



## Human Monkeypox - Spillover Event

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### ABSTRACT

Human monkeypox is a zoonotic disease mostly found in tropical rainforest areas of Central and West Africa. It belongs to the genus Orthopoxvirus and the Poxviridae family. Two clades of monkeypox have been seen, mainly the Central African Clade and the West African Clade. Transmission to humans occurs through close contact with an infected person or animal. There is no documented indication of domestic animal such as cats and dogs, being affected by monkeypox. In 2022, a spillover of monkeypox was the largest in history to occur outside of Africa. The first case of monkeypox in India is reported in Kerala. The case fatality rate is 3–6%. The number of positive cases in India has risen to 9 till today. The literature survey shows the symptoms of monkeypox are fever, body rash. Vaccination and antiviral treatment are going on to prevent the spillover of virus.

**Keywords:** Zoonotic disease, Monkeypox, Outbreak, Vaccination.

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### INTRODUCTION

Monkeypox virus, a zoonotic orthopox DNA virus related to the virus that causes smallpox, was first labelled in humans in 1970 in the Democratic Republic of Congo.<sup>1</sup> The virus belongs to the genus Orthopoxvirus in the Poxviridae family.<sup>2</sup> Random outbreaks of infection have been reported in Africa, typically originating from contact with wildlife reservoirs. Such outbreaks and travel-associated cases outside Africa have had limited secondary spread, and therefore human-to-human transmission has been deemed ineffective. Despite the fact that monkeypox virus has circulated for decades in regions where it has traditionally been widespread, research into monkeypox has been neglected. Since early May 2022, more than 3000 monkeypox virus infections have been reported in more than 50 countries across five regions, prompting the World Health Organization to announce monkeypox an “evolving threat of moderate public health concern” on June 23, 2022.<sup>1</sup> The disease is called monkeypox because it was first identified in colonies of monkeys kept for research in a Danish laboratory in 1958.<sup>3</sup> There are two different genetic clades of the monkeypox virus: the central African (Congo Basin) clade and the west African clade. The Congo Basin clade has generally caused more severe disease and was

thought to be more infectious. Various animal species have been identified as susceptible to monkeypox virus. This includes rope squirrels, tree squirrels, Gambian pouched rats, dormice, non-human primates and other species. Uncertainty remains on the natural history of monkeypox virus and further studies are needed to identify the particular source and how virus circulation is maintained in nature.

### Clinical Characteristics

Monkeypox Virus is same as that of Smallpox virus in terms of Incubation period, Prodromal period, symptoms. Incubation period of smallpox virus and monkeypox virus is 7-17 days, while prodromal period is about 1-4 days. Both the viruses shows same symptoms like fever headache except Lymphadenopathy. Lymphadenopathy seen only in monkeypox infection.<sup>4</sup>

### Epidemiology

Human monkeypox is zoonotic illness that was first discovered in captive monkeys in Denmark in 1958. Human infection with monkeypox virus is first described in central African in 1970. Transmission occurs from animal reservoirs like squirrels belongs to genera *Funisciurus* and *Heliosciurus*. It was reported that monkeypox virus neutralizing antibodies were detected in the domestic pig (*Sus scrofa*), Gambian rat (*Cricetomys emini*), elephant shrew (*Petrodromus tetradactylus*), Thomas's tree/rope squirrel (*Funisciurus anerythrus*), Kuhl's tree squirrel (*Funisciurus congicus*), and sun squirrel (*Heliosciurus rufobrachium*). Conditions that enable the occurrence of human cases of monkeypox include the constant circulation of the virus in wild animals in forests and agricultural areas surrounding human settlements, the use



of meat of wild animals as an important source of animal protein, as well as close contact of humans with wild animals.<sup>5-8</sup>

