

HUMAN MONKEYPOX: AN EMERGING AND NEGLECTED VIRAL ZOOONOSIS OF PUBLIC HEALTH CONCERN

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The world has witnessed several emerging and re-emerging infectious diseases. The recent COVID-19 pandemic is one of the biggest incidents that happened in human history. The war against COVID-19 is not over yet, and the sudden and unexpected outbreak of monkey pox has begun to invoke panic worldwide. Monkeypox is a rare viral zoonotic disease that occurs primarily in tropical rainforest areas of central and West Africa. With the eradication of smallpox in 1980 and subsequent cessation of smallpox vaccination and consequent drop of immunity against orthopoxviruses, monkeypox emerged as the most important virus for public health concern.^{1,2}

Monkeypox virus is an enveloped dsDNA virus with brick-like structure that belongs to the genus *Orthopoxvirus* of *Poxviridae* family, and is a sister virus of *Variola* (causes smallpox), *Vaccinia* virus (used for smallpox vaccination), and cowpox virus.³ The monkeypox virus is divided into two genetic clades: the more virulent Congo Basin (central African) clade (up to 10% mortality) and the less virulent West African clade (up to 1% mortality). Cameroon is the only country where both virus clades exist. Cumulatively, more cases of the central African clade have been reported to date than cases due to the West African clade in historical and ongoing outbreaks in the Democratic Republic of Congo. The West African clade has been isolated from cases in non-endemic countries in the current multi-country outbreak.⁴

Despite the name monkeypox, monkeys are not the primary reservoirs of the virus. Rope squirrels, tree squirrels, Gambian pouched rats, dormice, non-human primates (monkeys) are susceptible to monkeypox virus. The natural reservoir of monkeypox virus has not yet been identified. African rodents and monkeys may infect humans.^{1,2}

The disease was named monkeypox after two outbreaks of a pox-like disease in monkeys kept for research in Copenhagen, Denmark in 1958. Human monkeypox was first identified in humans in 1970 in the Democratic Republic of Congo in a 9-month-old boy during a period of intensified effort to eradicate smallpox. Human monkeypox had not been recognized prior to 1970. Over the past 50 years, sporadic outbreaks have been reported mainly in African countries. In 2003, an outbreak of monkeypox was reported in the USA infecting 70 people and was linked to contact with infected pet prairie dogs co-housed with infected Gambian pouched rats and dormice. Human monkeypox had never been reported outside Africa before.^{1,2,4,5}

In 2012, monkeypox virus was isolated from a dead infant mangabey monkey in West Africa.¹ In October 2018, one case occurred in a man who traveled from Nigeria to Israel.^{1,2} In May 2019, one case occurred in a man who traveled from

Nigeria to Singapore.^{1,2} In May 2021, a family returned to UK after traveling to Nigeria, and three family members became infected with the monkeypox virus.⁶ On July 15, 2021, a case of human monkeypox was confirmed by CDC in a US citizen who traveled from Nigeria to Texas, USA.⁷ Another case was confirmed on November 16, 2021 in a US citizen who returned to the Maryland, USA from Nigeria. In the present multi-country outbreak of monkeypox, 16,016 confirmed cases and five deaths have been reported from 75 countries from 1 January through 22 July, 2022.^{1,3,8}

The Monkeypox has not been reported from Nepal till date. As of July 25 2022, four cases of monkeypox has been reported from India. The first three cases in India were reported from the Southern state of Kerala; all of them had travelled to the state recently from countries in the Gulf region. India's fourth case of monkeypox has been reported in a man in national capital Delhi who has no history of foreign travel. The Union health ministry of Government of India released a guideline on managing the monkeypox, and advised officials to strictly screen all international arrivals at ports and airports. Indian Council of Medical Research (ICMR) has trained 15 research and diagnostic laboratories across the country for early virus detection.¹⁴

Monkeypox is transmitted to humans through close contact with an animal or infected person or with material contaminated with virus. Animal to human (zoonotic) transmission can occur by the bite or scratch, direct contact with body fluids or blood, cutaneous or mucosal lesions of infected animals. The main mode of human to human transmission is by large respiratory droplets. It can also be spread through direct contact with skin lesions, body fluids, internal mucosal surfaces such as mouth and throat contaminated materials such as bedding (fomites). Transmission can also occur via the placenta from mother to fetus (congenital monkeypox) or close contact during after birth. Curiously, vast majority of cases in the current outbreak have been in men who have sex with men. The virus did not spread well between people in the past but may have found a new niche in tightly connected sexual networks.⁸⁻¹⁰

