

## Review Based Study of Monkeypox Disease: A Public Health Emergency of International Concern.

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### Abstract

Monkeypox, a zoonotic disease, has become the hot topic spreading across the newspaper headlines like a forest fire. The disease is transmitted from one individual to another by close, intimate contact such as cuddling, kissing, or contact with fluids in the dermal lesions. Though it is a self-limiting disease with symptoms akin to Smallpox (but a milder version), some severe cases have been reported as well. WHO has reported the case fatality rate of Monkeypox infection to be around 3–6%, which is slightly higher than that of COVID-19. Incubation period of the disease is 6–13 days on an average (range of 5–21 days). The monkeypox virus, which was previously exclusive to West and Central African nations and caused endemic diseases in monkeys and people, has recently been linked to human infections in non-endemic areas including the United States of America (USA) and more than 30 additional countries. The monkeypox outbreak continues to be a worldwide health emergency, the highest degree of alert recognised by the World Health Organization. The Centers for Disease Control and Prevention (CDC) advises vaccination for those who have been exposed to the disease as well as those who may be at higher risk of contracting it, such as those who have been identified by public health officials as a contact of someone who has the disease.

**Keywords:** Monkeypox virus, Orthopox virus, Smallpox, Infection, COVID-19.

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### INTRODUCTION

Monkeypox, a DNA virus belonging to genus Orthopoxvirus, is a zoonotic disease which was first noticed in Congo as the human infection [1]. World Health Organization (WHO) has declared monkeypox as the danger to life on 23rd June 2022 due to the reporting of successive increase to about 3,000 cases in as much as 50 countries [2]. On July 23, 2022, the WHO declared Monkeypox outbreak as a Public Health Emergency of International Concern (PHEIC), because majority of the currently reported cases are from non-endemic countries and despite tremendous efforts for their containment, there has been a steep rise, despite the containment measures employed [3].

Several more outbreaks of monkeypox were documented in captive monkey colonies in the US and Netherlands between 1960 and 1968 [16]. Despite the deaths of many infected animals during these epidemics, no human cases were found, suggesting that people were

immune to monkeypox [16]. In 1970, the national smallpox surveillance and eradication programme was started in Africa where the first case of monkeypox in a human was reported [1]. The patient was a 9-month-old boy with fever, which was followed by centrifugal rash after two days (i.e., a rash with the majority of lesions on the arms and legs). Six further cases of monkeypox were found in humans in West African nations between September 1970 and March 1971. None of these patients had received a smallpox vaccination, and the majority were young children [17]. The last reported case of Mpox in India was in March 2024, from Kerala. Since the beginning of the outbreak in 2022, India has recorded a total of 30 confirmed Mpox cases. According to Economic Times Report, August 20, 2024 an official source stated, "At the moment, the risk of a surge in monkeypox infection is very low in India and there is no need to panic."

There have been various factors which are responsible for the human transmission which includes

contact with the fluids of body, lesions in cutaneous region. Transmission from infected animals through respiratory droplets is also responsible for infection either through direct contact or contaminated passive vectors (fomites). As the herd immunity is getting lower, there has been spike in the terror due to Monkeypox infection [4]. The practice of isolation in the hospital settings with provision of negative pressure room and awareness of standard Contact and droplet precautions has been under strong recommendation by the Centers for Disease Control and Prevention (CDC).

The monkeypox virus enters the human body through any of the routes like oropharynx, nasopharynx, or intradermal. After entering the body, the replication begins at the site of viral inoculation from where the virus enters the lymph nodes present locally. The other organs also get infected gradually due to viremia. The maximum incubation period of the infection is 21 days with usual range of 7–14 days [5]. There have been reports with cases of vertical transmission and death of fetus [6]. There has been increase in Monkeypox cases in males having sex with other males (MSM). The experts have raised worry also that this would lead to discrimination against gay men [7]. The sexual behaviour of the four Italian cases [8] and the initial distribution of lesions, primarily in the anal and vaginal regions, all point to the importance of intimate contact during sexual activity for virus transmission.

