

# A Review on Monkeypox

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## Abstract:

Monkeypox is a **re-emerging zoonotic disease caused by a DNA virus** that belongs to the orthopox virus genus of the Poxviridae family. After the eradication of smallpox in 1980, monkeypox has gradually emerged as the most important orthopox virus from a public health perspective. Monkeypox typically causes fever, chills, rash, and lesions on the face or genitals. MPXV (monkeypox virus) is considered a large virus that measures about 200–250 nm with the appearance “brick-like” or ovoid shape, The virus’s original source is wild animals. It can be found in a variety of mammals including squirrels, mangabey monkeys, and Gambian rats. Viral transmission can occur through direct and indirect contact with live or dead animals, including handling wild game, a bite or scratch, or contact with fluids or lesions from an infected animal. Human-to-human transmission likely occurs through contact with lesions, body fluids, contaminated bedding or clothing, and exposure to respiratory droplets from infected persons. Animal-to-human transmission of MPXV may occur via animal bites or scratches by infected small mammals, including rodents and nonhuman primates, or through the consumption of bush meat. Any patient with a fever and disseminated vesicular or pustular rash should be immediately placed on airborne and contact precautions, as these are the classic symptoms of Orthopox virus infections. smallpox antivirals with poxvirus activity, such as cidofovir, brincidofovir, and tecovirimat, are active against the monkeypox virus. Monkeypox is usually a self-limiting disease; however, new-borns, children, and people with underlying immune deficiencies may be at risk of more serious illness and death.

**Keywords:** Monkeypox, MPXV (monkeypox virus), Orthopox virus, Smallpox virus, DNA virus

## 1.Introduction:

Monkeypox is a **re-emerging zoonotic disease caused by a DNA virus** that belongs to the orthopox virus genus of the Poxviridae family.<sup>[1]</sup> The first recognized human case was of a boy aged 9 months in DR Congo in 1970. Between 1970 and 2017, several outbreaks and sporadic cases have been reported in several areas of central and west Africa, including Cameroon, Central African Republic, Congo Brazzaville, Côte d'Ivoire, DR Congo, Gabon, Liberia, Nigeria, Sierra Leone, and South Sudan. The first outbreak outside Africa occurred in the USA in 2003, where 47 human cases were attributed to close contact with prairie dogs infected by rodents imported from Ghana. After the eradication of smallpox in 1980, monkeypox has gradually emerged as the most important orthopox virus from a public health perspective, because it is the most prevalent in human beings.<sup>[2]</sup> The disease is described clinically as very similar to smallpox (pustular rash, fever, respiratory symptoms) except for marked lymphadenopathy. With smallpox eradicated, a differential clinical diagnosis must distinguish between monkeypox and varicella (chickenpox). In varicella, the pocks appear gradually and in different stages of development, mainly on the trunk of the body. In typical human monkeypox, the pocks concentrate on the face, arms, and legs. They all appear within a 1–2 days period and develop uniformly so that, contrary to varicella,

scabs, and vesicles are not seen simultaneously.<sup>[3]</sup> MPXV (monkeypox virus) is one of the 4 orthopox virus species pathogenic for humans, the other 3 beings are (1) variola major virus (VARV), the causative agent of smallpox, now eradicated, (2) variola minor virus, and (3) cowpox virus (CPXV). There is a range of animal poxviruses, several of which have zoonotic potential. Infections in humans have been described for vaccinia virus, cowpox virus, buffalopox virus, and sporadic cases of camelpox. Monkeypox infects a wide range of mammalian species, but its natural host reservoir remains unknown.<sup>[4]</sup> Monkeypox virus was discovered in 1958, when it was isolated from the lesions of a generalized vesiculopustular disease among captive monkeys at the State Serum Institute, Copenhagen. The close resemblance between smallpox and monkeypox in captive primates focused attention on the monkeypox virus as a potential threat to smallpox eradication.<sup>[5]</sup>

