

Review Article

The world faces a new viral threat: monkeypox

Archana Reddy Bongurala^{1*}, Sandhya J. Kadam², Vy Nguyen³, Mira Patel³,
Rishika Sharma², Anshuman Srivastava²

¹Department of Pediatrics, Omni Family Health, Bakersfield, CA, USA

²Family HealthCare Network, Visalia, California, USA

³Western University of Health Sciences, California, USA

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*Correspondence:

Dr. Archana Reddy Bongurala,

E-mail: drarchanareddy@gmail.com

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ABSTRACT

Monkeypox, a zoonotic viral disease, has re-emerged globally, presenting a significant public health challenge. Initially affecting primarily men who have sex with men, the virus has demonstrated broader transmission patterns, raising concerns about its potential to become endemic. The recent outbreak has highlighted the rapid spread of Monkeypox through close contact, particularly during sexual activity. This shift in transmission dynamics necessitates a robust global response, including surveillance systems, contact tracing, and vaccination campaigns. Understanding the virus's epidemiology, clinical manifestations, and transmission routes is crucial for effective prevention and control. While supportive care remains the primary treatment, antiviral medications and vaccines offer additional tools to mitigate the impact of Monkeypox outbreaks. Continued vigilance and timely interventions are essential to prevent further spread and protect public health.

Keywords: Monkeypox, Zoonotic disease, Global outbreak, Public health, Prevention

INTRODUCTION

Monkeypox virus (MPXV) is a double-stranded DNA zoonotic virus that belongs to the *Poxviridae* family, *Chordopoxvirinae* subfamily, and *Orthopoxvirus* genus.^{1,2} The MPXV shares clinical similarities with smallpox, likely due to its frequent infection with the Variola virus.^{2,3} The MPXV is classified into two clades: Central African/Congo Basin and West Africa. Various *Orthopoxviruses* can be differentiated with the help of PCR testing.⁴

By June 2022, the Pan American health organization (PAHO) and WHO (PAHO/WHO) had recorded a total of 1423 confirmed cases of MPX in 31 non-endemic countries.⁵ Smallpox and MPXV share antigenic and genetic components. Therefore global campaign carried out for smallpox eradication also provided substantial immunity against MPXV.^{2,3} However, the discontinuation of smallpox vaccination has led to decreased herd

immunity, making populations more susceptible to MPXV outbreaks.^{3,4} Since the first human infection in 1970 in the Democratic Republic of Congo (DRC), monkeypox has become endemic in both West Africa and Central Africa, with a mortality rate between 1 and 10%.² At the beginning of 2022, the world health organization (WHO) reported the alarming re-emergence of MPX with the confirmed outbreak in Africa and non-endemic countries worldwide.

HISTORY

MPXV was first isolated in Copenhagen in 1958 after two outbreaks of smallpox-like disease in cynomolgus monkeys.⁶ Several consequent outbreaks of monkeypox were identified in 1960 and 1968 in colonies of captive monkeys in the United States and the Netherlands. In 1970, the first reported case in humans was reported in a 9-month-old boy with fever, rash, lymphadenopathy and ear infection in the Democratic Republic of Congo. He

was the only member of the family who did not receive the smallpox vaccine. Six additional cases of monkeypox were reported only in young children between September 1970 and March 1971 in West African countries.⁷ From 1970 to 1990, monkeypox in humans remained confined in Africa with more than 400 additional cases documented mainly in DRC.² In 2003, monkeypox began to garner worldwide attention when 37 confirmed cases were reported in the United States due to viral transmission from prairie dogs, infecting primarily young adults and children.^{2,7} In the same year, the Republic of Congo (ROC) reported the first outbreak of human monkeypox, in which 11 cases were reported to be younger than 18 years of age.² From 2017 to 2018, a large outbreak in Nigeria led to a surge in infection in other countries including the United Kingdom, Israel, and Singapore. Nonetheless, monkeypox remained in Africa with rare sporadic cases arising in the United Kingdom and the United States. In 2022, a series of cases were reported in the United Kingdom, Portugal, and Italy involving homosexual men, establishing the start of a new outbreak.⁷ As of 13 September 2022, 57,995 MPXV infections have been reported in >100 countries or regions.⁸