### Outbreaks

Human monkeypox was first identified in humans in 1970 in the Democratic Republic of the Congo in a 9-month-old boy in a region where smallpox had been eliminated in 1968. Since then, most cases have been reported from rural, rainforest regions of the Congo Basin, particularly in the Democratic Republic of the Congo and human cases have increasingly been reported from across central and West Africa. Since 1970, human cases of monkeypox have been reported in 11 African countries: Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon, Cote d'Ivoire, Liberia, Nigeria, the Republic of the Congo, Sierra Leone and South Sudan. Since 2017, Nigeria has experienced a large outbreak, with over 500 suspected cases and over 200 confirmed cases and a case fatality ratio of approximately 3%. Cases continue to be reported until today. 70 cases of monkeypox in the U.S. Monkeypox has also been reported in travelers from Nigeria to Israel in September 2018, to the United Kingdom in September 2018, December 2019, May 2021 and May 2022, to Singapore in May 2019, and to the United States of America in July and November 2021.<sup>9,10</sup> The outbreak was first reported in India on 14 July 2022 when Kerala's State Health Minister Veena George announced a suspected imported case which was confirmed hours later by the NIV. India was the tenth country to report a monkeypox case in Asia and the first in South Asia. Currently, India has reported four confirmed

cases of monkeypox, three of them in Kerala and one in Delhi, and eight suspected cases, one case each in Delhi and Telangana, two in Bihar and four in Uttar Pradesh. On 24 July, the first locally transmitted case was reported in Delhi.<sup>11</sup>

### Transmission

Monkeypox virus can spread from animal to human from direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals. Human cases are often found close to tropical rainforests where there are animals that carry the virus.

Human-to-human transmission can occur from close contact with respiratory secretions, skin lesions and saliva of an infected person or recently contaminated objects—clothing, bedding, towels or objects like eating utensils/dishes. More studies are needed on whether the virus can spread from breathing and talking. Ulcers, lesions or sores present in the mouth or throat can be infectious, meaning the virus can spread through saliva and respiratory droplets. [Figure.1]

The virus can also spread from mother to fetus through the placenta (congenital monkeypox) or from an infected parent to child during or after birth through close contact.

It is currently not known whether monkeypox can be spread through sexual transmission routes (e.g., through semen or vaginal fluids), but direct skin-to-skin contact with lesions during sexual activities can spread the virus.<sup>11-14</sup>

