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# Human Monkeypox: What do we know so far?

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## ABSTRACT

The first known human infection of monkeypox was recorded in 1971. MPXV has been found in a number of human instances in West Africa. The majority of confirmed cases with travel histories indicated travel to Europe and North America rather than West or Central Africa, where the monkeypox virus is endemic. Monkeypox virus (MPXV) is a type of Orthopoxvirus, which also includes camelpox, cowpox, vaccinia, and variola viruses. Two oral drugs, brincidofovir and tecovirimat, have been approved for the treatment of smallpox. MPXV can infect people in areas that were previously known to be free of smallpox. In 2003, MPXV-infected West African rats brought into the U.S. infected prairie dogs intended for sale in the pet business. Although there were no fatalities, the virus was of a less dangerous West African strain. Since 1970, eleven African nations have recorded human cases of monkeypox. Most cases have been recorded from rural, rainforest parts of the Congo Basin. Nigeria has seen a significant epidemic, with over 500 suspected cases, over 200 confirmed cases and an approximate 3% case fatality rate. People living in or near wooded regions may be exposed indirectly or at a low level. Consuming meat and other animal products from diseased animals that have been improperly cooked is a potential risk factor. The longest known chain of transmission in a community has increased from six to nine person-to-person infections. Monkeypox is prevented by increasing public knowledge of risk factors and teaching individuals about the actions they may take to decrease their exposure.

***Keywords:*** Human monkeypox, monkeypox virus, orthopoxvirus, viral zoonosis

## INTRODUCTION

Cynomolgus monkeys kept in captivity were found to have the monkeypox virus (MPXV), an orthopoxvirus, in 1958 in Copenhagen, Denmark [1, 2]. A patient from the Democratic Republic of the Congo was the victim of the first known human infection with MPXV, which was recorded in 1971 [3]. There have been other outbreaks, such as a significant one in the US in 2003 following the importation of wild rodents from Ghana, which resulted in the identification of 47 confirmed and probable human cases of MPXV infection [4]. The Congo Basin and West African clades of MPXVs have been identified by phylogenetic analysis. Human MPXV infections have also grown in Central and West Africa over the past ten years [5]. In West Africa, MPXV has been found in a number of human instances, including one in Sierra Leone in 1970 and another in March 2014 [6]. Between May 13 and June 2, 2022, 780 monkeypox cases with laboratory confirmation were reported to or detected by WHO from 27 Member States in four WHO regions where the monkeypox virus is not endemic. Epidemiological studies are still being conducted [7]. To date, the majority of documented cases have involved primarily, but not exclusively, males who have had sex with men and have sought sexual health or other health services in primary or secondary health care facilities (MSM) [8]. Despite the fact that the West African lineage of the virus has so far been identified from samples of patients, the majority of confirmed cases with travel histories indicated travel to regions of Europe and North America rather than West

or Central Africa, where the monkeypox virus is endemic [9]. It is unusual to have monkeypox confirmed in people who have not visited an area where the disease is endemic, and even one case of the disease in a non-endemic nation is regarded as an epidemic [10]. While most cases are not related to travel from endemic regions, Member States are also reporting a limited number of cases in travellers from Nigeria, as has previously been seen [11]. Given that there have never been so many cases and clusters of monkeypox, the WHO rates the risk at the global level as moderate [12, 13].
Human monkeypox cases are uncommon outside of West and Central Africa [14]. There is little data on viral kinetics or the duration of viral shedding, and there are no licensed treatments [15]. Two oral drugs, brincidofovir and tecovirimat, have been approved for the treatment of smallpox and have shown efficacy in animal studies against monkeypox [16]. The aim of this review is to study and understand the history of chickenpox smallpox, an outbreak including methods of treatment and prevention of smallpox [8, 17].