The Congo Basin (CB) clade, also known as the Central Africa clade, and the West African (WA) clade are two additional genetic subgroups of the monkeypox virus [9]. While the WA clade has been documented from Western Cameroon to Sierra Leone, the CB clade has been found from Central and Southern Cameroon to the Democratic Republic of the Congo. The CB clade is thought to be more virulent with extremely high rates of interhuman transmission, serial transmission events, and secondary attack rates, whereas the WA clade is the milder one [10].

Infection with the monkeypox virus activates cellular and humoral immune responses that limit the replication of virus and create long-lasting protection in patients who have recovered. After a natural infection with monkeypox the body produces orthopoxvirus-specific IgM and IgG antibodies against a variety of antigen targets, along with long-lasting residual IgG-memory B cells [11-13] that guard against re-infection or the onset of severe disease. A rapid increase in activated effector CD4+ and CD8+ T cells is a hallmark of the cellular immune response following monkeypox infection or vaccination against the vaccinia virus [12][14][15]. This increase is followed by a gradual decline that typically returns to normality 12–20 days after the onset of symptoms [12]. The majority of patients have specialised T cells that may release a variety of Th1 inflammatory cytokines (including MCP-1, IFN-, IL-1, IL-6, and IL-8).

## Epidemiology

In the current outbreaks being reported, the WHO claims that this is the first time that chains of transmission have been reported in Europe without known epidemiological connections to West or Central Africa. In several other central and western African nations, including Cameroon, Central African Republic, Cote d'Ivoire, Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Republic of the Congo, and Sierra Leone, monkeypox has been documented as being endemic. The United States, the United Kingdom, Belgium, France, Germany, Italy, the Netherlands, Portugal, Spain, Sweden, Australia, Canada, Austria, the Canary Islands, Israel, and Switzerland are just a few of the non-endemic nations where this has been documented. As of May 31st, 2022, India has not had any cases of the monkeypox virus reported [18]. With the first case in India, there has been progressive rise in the cases in various parts of India.

As of now, no new cases of Mpox have been reported in India since March 2024. Officials maintain that the risk of a large-scale outbreak with sustained transmission remains low. The Health Ministry continues to focus on enhancing surveillance and ensuring that healthcare providers are aware of the symptoms and protocols related to Mpox. According to WHO, there have been 99,176 Mpox cases and 208 deaths reported globally from 116 countries since 2022. The number of cases and deaths has increased significantly this year, with over 15,600 cases and 537 deaths reported so far in 2024.

## Complications

The presence of swollen glands helps to distinguish the sickness from chickenpox, measles, and smallpox. Early symptoms often include a headache, muscle aches, fever, and fatigue. After a few days of the fever, lesions frequently start on the face and then spread centrifugally to other parts of the body, like the soles of the feet and palms of the hands [33-35, 56-58]. Before converting into scars when the lesions have healed, they may leave behind pale traces [35]. Possible consequences include pneumonia, encephalitis, blindness, and subsequent infections. There's a chance of stillbirth or birth defects if an infection develops during pregnancy [36]. In people who received a smallpox vaccination as youngsters, the illness might be less severe [37].

## Diagnosis

When rash diseases including syphilis, measles, chickenpox, bacterial skin infections, scabies, and drug allergies are present, it is possible to make a clinical diagnosis of monkeypox infection. One distinguishing hallmark of monkeypox infection from chickenpox or smallpox infection is the presence of lymphadenopathy during the prodromal stage of illness. The polymerase chain reaction (PCR), the standard laboratory test for skin lesion samples, can be used to check for the