## 2. Sign and Symptoms:

Monkeypox typically causes fever, chills, rash, and lesions on the face or genitals. It can be spread through close contact with an infected person or their clothing or bedsheets, but sexual transmission has not yet been documented.<sup>[6]</sup> Prior to, and concomitant with, rash development is the presence of maxillary, cervical, or inguinal lymphadenopathy (1– 4 cm in diameter) in many patients (Figure 2.1.). Enlarged lymph nodes are firm, tender, and sometimes painful. Fever often declines on the day of or up to 3 days after rash onset. Often, the rash first appears on the face and quickly appears in a centrifugal distribution on the body. The distinctive lesions (Figure 2.2.) often present as first macular, then papular, then vesicular, and pustular. The number of lesions on a given patient may range from a few to thousands. Lesions are often noted in the oral cavity and can cause difficulties with drinking and eating. The skin of patients has been noted to be swollen, stiff, and painful until crusts appeared. Patients have been observed with pulmonary distress or bronchopneumonia, often late in the course of illness, suggestive of secondary infection of the lungs. Vomiting or diarrhea can occur by the second week of illness and can contribute to severe dehydration. Ocular infections can occur and may result in corneal scarring and permanent vision loss.<sup>[7]</sup>



Figure 2.1. Cervical lymphadenopathy in a patient with active monkeypox during a monkeypox outbreak in Zaire, 1996–1997. Photograph credit: Dr. Brian W. J. Mahy.



Figure 2.2. A patient with monkeypox showing characteristic lesions. Photograph credit: Dr. Marcel Pie Balilo.

### 3.Virology:

Monkeypox virus is an enveloped double-stranded DNA virus that belongs to the Orthopox virus genus of the Poxviridae family. There are two distinct genetic clades of the monkeypox virus: the central African (Congo Basin) clade and the west African clade.<sup>[8]</sup> It has a characteristic ultrastructure with mature mulberry-shaped viral particles (Figure 3.1.). Although MPXV has a low mutation rate, under certain selective pressure, adaptive mutations of the MPXV may occur, and that might have enhanced its transmissibility. Additionally, recent studies indicate that the MPXVs in this outbreak exhibit single nucleotide alterations and frameshift mutations compared to those in previous episodes.<sup>[9]</sup> The Orthopoxviruses are antigenically and genetically similar, with open reading frames (ORFs) having >90% sequence identity amongst its members.<sup>[10]</sup> The Poxviridae family consists of complex, large, enveloped, and linear double-stranded DNA viruses. The Poxvirus family is a large group of viruses that infect a wide range of animals. The variola virus and Molluscum Contagiosum virus are human-specific. The Poxviridae family has two subfamilies: Chordopoxvirinae, which causes infection in vertebrates, and Entomopoxvirinae, which infect insects. The subfamily Chordopoxvirinae has been subdivided into eighteen genera the Orthopoxvirus genus. Orthopox viruses are large viruses (size range: 140–450nm) Generally, brick or oval-shaped forms.

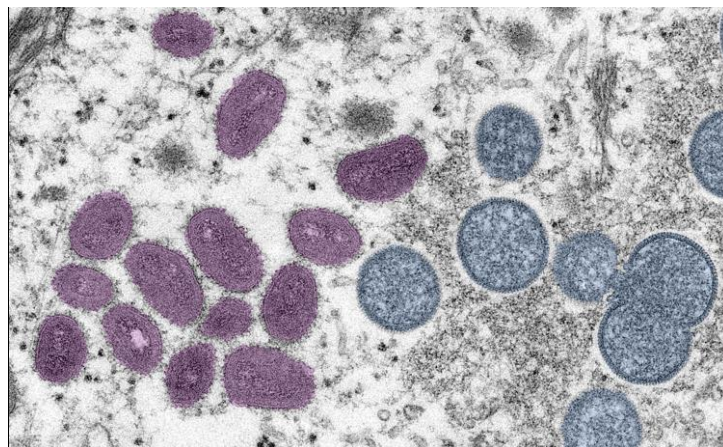


Figure 3.1 –virus particles (pink) and the immature particles (blue) from a skin lesion of a patient with

monkeypox. (Photo credit: Cynthia S. Goldsmith, Russell Regnery; Courtesy CDC Image library.) Monkeypox belongs to the Orthopoxvirus genus and is one of the four humans pathogenic Orthopoxvirus species.<sup>[11]</sup> MPXV is considered a large virus that measures about 200–250 nm with the appearance “brick-like” or ovoid shape. MPXV has two distinguished hereditary subgroups, the West African and the Central African (Congo Basin) which motivate more serious infection and is believed to cause a higher infective possibility. In spite of the fact that there are different geographical incidence locations between the two

virus categories, they both occurred in the same country “Cameroon”. The virus’s original source is wild animals. It can be found in a variety of mammals including squirrels, mangabey monkeys, and Gambian rats. Even though the essential host continues to be not clear, the rodents are believed to be the host reservoir rather than monkeys.<sup>[12]</sup>