**Overview of monkeypox**

Monkeypox virus (MPXV) is a type of Orthopoxvirus, which also includes camelpox, cowpox, vaccinia, and variola viruses [18]. The virus is the most common Orthopoxvirus affecting human populations since the eradication of smallpox in 1980, as confirmed by the World Health Organization [19]. Clinical recognition, diagnosis, and prevention continue to be difficult in resource-limited endemic areas where monkeypox is found [20]. Studies conducted at the end of smallpox eradication have informed monkeypox epidemiology, but new assessments are required now that routine smallpox vaccination has ended and there is associated waning herd immunity [21]. Furthermore, foundational ecological studies are required to better understand the animal species involved in virus transmission and maintenance, as well as to inform prevention measures [22]. Monkeypox is a viral zoonosis (a virus transmitted to humans from animals) with symptoms similar to smallpox patients in the past, but it is clinically less severe [11]. Monkeypox has emerged as the most important orthopoxvirus for public health since the eradication of smallpox in 1980 and the subsequent cessation of smallpox vaccination [23]. Monkeypox is primarily found in central and western Africa, often near tropical rainforests, and is becoming more common in urban areas [19, 24]. A variety of rodents and non-human primates serve as hosts [2].
MPXV is an enveloped double-stranded DNA virus in the Poxviridae family's Orthopoxvirus genus [25]. The monkeypox virus has two distinct genetic clades: the central African (Congo Basin) clade and the west African clade [26]. Historically, the Congo Basin clade caused more severe disease and was thought to be more transmissible [27]. So far, the geographical divide between the two virus clades has been found in Cameroon, the only country where both virus clades have been discovered [28]. Several animal species have been identified as monkeypox virus susceptible. Rope squirrels, tree squirrels, Gambian pouched rats, dormice, non-human primates, and other species are included [29]. The natural history of monkeypox virus is still unknown, and more research is needed to determine the exact reservoir(s) and how virus circulation is maintained in nature [30].

**Human Monkeypox**

For the most of the 1960s, scholarly research on MPXV remained the main focus. When it was discovered that MPXV could infect people in areas that were known to be smallpox-free, attitudes drastically changed [26]. This led to worries that MPXV might occupy the space left by VARV [2]. A WHO-led campaign, however, indicated that this was improbable [31]. Before VARV was eliminated, it was widely believed that MPXV infections in

humans were present, but they went unnoticed because of smallpox [32]. While attenuated human infections have typically occurred in West African nations, the most severe human MPXV infections have been documented in the Congo Basin region of Africa [33]. Although human-to-human transmission has been documented, touching MPXV-infected animals (such as bush meat) typically causes human illnesses [11]. When MPXV-infected West African rats were brought into the USA and later infected native prairie dogs intended for sale in the pet business, an MPXV outbreak happened in 2003 [34]. There are various ways that human infections are started, and these different ways seem to have an impact on how the disease manifests clinically [7]. Although there were no fatalities, the virus was of a less dangerous West African strain. Nevertheless, this occurrence showed how easily MPXV can cross the interspecies barrier [35, 36].

**Outbreaks**

A 9-month-old boy in a location where smallpox had been eradicated in 1968 was the first person to be detected with monkeypox in 1970 in the Democratic Republic of the Congo [3]. Since then, most cases have been recorded from rural, rainforest parts of the Congo Basin, mainly in the Democratic Republic of the Congo, and a growing number of human cases have been documented throughout central and western Africa [37]. Since 1970, eleven African nations have recorded human cases of monkeypox: 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 [38]. The actual impact of monkeypox is unknown [38]. For instance, in 1996–1997, the Democratic Republic of the Congo reported an epidemic with a lower case fatality ratio and a higher attack rate than usual [38]. An epidemic of chickenpox (produced by the varicella virus, which is not an orthopoxvirus) and monkeypox was discovered, which might explain alterations in transmission dynamics, whether actual or perceived [39]. Since 2017, Nigeria has seen a significant epidemic, with over 500 suspected cases, over 200 confirmed cases, and an approximate 3% case fatality rate.