Persons at increased risk of developing disease upon exposure to monkeypox virus are those living in forested areas, male gender, less than 15 years of age, and those who are not immune to smallpox.⁸⁻¹⁰

The incubation period (interval from infection to onset of symptoms) of monkeypox is usually from 6 to 14 days but can range from 5 to 21 days. The sickness starts with a febrile stage that lasts 1-5 days, characterized by fever, severe headache, lymphadenopathy, back pain, myalgia, and intense asthenia. The febrile stage is followed by the formation of a rash, which

DOI: <https://doi.org/10.3126/jucms.v10i01.47113>

usually begins on the face and then spreads to other areas of the body and lasts 2 to 4 weeks. The rash usually starts in the mouth (oral mucus membranes), and then spreads to the face and extremities, including palms and soles rather than on the trunk. Also affected are genitalia, and conjunctiva, as well as the cornea. The rash evolves sequentially from macules (lesions with a flat base) to papules (raised firm painful lesions), vesicles (filled with fluid), pustule (filled with pus), and scabs or crusts which dry up and fall off. The number of lesions varies from a few to several thousand. In severe cases, lesions can coalesce until large sections of skin slough off.^{1,8,11}

Monkeypox is usually a self-limited disease and resolves with the symptoms lasting for 2 to 4 weeks. Severe cases can occur. In recent outbreaks the case fatality rate has been around 3-6%. Underlying immune deficiencies may lead to worse outcomes. Rare complications of monkeypox include secondary bacterial infections, bronchopneumonia, sepsis, encephalitis, conjunctivitis/keratitis. The clinical presentation of monkeypox resembles that of smallpox, a related orthopoxvirus infection which was declared eradicated worldwide in 1980. The basic difference is that monkeypox causes lymphadenopathy, but smallpox does not. Monkeypox is less contagious than smallpox and causes less severe illness.^{1,8,11}

The skin lesions of monkeypox may be confused with chicken pox, molluscum contagiosum, herpes simplex virus infection, measles, syphilis, impetigo, rickettsial diseases, and drug associated eruption and differential diagnosis must be done.^{4,8,11}



Figure 1. Electron micrograph showing monkeypox virus¹⁵



Figure 2. Monkeypox skin eruption¹

The laboratory test for monkeypox diagnosis is the detection of virus DNA using PCR. The optimal diagnostic samples are from skin lesions (roof or fluid from the vesicles and pustules and dry crusts) and biopsy where feasible. Cultivation in cell cultures is restricted to accredited biosafety level 3 reference laboratories. As orthopoxviruses are serologically cross-reactive, serology and antigen detection methods may not be useful for diagnosis. Persons those who received smallpox vaccination may give false positive results.^{1,11}

Treatment is mainly supportive care and symptomatic management. Patients should be offered fluids and food to maintain adequate nutritional status. Secondary bacterial infections should be treated. The oral DNA polymerase inhibitor brincidofovir, oral intracellular viral release inhibitor tecovirimat and intravenous vaccinia immune globulin have been approved for treatment of small pox and have demonstrated efficacy against monkeypox in animals.^{1,2,8}

The preventive measures include avoiding contact with infected animals, as well as animals that are sick or have been found dead in the infected areas, avoiding touching any objects that have come into contact with a sick animal, such as bedding, isolating infected patients from those who could be at risk of infection. After coming into contact with infected animals or humans wash your hands with soap and water or use an alcohol based hand sanitizer. Raising awareness of risk factors and educating people about the measures they can take to reduce the exposure to the virus is the main prevention strategy for monkeypox.⁴

Smallpox vaccine is 85% effective in preventing monkeypox. Post-exposure vaccination with modified vaccinia, Ankara vaccine (smallpox and monkeypox vaccine, live attenuated, non-replicating) (trade name JYNNEOS) has been approved and given in two doses, four weeks apart.^{1,11,12}

Health care professionals worldwide should become familiar with the clinical presentation and management of this viral infection. It is time for us to recognize a growing reality, and take rapid action before the virus can be allowed to further establish itself as a human pathogen with efficient person to person transmission. Whereas smallpox no longer occurs naturally, the health care professionals must remain vigilant in the event it could reappear through natural mechanisms.^{8,13}

On July 23, 2022 the WHO declared the escalating global monkeypox outbreak a Public Health Emergency of International Concern (PHEIC).¹ But in my opinion, the Monkeypox outbreak is now a pandemic. Unless we act quickly to control it, we risk repeating the same mistakes we made with our covid-19 battle.

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