ETIOLOGY

The origin of monkeypox remains unknown; however, it was first seen in a laboratory in Denmark in 1968 where a group of monkeys had classic vesicular rash. The first human case was in 1970 in the Republic of Congo and it first became widespread globally in 2022.²

The MPXV is a fairly large (200-250 nanometers) double stranded DNA virus enveloped within lipoprotein, resembling bricks. It is part of the Poxviridae family.⁹ Since it is fairly large, the MPXV (although a DNA virus) typically hijacks host ribosomes and is able to replicate within the cytoplasm utilizing its own proteins otherwise. The virus initially replicates in its inoculation site then causing local and regional lymphadenopathy for systemic infection.⁹

It is a zoonotic infection and thus disease can be transmitted from animals to humans. Common animal reservoirs include: monkeys, squirrels, rats, small primates, and prairie dogs.¹⁰ MPXV types- divided into Clade 1 or Clade 2.¹⁰ Clade 1 causes more serious disease with increased mortality up to 10% and is endemic to Central Africa. Clade 2 causes less severe disease with a mortality of <1%, was commonly seen with global spread in 2022, and is endemic to West Africa. Clade 1 seems to have less human-to-human transmission compared to clade 2.¹⁰

EPIDEMIOLOGY AND TRANSMISSION

Monkeypox is a zoonotic disease most endemic to Central and West Africa, though in recent years (since 2022) there has been an increase in global spread of the

MPXV. Currently, the Democratic Republic of Congo is having its largest outbreak of monkeypox with more than 12000 suspected cases and more than 581 deaths since January of 2023.¹¹

In early years (1987-1989), monkeypox was more common in young children with the most affected group between age 4-5 years, which increased to 10 years of age in 2009, and in recent years monkeypox most commonly affects young adults.³ Currently the most common subtype of monkeypox is clade 2 with associated low mortality and low level of transmission.¹² There has been an increasing rate of monkeypox in the United States. Most commonly monkeypox has affected age groups between 25 and 40 years.¹³ For the year of 2024, there have been 744 cases reported thus far compared to 335 in 2023. Cases of monkeypox have been commonly seen in California (72), Texas (55), Illinois (64), Florida (59), New Jersey (51), and New York (151)-states where travel is frequently common.¹⁴ Last updated in January 2023, there have been a total 32,063 cases within the United States with 58 associated deaths and over 95,000 cases worldwide.¹³

Outbreaks in the United States include: Forty-seven probable and confirmed cases of monkeypox were reported in year 2003 from Illinois, Kentucky, Indiana, Missouri, Ohio, and Wisconsin. July 15, 2021: a case from US citizen who traveled from Nigeria to US on two commercial flights. November 16, 2021: a case from Maryland of US resident who recently returned from Nigeria. Last updated on August 28, 2023 since the most common form of monkeypox right now is Clade 2 which has less associated mortality.¹⁵

Risk factors for severe disease include: currently pregnant females, children younger than 1 years of age, severely immunocompromised, and a history of asthma or eczema.¹

Monkeypox can be transmitted from person-to-person via direct contact, such as touching, kissing, or vaginal/anal/oral sexual contact, or short-range aerosol respiratory droplets (such as talking short distances or coughing/sneezing droplets).¹