#### 4.Pathophysiology:

Monkeypox is a double-stranded DNA virus of the Orthopox virus genus, similar to smallpox and cowpox, and is the most important active virus remaining in the genus in the post-smallpox eradication era. Transmission of monkeypox occurs through contact with an infected animal or human or through contact with material contaminated by the virus. Viral transmission can occur through direct and indirect contact with live or dead animals, including handling wild game, a bite or scratch, or contact with fluids or lesions from an infected animal. Human-to-human transmission likely occurs through contact with lesions, body fluids, contaminated bedding or clothing, and exposure to respiratory droplets from infected persons. In addition, emerging evidence suggests aerosolized transmission may be possible. Localized genital lesions have occurred in many patients during the current outbreak, disproportionately among young adult males who reported having sex with males; this suggests that sexual transmission plays a role in the current outbreak. A systematic review estimated the secondary attack rate to be between 0.3% to 10.2%, though data suggest it could be as high as 50% among household contacts. However, it can be as low as 0% with appropriate personal protective equipment. The time from exposure to the onset of symptoms is approximately 12 days. During this incubation period, the virus replicates at the inoculation site and then spreads to the lymphatic system. A viremia develops, allowing the virus to spread to other organs and ultimately resulting in the onset of symptoms.<sup>[13]</sup>

#### 5.Etiology:

Monkeypox is a rare disease caused by MPXV infection. MPXV is an enveloped, linear, double-stranded DNA virus, which is a member of the Orthopox virus genus, of the Chordopoxvirinae subfamily, within the Poxviridae family. Having the same morphological characteristics as other orthopox viruses, virions are ovoid or brick-shaped particles. MPXV is among the largest and most complex animal viruses, ranging from 200 to 250 nm in length when viewed by electron microscopy. The virus consists of 4 main components: the core, lateral bodies, the outer membrane, and the outer lipoprotein envelope. Virions are enclosed by a geometrically corrugated lipoprotein outer membrane, the core is described as biconcave and contains a large double-stranded DNA genome, with a lateral body on each side. The MPXV genome is approximately 197 kb and encodes 200 proteins. The ends of the genome contain an identical but oppositely oriented sequence called an inverted terminal repeat (Figure 5.1.). The genome has close hairpins on both ends and contains about 190 nonoverlapping open reading frames of >180 nt in length. Four open reading frames at the left side of the genome are located within the inverted terminal repeat and thus have counterparts on the right side of the genome. Although MPXV is a DNA virus, its entire life cycle occurs in the cytoplasm of infected cells. All of the proteins required for viral DNA replication, transcription, virion assembly, and egress are encoded by the MPXV genome. Phylogenetic trees showed that MPXV sequences were classified into 2 genetic clades, named the West African clade and the Central African clade (Congo Basin clade). The genomes of monkeypox strains from Central and West Africa were compared because of the difference in virulence and the results revealed a 0.55%–0.56% nucleotide difference between the 2 types of strains. MPXV is resistant to ether and drying, while easily inactivated by chloroform, methanol, and formalin. In addition, heating at 56°C for 30 minutes inactivates the virus. The virus can be stored at 4°C or – 20°C over a short time period or at – 70°C over a long time period.<sup>[14]</sup>

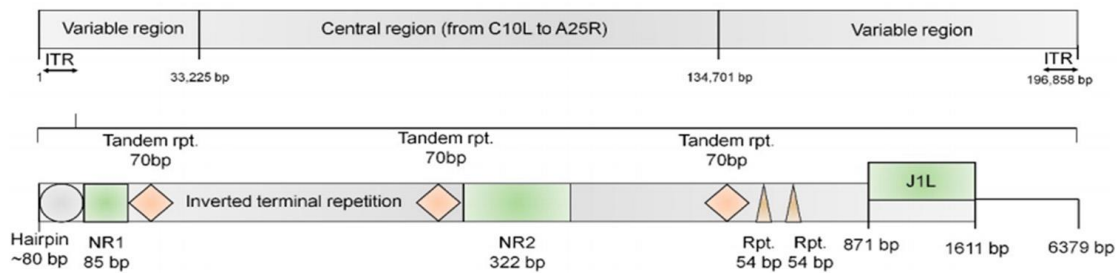


Figure 5.1. The structure of the MPXV genome. The ends of the genome possess a 6379- bp inverted terminal repeat (ITR), NR1, NR2, 2 short tandem repeats, and the coding region.