monkeypox virus in order to confirm the diagnosis. Since the virus cannot persist in blood for an extended period of time, PCR blood tests are typically inconclusive. To interpret test results, it is necessary to know the patient's age, the date the fever first appeared, the rash's current stage, and the date the samples were taken [30]. The majority of positive PCR results (97%) came from cutaneous or anogenital lesions; fewer samples were taken from other sites. The percentages of positive PCR results for nasopharyngeal specimens (26%), urine specimens (3%), and blood specimens (7%), respectively, were reported. A total of 32 people from five clinical sites had their semen examined, and a total of 29 of them had PCR positive results (4 of these instances have previously been reported) [8]. In contrast, tests which can demonstrate the presence of orthopoxvirus in a patient specimen and has the potential to prohibit the exposure of the monkeypox infected person to another virus of the same genus, can form an important part of the diagnosis. These tests include detection by electron microscopy, staining methods for orthopoxvirus antigens such as immunohistochemical staining, and diagnosis of antibodies: anti-orthopoxvirus IgM and IgG for recent exposure and vaccination/past exposure respectively [30]. If the patient has not been exposed to another orthopoxvirus of the same genus, serum anti-orthopoxvirus IgM antibody testing may be sufficient for diagnosis in low-income nations [31].

The cases of the monkeypox virus are categorized as suspected, probable, and verified according to Indian criteria of Ministry of Health and Family Welfare (MOHFW). Any individual, regardless of age, who has been to one of the affected nations during the preceding 21 days and has an unexplained rash in addition to one or more of the crucial signs and symptoms is deemed to be a suspected case (fever, headache, body ache, swollen lymph nodes, and weakness). The word "potential case" refers to a suspected case with a clinically comparable illness and denotes a probable epidemiological relationship, such as direct contact with skin or skin lesions, sexual intercourse, or contact with contaminated clothing, utensils, or bedding. A monkeypox case is considered to be validated if it has been identified using PCR or sequencing [18]. According to Indian recommendations, even one case of monkeypox will be regarded as an outbreak. These guidelines also include specific surveillance measures to quickly identify and control cases and clusters of infection as soon as feasible. In addition to contact tracing and testing of all symptomatic cases after the detection of probable or confirmed cases, the core surveillance tactics include hospital-based and targeted surveillance [32].

### Treatment

As first-line antiviral therapy and supportive care, British Medical Journal (BMJ) Best Practice suggests using the two Food and Drug Administration-approved medications tecovirimat or the smallpox

medicine brincidofovir (including oxygenation, antipyretic, and fluid balance) [38]. If a bacterial infection or subsequent varicella-zoster is suspected, aciclovir or empirical treatment may be used [39]. The United States Food and Drug Administration (USFDA) and CDC have licensed the antiviral Tecovirimat (a protein inhibitor that targets the gene encoding p37—an envelope protein) [40] for the treatment of patients of monkeypox [41]. Also, because both viruses are members of the same family (Orthomyxovirus), prior studies and fieldwork have demonstrated that the smallpox vaccine may be quite helpful in preventing occurrences of monkeypox [42]. The Indian Council of Medical Research (ICMR) in India has asked pharmaceutical companies to develop diagnostic tools and vaccinations for monkeypox. India has so far primarily advised supportive management and isolation of the confirmed cases, including protection of the compromised mucous membranes and skin (rash, conjunctivitis, oral, and genital ulcers), oral rehydration and adequate nutrition, and symptom relief for fever, nausea/vomiting, pruritus, malaise/headache, and other symptoms using paracetamol, antihistaminics, topical ointments, antiemetics, etc. Close monitoring of the side effects, such as eye pain or blurred vision, dyspnea, changed consciousness, seizures, poor oral intake of meals, and excessive lethargy, is also necessary [18].