CLINICAL FEATURES AND PHYSICAL EXAM FINDINGS

Usual incubation period of monkeypox is 5-14 days. An initial prodrome of fever, headache, and fatigue often occurs before the appearance of the rash. A hallmark of Monkeypox is the development of swollen lymph nodes in the neck, groin, or under the jaw. This is a key distinguishing feature from smallpox, which does not typically cause swollen lymph nodes.¹⁶ Following the prodromal phase, a maculopapular rash typically erupts, often initiating on the face and oral mucosa. This rash subsequently spreads centrifugally to other body parts, coinciding with the period of peak transmissibility.¹⁷ The

characteristic lesions progress through a series of stages: macular, papular, vesicular, and pustular. The number of lesions can vary widely, ranging from a few to several thousand. Over the next 7 to 14 days, the lesions begin to form scabs. These scabs eventually fall off, and most people recover completely within 3 to 4 weeks after the initial symptoms. Once all scabs have fallen off, a person is no longer considered infectious.¹⁸

EVALUATION OF SUSPECTED MONKEY POX

A thorough history and physical examination form the cornerstone of diagnosis of monkeypox. History should focus on travel to endemic countries, encounter with humans or animals with symptoms of monkey pox or animals imported from endemic countries. Since it is transmitted through close, sustained physical contact almost exclusively associated with sexual contact during the 2022-23 global outbreak, a detailed sexual history is critical. A thorough physical exam, including a careful examination of the mouth, anus, and genitals, is essential to detect monkeypox lesions. These lesions may be subtle or in areas that patients may not notice.¹⁶ In suspected

patients CDC recommends collecting two specimens, each from multiple lesions at different sites. While PCR testing for mpox virus DNA is the definitive diagnostic method, non-variola *Orthopoxvirus* testing followed by further characterization at CDC can also be considered.¹⁹

TREATMENT AND PREVENTION

Treatment for monkeypox is primarily supportive and symptomatic. This includes staying well-hydrated, taking over-the-counter pain medications like acetaminophen or ibuprofen to relieve fever and aches, and using topical creams or lotions to soothe itchy skin lesions.

Individuals who are at increased risk of severe illness or death from monkeypox can benefit from antiviral medication like Tecovirimat (TPOXX or ST-246).¹⁶ Early and supportive care helps to avoid further complications. Monkeypox vaccine is recommended for pre-exposure prophylaxis of people at high-risk of getting monkeypox, especially during an outbreak. Healthcare workers, household contacts, and people with multiple sex partners, including men who have sex with men and sex workers, are at higher risk.²⁰

Table 1: WHO recommendations to prevent spread of monkeypox.²¹

Do	Do not
Suspicion or possible symptoms contact health care provider	Touch and worsen skin lesions
Maintain personal hygiene, wear mask, wash hands	Shave the areas with sores
Self-isolate in well ventilated room	Sexual activity with new partners
Skin care	Direct or skin to skin contact
Symptomatic treatment	Delay to seek the treatment

The resurgence of monkeypox, a zoonotic viral disease, poses a significant and ongoing burden on global public health. While the initial outbreak in 2022 primarily affected men who have sex with men, the virus has demonstrated a broader capacity for transmission, raising concerns of an endemic disease.

SHIFT OF PARADIGM

While monkeypox can spread through various routes, recent outbreaks have highlighted sexual activity as a major mode of transmission via close contact. This change in transmission patterns required a rapid and coordinated global response. Health organizations across the world established comprehensive surveillance systems, contact tracing protocols, and vaccination campaigns to help limit the virus's spread.

CONCLUSION

The recent monkeypox resurgence demonstrates the dynamic nature of zoonotic diseases and the critical need for adaptable public health responses. The changing transmission patterns, especially via sexual contact, have

broadened the virus's impact, demanding comprehensive global surveillance, rapid contact tracing, and targeted vaccination. Understanding the virus's epidemiology, clinical presentation, and clade-specific disease severity has been crucial for developing effective prevention and treatment strategies. This review article advances knowledge by highlighting the ongoing need for vigilance, improved diagnostics, and strengthened global collaboration to control monkeypox, prevent future outbreaks, and bolster public health preparedness in our interconnected world.

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