand hygiene, and wearing gloves and a well-fitting mask or respirator while caring for the pet. More details can be found on the CDC website.⁴³

Conclusions

Transmission during the current outbreak is largely by direct contact and infectivity is relatively low. While most cases at this time are in MSM, this does not mean that monkey pox cannot be transmitted to other individuals. Identification, tracing, and isolation are important in combating transmission. In addition, healthcare professionals should take proper history, signs and symptoms suggestive of monkey pox when seeing patients. Dental professionals are uniquely qualified to identify oral and peri-oral lesions, as well as oropharyngeal lesions. As such, dental professionals can play a principal role in the early identification and referral for testing of individuals suspected of having monkey pox. Early identification of potential cases together with earlier isolation for suspected and confirmed cases lead to reduced opportunity for further transmission.

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