The relevance of monkeypox to global public health is demonstrated by the fact that it affects not only nations in west and central Africa but also the rest of the world [40]. The first monkeypox epidemic outside of Africa occurred in the United States in 2003 and was caused by contact with sick prairie dogs kept as pets [41]. Ghana-imported Gambian pouched rats and dormice were kept with these animals. In the United States, this outbreak caused about 70 cases of monkeypox [9]. In addition, visitors from Nigeria were diagnosed with monkeypox in Israel in September 2018, the United Kingdom in September 2018, December 2019, May 2021, and May 2022, Singapore in May 2019, and the United States in July and November 2021 [33]. Multiple cases of monkeypox were reported in non-endemic nations in May 2022 [42]. Currently, research is being conducted to comprehend further the epidemiology, infection origins, and transmission patterns [43].

**Transmission**

Direct contact with the blood, body fluids or cutaneous or mucosal lesions of infected animals can result in zoonotic transmission [44]. Evidence of monkeypox virus infection has been discovered in several African animals, including rope squirrels, tree squirrels, Gambian pouched rats, dormice, and other kinds of monkeys [45]. The natural reservoir of monkeypox has not been discovered, but it is most likely rodents [45]. Consuming meat and other animal products from diseased animals that have been improperly cooked is a potential risk factor [45]. People living in or near wooded regions may be exposed to sick animals indirectly or at a low level [46]. Transmission from person to person can occur through intimate contact with

respiratory secretions, skin lesions, or recently contaminated objects [47]. Transmission by respiratory droplet particles often necessitates prolonged face-to-face contact, putting health professionals, household members, and other close contacts of active patients at increased risk [34]. In recent years, the longest known chain of transmission in a community has increased from six to nine subsequent person-to-person infections [32]. This may result from the suspension of smallpox immunisation in all populations, which leads to a decline in immunity [48]. Transmission can also occur via the placenta from mother to foetus, resulting in congenital monkeypox, as well as during and after delivery through intimate contact [49]. Although close physical contact is a well-known risk factor for transmission, it is still unknown if monkeypox may be transferred, primarily through sexual pathways [50]. There is a need for research to comprehend this risk better [40, 51].

**Physical examination**

The most consistent clinical symptom distinguishing monkeypox from smallpox and chickenpox is lymph node enlargement, particularly in the submental, submandibular, cervical, and inguinal regions [48]. Enanthema has been associated with nonspecific lesions and inflammation of the pharyngeal, conjunctival, and vaginal mucosae [52]. In the exanthema stage, lesions grow synchronously over 14–21 days in a specific body area, comparable to the progression of lesions in smallpox [53]. Unlike smallpox, though, crops may develop skin sores [29]. In contrast to smallpox, the distribution of the lesions is not strongly centrifugal [29]. The progression of lesions from macules to papules to vesicles and pustules is followed by umbilication, crusting, and desquamation [29]. The majority of lesions have a diameter of between 3 and 15 millimetres [29]. The head, face, trunk, and limbs are all affected. There are lesions in both covered and uncovered areas [54]. There are lesions on the palms and soles. There may be necrosis, petechiae, and ulceration as symptoms [44]. Pain is uncommon, and when it does occur, it is frequently caused by a subsequent bacterial infection [30]. Pruritus is possible [26]. Patients who have been vaccinated against smallpox get a lesser form of the disease [26]. Lesions in youngsters may manifest as nonspecific, erythematous papules ranging in width from 1 to 5 mm, indicative of arthropod bite responses [26]. A faint umbilication may be observed [40]. Twenty per cent of unvaccinated patients in the African outbreaks had a confluent, erythematous eruption on the face and upper torso, which some writers refer to as the septicemic rash of monkeypox [55]. The hemorrhagic and flat forms of smallpox, which have been documented in individuals with smallpox, have not been observed in patients with monkeypox. As lesions heal, they may leave behind deep pockmarks [55]. During the monkeypox epidemic in 2022, a substantial percentage of sufferers were guys who had sex with other men [15, 44]. In a few cases, the perianal and vaginal regions were the initial locations of lesion manifestation [36]. With the detection of typical lesions in these regions, clinicians should have a high suspicion of monkeypox, especially if the patient has a recent travel history [32, 56].