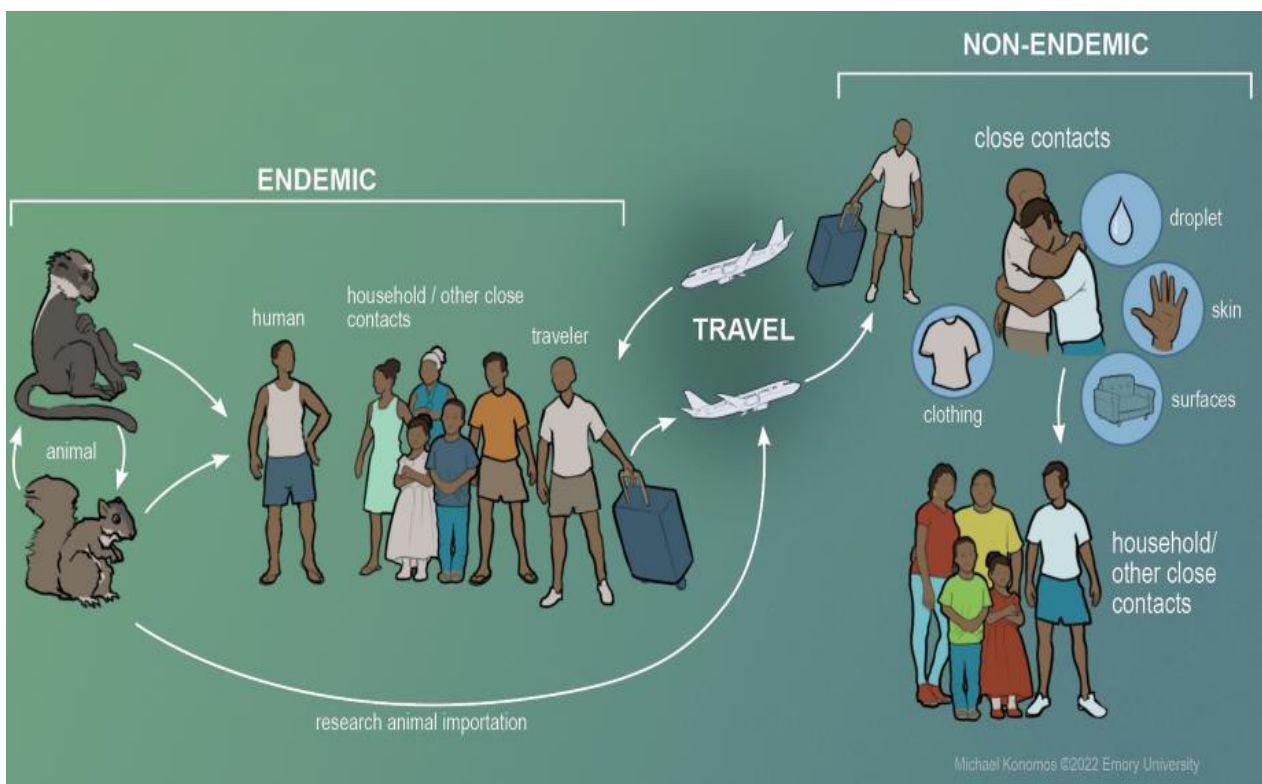


Figure 1

**Symptoms**

The incubation period of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days. The first 0-5 days of infection is characterized by fever, intense headache, lymphadenopathy (swelling of the lymph nodes), back pain, myalgia (muscle aches) and intense asthenia (lack of energy). The skin eruption usually initiates within 1–3 days of presence of fever. The rash affects the face (in 95% of cases), and palms of the hands and soles of the feet (in 75% of cases). Moreover, affected are oral mucous membranes (in 70% of cases), genitalia (30%), and conjunctivae (20%), as well as the cornea.

Also shows Fever, Headache, Muscle aches and backache Swollen lymph nodes, Chills, Exhaustion. The illness typically lasts 2-4 weeks.<sup>11,13,15,16</sup>

Lesions improvement through first macules (flat lesion less than 1 cm in diameter) to papules (Elevated lesion less 1 cm in diameter) within 1-2 days. Elevated lesion converted to vesicles. Vesicles converted to pustules (containing purulent material) within 5-7 days. In next 7-14 days hard coating on the skin formed during the wound healing is known as Scabs. [Figure.3]



**Figure 2**

**Diagnosis**

1. Lymphadenopathy (swollen lymph nodes) during the prodromal stage of monkeypox can distinguish it from chickenpox or smallpox.

2. Detection of viral DNA by polymerase chain reaction (PCR) is the favored laboratory test for monkeypox.
3. In India, All the clinical specimens are tested by the Apex Laboratory of ICMR-NIV (Pune) channeled through the Integrated Disease Surveillance Programme (IDSP) network of the respective district/state.
4. Virus Neutralisation Test (VNT) is the suggested diagnostic test for detecting poxvirus antibodies. It takes 2-3 days to do an *Orthopoxvirus* VNT and a fluorescently tagged VACV strain can be used to make identification easier.<sup>4,11,15,17,18,19,20</sup>