### Preventive Measures

1. **General Measures:** The management of monkeypox cases is possible by proper academic training for medical practitioners. It is necessary to promote health in vulnerable populations with targeted testing and education that is compassionately supported. To ensure that public health measures are appropriate and non-stigmatizing and to avoid messaging that will push the outbreak underground, communities must be involved from the beginning in structuring their implementation. Following infection, condom use is encouraged according to UKHSA guidelines for 8 weeks; however, further research is needed to determine the probable length and contagiousness of viral shedding in semen [43].
2. **Vaccination:** In the UK, New York City, and Canada, vaccines are currently being provided to people who are at a high risk of contracting an infection [39]. Anybody who has had close or personal contact with monkeypox-infected people or animals is also advised to get vaccinated [44]. ACAM2000 and MVA-BN are the available vaccines for controlling the current outbreak. The Food and Drug Administration (FDA) has given the second generation live, attenuated vaccinia virus vaccine ACAM2000 (Emergent BioSolutions) approval for use either before or after exposure to monkeypox. Although there is a chance of cardiac complications, it is effective [45]. The JYNNEOS vaccine, which is presently being used to treat monkeypox, was developed using the modified

vaccinia ankara (MVA) employed in the 1970s German smallpox eradication campaign to immunise more than 100,000 people [46]. Developed by Bavarian Nordic, MVA-BN is a third-generation live, attenuated, non-replicating, modified vaccinia Ankara vaccine. The vaccine was granted FDA approval in 2019 for use in preventing monkeypox in addition to the prevention of smallpox in the United States and Europe [47].

## FUTURE PERSPECTIVES

Ministry of Health and Family Welfare (MOHFW) had proposed guideline to tackle monkeypox in three significant government hospitals in Delhi. The government had also taken steps to make isolation rooms operational. It was then enlarged to include some more hospitals in Delhi. In India, National Institute of Virology (NIV) Pune has been the nodal centre for monkeypox diagnosis by RT-PCR [48, 49]. With due course of time, ICMR has given permission to 15 additional institutions to conduct the RT-PCR test for confirmation [50, 51]. All of the recovered monkeypox virus (MPXV) sequences from India are lineages of the A2 which is of clade 2b, according to ICMR research.

No matter how the monkeypox medications are approved, randomised clinical trials are required to assess their efficacy. Such experiments are being carried out by the WHO and various nations, particularly using tecovirimat [52, 53]. This assessment needs to be carried out not only in the nations where the present outbreak is occurring, but also in regions where the illness is endemic. Given the possibility for first-line medicines to develop resistance, availability of second-line medications may be crucial. In the United States, Vaccinia immune globulin, pure plasma gamma globulins extracted from individuals immunised with live vaccinia virus vaccine [54], is approved for the treatment of smallpox vaccination sequelae. Monoclonal antibodies and chemical compounds are two other treatments that are currently in development. Phase I studies for the synthetic tecovirimat counterpart NIOCH-14 were successful [55]. Preclinical trials for monoclonal antibodies are already underway in numerous facilities [55].

The Health Ministry's warning given to the hospitals and doctors helps in early detection and handling of any probable instances. This approach is in consonant with standard world practices in infectious disease control because of emphasis on surveillance and speed. Also, the government is contemplating increasing the production of large-scale test kits and ensuring that there is quick identification of individuals who are infected particularly within the high-risk zones to avoid contamination of the community with the virus. Another strategic instance that will be crucial in stopping an outbreak in India will be awareness campaigns. Informing the public about the signs, ways through which monkeypox spreads, and how it can be prevented

will help control spread the virus and encourage people with such symptoms to seek medical assistance.

## CONCLUSION

India preparedness strategy has elements of identification, control, and prevention, and awareness promotion. The Health Ministry's warning given to the hospitals and doctors helps in early detection and handling of any probable instances. In some areas where the disease is endemic, an increase in the prevalence of monkeypox may be partially explained by a gradual loss of immunity to smallpox. But the present pandemic serves as a timely reminder that viral emergence is a constant phenomenon without bounds that is frequently unforeseen in its origin, aim, and scale. There is need to further have in depth understanding of vaccination which is possible by encouragement of manufacturers to routinely test dosage administration in next clinical vaccine trials and vaccination of high risk patients. For now, the situation in India is stabilized, however, the aggravating circumstances are that Africa has the virus of a more malignant modification of monkeypox. Furthermore, community education and appropriate actions to be provided by the health organizations will remain crucial for preventing the population from this emerging health threat.

**Conflict of Interest:** Authors declare they have no conflict of interest.

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