## 6.Epidemiology:

By the end of 2019, a total of 1347 cases and an additional 28,815 suspected cases of monkeypox had been reported. In the 1980s, the number of confirmed and probable monkeypox cases in the DRC had increased 9- fold compared with that in the 1970s. Monkeypox cases continued to increase in the 1990s. From 2000 to 2009, 3 African countries reported 92 confirmed cases, while during 2009–2019, 7 African countries reported 277 confirmed cases. Compared with the last 3 decades of the 20th century, outbreaks as of the year 2000 were greater in terms of the total number of cases, but there were fewer single-case reports. In Africa, outbreaks of monkeypox have been frequent. From 1996 to 1997, an unprecedented outbreak occurred in the DRC (511 cases), with a peak incidence rate in August 1996. The majority of cases were secondary cases resulting from the person-to-person transmission, with clinically milder disease. In September 2017, the largest monkeypox outbreak was recorded in Nigeria, which was caused by a strain belonging to the West Africa clade.<sup>[15]</sup> This resurgence occurred after 40 years of no cases being reported. Between 2017 and 2019, 183 cases were diagnosed, with most cases being among those aged 21–40 years, whereas historically, the disease was more prevalent among < 15-year-olds.<sup>[16]</sup> A total of 502 confirmed cases and 8 deaths were reported from September 2017 to October 2021.<sup>[17]</sup> Recently, monkeypox outbreaks have occurred in non-endemic countries, with most cases having no direct travel links to an endemic area. Whereas, prior to this outbreak, confirmed cases in non-endemic countries usually had a travel history to endemic countries. It was not until 2003 that the first monkeypox outbreak occurred outside of Africa, with 47 confirmed or possible cases being reported in the USA. These cases occurred after contact with an infected pet marmot, which was infected with MPXV from an infected exotic animal imported from Ghana.<sup>[18]</sup> Seven international monkeypox cases were confirmed from 2018 to 2021, and all cases had a history of travel and exposure in Nigeria, of these: 3 were in the UK (May 2021), 2 were in the USA<sup>[19]</sup> (July 2021, and November 2021), one was in Israel (October 2018),<sup>[20]</sup> and one was in Singapore (May 2019).<sup>[21]</sup> Before the 2017 Nigeria outbreak, most human monkeypox cases occurred in rural, forested areas in Africa. However, monkeypox cases occurred in urban areas in Nigeria. This change indicated that human-to-human transmission increases the risk of MPXV spread.<sup>[22]</sup> Since the discovery of the monkeypox virus and its isolation from *Cynomolgus* monkeys in Copenhagen in 1958, this poxvirus infection has remained a zoonosis,<sup>[23]</sup> being chiefly confined to African countries. The first human infection due to the monkeypox virus was recorded in a child in the Democratic Republic of Congo in 1970. Soon, it was followed by other sporadic cases from Liberia, Nigeria, and Sierra Leone.<sup>[24-27]</sup> Since then, human monkeypox infection was occasionally reported in African countries for the next few decades (Figures 6.1.-6.6.). Unfortunately, there are an alarming number of human monkeypox cases now reported from non-African countries. The first outbreak of human monkeypox was reported in the Democratic Republic of Congo in 2003,<sup>[28]</sup> followed by South Sudan in 2005.<sup>[29]</sup> Then there was a lull in human monkeypox infections. Similarly, in Nigeria, several cases were reported from 2017 onward, after the first reported case 39 years ago. Outside of Africa, the Midwest states of the United States recorded 47 cases in 2003, when Gambian pouch rats were imported as exotic pets from Ghana.<sup>[30]</sup> Soon after, isolated cases

from the United Kingdom, Israel, and Singapore were reported.<sup>[31]</sup> A significant feature of these patients indicates that they are chiefly men who have sex with men (MSM) and live in urban areas.<sup>[32]</sup>



Figure 6.1. A 7-year-old girl with monkeypox from Equateur Region, Zaire. Front view, during day 8 of rash.