**Prevention**

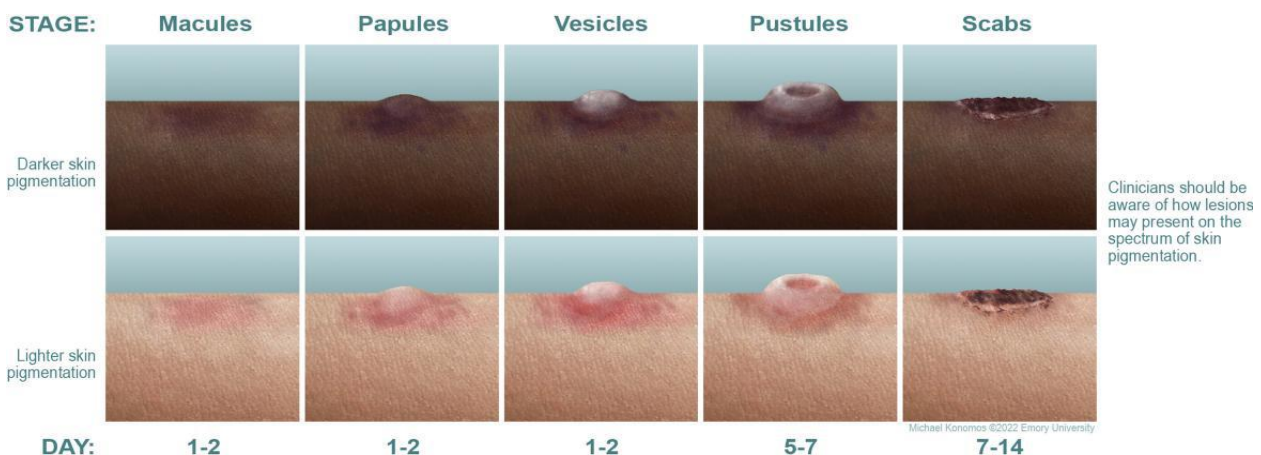
Prevention is better way to avoid the wide spread of virus. Some countries have, or are developing policies to offer vaccine to persons who may be at risk such as laboratory personnel, rapid response teams and health workers.

**Reducing the risk of human-to-human transmission**

Surveillance and rapid identification of new cases is critical for outbreak virus. The most significant risk factor of monkeypox virus infection is close contact with previously infected patient. Health workers who handled the suspected or confirmed cases are at a greater risk of infection. Patient specimens must be safely prepared for transport with triple packaging in accordance with WHO guidance for transport of infectious substances.

**Reducing the risk of zoonotic transmission-**

Over time, most human infections have resulted from a primary, animal-to-human transmission. Unprotected contact with wild animals, especially those that are sick or dead, including their meat, blood and other parts must be avoided. Additionally, all foods containing animal meat or parts must be carefully cooked before eating. Ensure that all waste, including medical waste is disposed of in a safe manner and that it is not accessible to rodent and other scavenger animals.<sup>3,10,11,12</sup>



**Figure 3**

**Table 1**

|  |  |   |
|--|--|---|
| <b>Viral culture/isolation:</b> Live virus is grown and categorized from a patient specimen.     | Can yield a pure, live culture of virus for perfect classification of the species. Orthopoxviruses produce distinctive “pocks” on chorioallantoic membranes; and other cell-based viral culture methods can be used. | The assay takes numerous days to complete. Further characterization must be done for viral identification. Must be performed at a major laboratory with expert technicians. |
| <b>Electron microscopy:</b> Negative staining produces a clear image of a brick-shaped particle. | Can be used to identify viral particles in a biopsy, specimen, scab material, vesicular fluid, or viral culture. Can distinguish an Orthopoxvirus from Herpesviridae.  | Orthopoxviruses are morphologically indistinguishable from each other.  |
| <b>Immunohistochemistry:</b> Tests for the presence of Orthopoxvirus specific antigens.          | Can be used to identify antigens in biopsy specimens. This technique can be used to identify other suspect agents.   | Can be used to identify antigens in biopsy specimens. This technique can be used to identify other suspect agents.  |
| <b>PCR, including real-time PCR:</b> Tests for the presence of monkeypox-specific DNA            | Can analyze an active case using lesion material from a patient. The assay uses viral DNA, which is stable if a specimen is kept in dark, cool conditions. Designed to be specific for monkeypox virus.              | These assays require expensive equipment and reagents.  |