**Therapy for Monkeypox**

There are currently no clinically validated specific therapies for monkeypox infection. However, there are preventative steps that can aid in preventing an epidemic [57]. As with the majority of viral infections, therapy consists of symptom control [13, 42]. The infected person should stay in isolation, wear a surgical mask, and keep the lesions covered as much as possible until all crusts have gone off spontaneously and a new skin layer has grown [39]. The effectiveness of the oral DNA polymerase inhibitor brincidofovir, intracellular viral release inhibitor tecovirimat, and vaccinia immune globulin against the monkeypox virus is uncertain [30]. In extreme instances,

medicines having established efficacy against orthopoxviruses in animal trials and severe vaccinia vaccination sequelae may be evaluated for exploratory usage [34]. Due to the recognised top limit of the monkeypox incubation period, those exposed to the virus should check their temperature and symptoms twice every day for 21 days [24]. Infection coincides with the development of symptoms; consequently, close contacts do not require isolation when asymptomatic [44]. In some instances, post-exposure immunisation with modified vaccinia, Ankara vaccine (live, non-replicating smallpox and monkeypox vaccine) is suggested [58]. Broken skin or mucous membranes in contact with an infected patient's bodily fluids, respiratory droplets, or scabs constitute a "high risk" exposure necessitating immediate post-exposure immunisation [59]. According to the CDC, immunisation within four days of exposure may prevent the development of sickness, and vaccination within fourteen days may minimise the severity of the condition [17]. The replication-defective modified vaccinia Ankara vaccine has a higher safety profile than first- and second-generation smallpox vaccinations and is administered in a two-dose series four weeks apart [54]. In contrast, to live vaccinia viral preparations, the administration of modified vaccinia, Ankara, does not result in skin lesions or represent a danger of local or generalised dissemination [54]. In addition, clinical investigations have demonstrated that modified vaccinia Ankara is safe and increases antibody production in individuals with atopy and weakened immune systems, which are known contraindications for administering live vaccines [29, 54]. Further data collection and feasibility research are required to determine the possible advantages and downsides of prophylactic immunisation against monkeypox in endemic areas [54]. Access to medical treatment, diagnostic capabilities, and infrastructure hinders the capacity to make well-informed judgments on the most effective method of combating this neglected tropical illness [54, 60].

**Vaccination and prevention**

Several observational studies have found that smallpox vaccination is approximately 85% effective in preventing monkeypox [24]. Therefore, previous immunisation against smallpox may result in a lesser disease [15]. A scar on the upper arm indicates that a person has been vaccinated against smallpox [1, 48]. The original (first-generation) smallpox vaccinations are now unavailable to the general population. Some laboratory or health employees may have gotten a more modern smallpox vaccine to protect them in the case of occupational exposure to orthopoxviruses [61]. In 2019 we saw the approval of a vaccine based on a modified, attenuated vaccinia virus (Ankara strain) to prevent monkeypox [25, 50]. This vaccination requires two doses, and its availability remains restricted [62]. Because of the cross-protection given by the immune response to orthopoxviruses, formulations of smallpox and monkeypox vaccines are derived from the vaccinia virus [23].

Primarily, monkeypox is prevented by increasing public knowledge of risk factors and teaching individuals about the actions they may take to decrease their exposure to the virus [26]. Currently, scientists are evaluating the viability and suitability of vaccination for the prevention and control of monkeypox [48, 63]. Some nations have or are establishing programmes to provide vaccinations to those who may be at risk, including laboratory technicians, fast response teams, and health care professionals [15, 64].

## CONCLUSION

In conclusion, the new introduction of the monkeypox virus in the United States necessitates that the disease's histologic characteristics not be attributed to another viral activity but rather be included in the dermatopathologic diagnostic repertory. Patient and medical staff education is of the highest significance in countries where the

monkeypox virus is prevalent. Local confinement is the most effective barrier against the global spread. Historically, the capacity of the monkeypox virus to spread between people has been restricted. Notwithstanding, the dwindling number of people immunised against smallpox sets the stage for an increase in human monkeypox incidence, hence increasing the likelihood of viral mutation. Therefore, boosting patient awareness of this disease, reporting integrity, and access to diagnostic capabilities are crucial for gathering the data required to obtain more profound knowledge of monkeypox and bolster its defences.

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