Figure 6.2. A 7-year-old girl with monkeypox from Equateur Region, Zaire. Rearview



Figure 6.3. The old scar on the arm is not due to vaccination



Figure 6.4. The heavy concentration of lesions on the hands, inguinal lymphadenopathy, and pustules on the genitalia



Figure 6.5. Swollen lower face and neck due to cervical and submandibular lymphadenopathy.



Figure 6.6. Lesions on lips, tongue, and eyelids.

## 7. Distribution of the disease:

### 7.1. Sources of infection:

Monkeypox is a zoonotic infectious disease, which usually occurs sporadically in forested areas of Central and West Africa. It is caused by MPXV of the Orthopox virus family. Monkeypox can be spread by contact and by large droplets of exhaled fluid. Most cases of infection occur from a reservoir host or infected animals. Humans are the sole reservoir host of variola virus, with no known animal reservoirs, whereas MPXV has a wide range of permissible animal reservoir(s), including rodents, mammals, and primates. Specific animal reservoirs include Kenyan vervet monkeys, chimpanzees, African elephants, wild boars, antelope, Gambian poached rats, pet prairie dogs, West African squirrels, and anteaters. The natural reservoir of monkeypox has not yet been identified, and the mode of transmission in nature remains

unknown. However, African rodents are suspected to play a role in the transmission of monkeypox to humans.

### **7.2. The mode of transmission:**

MPXV spreads when a person is exposed to the virus from an infected animal, infected person, or virus-contaminated material. Transmission of MPXV occurs via the animal-to-human and human-to-human routes. The virus can also spread from a mother's placenta to a fetus. MPXV may be transmitted from animal to human through direct contact with the blood, body fluids, or cutaneous or mucosal lesions from bites or scratches of infected animals, treatment of wild animals, or the use of products made from infected animals. Monkeypox is mainly transmitted from person to person through direct contact with infectious ulcers, scabs or bodily fluids, or materials that have been exposed to bodily fluids or ulcers, such as clothing or linen. In long-term face-to-face contact, it can also be transmitted through respiratory secretions. MPXV also can spread during close contact between people, including during sexual intercourse, kissing, hugging, or touching body parts with monkeypox, the MPXV transmission mode from 1970 to 2019. Throughout history, monkeypox mainly occurred in Africa, and the mode of transmission was animal-to-human, while the human-to-human transmission was limited, with cases of secondary human-to-human transmission accounting for about 28% of cases. However, during this outbreak, the mode of transmission is human-to-human transmission, and most cases have been diagnosed in GBMSM. Although the disease is not generally considered a sexually-transmitted infection, inter-human transmission has been proven through close contact. Therefore, there is a risk of community transmission.

### **7.3. Susceptible population:**

The contemporary susceptible population is composed mainly of individuals who are unvaccinated for the vaccinia virus (approximately 80%–96% of the population). Although the vaccinated population has some immunity to MPXV, protection may have waned over time, and there is still a risk of infection. Historically, vaccination against smallpox (vaccinia) was shown to be 85% effective in preventing MPXV and the case fatality rate of people who are unvaccinated against vaccinia is 9.8%.<sup>[14]</sup>

### **8. Diagnosis:**

To diagnose cases of monkeypox, epidemiological and clinical characteristics are required. Usually, patients have travelled to an endemic country or have been in contact with infected animals and patients in the previous 21 days. Outbreaks of MPXV infection have been ongoing in non-endemic countries since the beginning of May 2022. Moreover, almost all of these cases had no travel history to endemic countries. Therefore, the WHO has developed surveillance case definitions for the current monkeypox outbreak in non-endemic countries.<sup>[14]</sup> In order to diagnose monkeypox, health providers should collect a proper specimen and send it carefully to a capable lab. Verifying human MPX virus relies on the sample type and the available laboratory tests. As the illness symptoms are still difficult to identify and hard to minimize in low-income countries. It poses a world challenge since these areas are considered endemic to this disease. The confirming techniques that are used for analyzing specimens and determining MPX include genetic, phenotypic, and immunological methods. The diagnostic methods that can be used to identify human MPX. These approaches work better when combined with the medical and epidemiological information including the patient's immunization history. A detailed medical history with a focus on specific information, such as recent traveling to an endemic area, vaccination with the smallpox vaccine, along with linking clinical information to the existing symptoms, can be extremely directing to the disease diagnosis, but it is not sufficient to establish a definitive one. The golden test to establish the diagnosis is the polymerase chain reaction. Besides its high accuracy and sensitivity, the viral DNA within the lesion