**Vaccines**

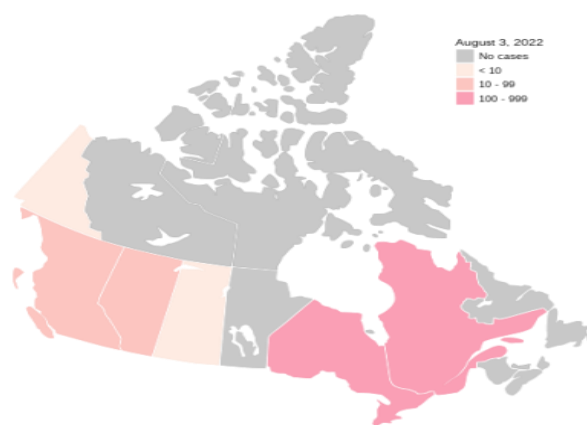
- ACAM2000:** Live vaccinia virus which is licensed vaccination in the United States.
- Modified vaccinia Ankara; IMVAMUNE (US); IMVANEX:** European Commission has authorized marketing for immunization of the general adult population.
- LC16m8:** It is a Attenuated vaccine virus: licensed for use in Japan.
- Cidofovir:** Cidofovir is a strong antiviral drug used in monkeypox infection. It acts by inhibiting DNA polymerase, has been used to treat other poxvirus infections.
- CMX-001:** It is a Modified cidofovir compound which inhibits DNA polymerase. Now it is in development stage.
- ST-246:** Available for other Orthopoxvirus infections under an investigational protocol.<sup>21,22,23,24,25</sup>

**Spillover Countries**

Till today's date the number of cases are increase all over the world. In United states-13452, Spain-5792, Germany-3213, Brazil- 3184, England-3050, Canada-1076, Peru-891, Italy-662, France-2735, Mexico- 252, Switzerland-399, India-10, Japan-04, Ghana-47 have confirmed cases.<sup>[26]</sup>

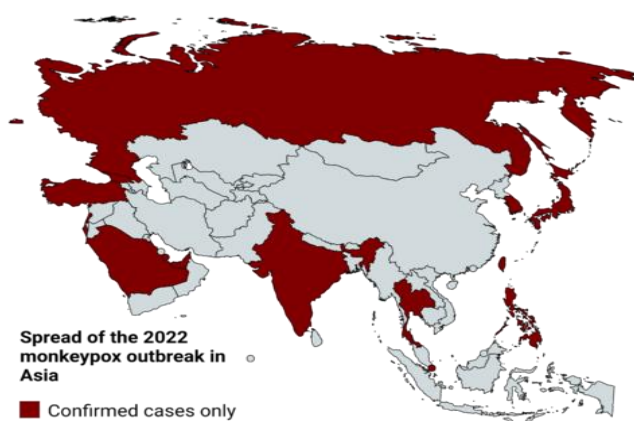


**Peru [Figure.4]**

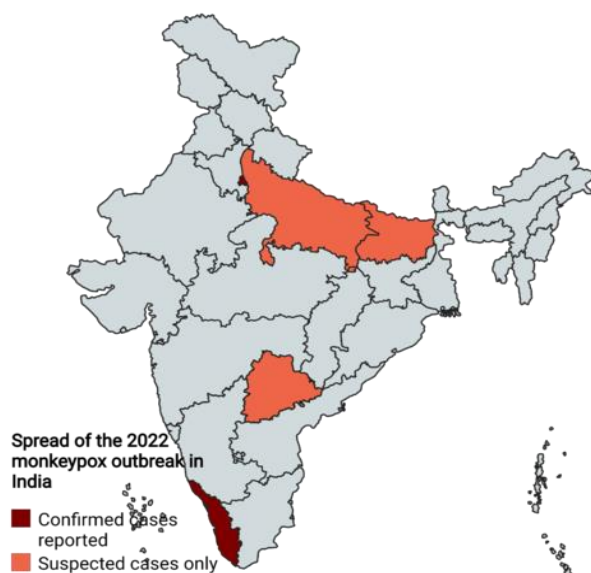


**Canada [Figure.5]**





Outbreak in Asia [Figure.6]



Outbreak in India [figure.7]

## CONCLUSION

It has been noticed that the newer pox virus should be similar to smallpox virus which produce a powerful life threat infection in human being. In the era of globalization, there is a continual compactness of individuals, carrying a potential for expand of monkeypox. So, this movement of individuals cause concerns for shifting of virus into an area without monkeypox. However, the occurrence of human illness requires additional assessment and examinations with further studies to better understand the area of disease communication and spread. Thus, improving our understanding of this predominant zoonosis will help better for prevention strategies. Also, there is a future need to develop vaccines to fight with this spillover attack.

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