persists constantly for a long time if kept in a dark and comparatively cool atmosphere. As Real-time PCR needs high quality labs which are hard to be found in low-resource countries. The upcoming technologies are relied on to develop the PCR and qPCR to overcome their consequences and become available outside the large laboratories, which allows having an accurate diagnostic tool within the reach of all medical staff, even those in poor countries. Establishing the source of the condition requires antibody-based diagnosing. Immunological tests against orthopox viruses have cross-reactivity with other Orthopox viruses. Still, these tests may be valuable when there is a previous indication to explain the disease's cause. Although IgG alone cannot provide a definitive diagnosis to a patient who has been exposed to orthopox virus during his life through vaccination, IgM is considered more effective in diagnosing newly infected patients retrospectively. MPX patients often pursue medical help at countryside health centers or hospices which are not provided with electricity; therefore, it is a requirement to improve the current tests so they can be used in developing countries where there is a lack of resources and human performance.<sup>[12]</sup> In light of the ongoing outbreak, clinicians evaluating patients with new-onset fever and rash should consider MPX, particularly if lymphadenopathy is also present. Typically, serum antibodies are detected around 2 weeks postexposure, when oral or skin lesions appear. A swab is used to collect crust or exudate from the lesion to isolate viral nucleic acids for diagnosis. The swabs and lesion aspirates demonstrate the strongest correlation with both infectiousness and the clinical course of infection. The western blot method, on the other hand, uses MPX virus proteins to verify their presence. The recommended test for identifying MPXV during acute infection, as per the World Health Organization, is the real-time polymerase chain reaction test. In general, these tests are available at state laboratories for public health in the developed world. Commercial tests are not available at this point.<sup>[9]</sup> Monkeypox infection can be confirmed by using PCR for monkeypox DNA from the patient's specimen. Orthopox viruses in the specimen can be visualized using electron microscopy; viral culture isolation can also be undertaken. Immunohistochemical staining for Orthopox viral antigens, serum studies for anti-Orthopox virus IgM (for recent infection), and anti-Orthopox virus IgG (for prior exposure/vaccination) are other important laboratory studies. The differential diagnoses include chickenpox, measles, secondary syphilis, hand-foot-mouth disease, and infectious mononucleosis. Genital human monkeypox can be confused with chancroid, donovanosis, and other nonvenereal genital ulcers.<sup>[33]</sup>

## 9. Management:

As MPX is a self-limiting infection, management is essentially symptomatic, and no specific antiviral agents are available. Nevertheless, the smallpox vaccine and the antiviral agents' cidofovir, brincidofovir, and tecovirimat have activity against MPX and could be prescribed for patients with comorbidities. Passive immunization with immune globulin vaccinia (6000 UI/kg to 24,000 UI/kg) has been successful.<sup>[9]</sup> There is no specific clinically proven therapy for monkey pox disease. Tecovirimat (S.T.-246 and Brincidofovir are the two antiviral preparations approved by the US Food and Drug Administration (FDA) for smallpox. Their use in human monkeypox has insufficient data but suggests that Tecovirimat is more effective than Brincidofovir. The preventive measures include isolation of the patient, keeping lesions covered, proper, and disposing of infectious materials with appropriate precautions. Contact tracing and monitoring for a reasonable duration will assist in controlling the spread of the disease, A concerted two-decade effort of the United States government to develop antivirals and next-generation vaccines against smallpox resulted in two FDA-approved antivirals and two next-generation vaccines.

1. The first next-generation smallpox vaccine called ACAM-2000 is similar to the discontinued Dryvax vaccine, known to generate long-lasting immunity and provide 85% protection against human monkeypox.
2. The second next-generation smallpox vaccine is MVA - BN (JYNNEOS in the United States), manufactured with the Modified Vaccinia Ankara strain and administered by two subcutaneous injections, 4 weeks apart. While the former vaccine is contraindicated in pregnancy, atopic dermatitis, and various immune deficiencies, the latter displayed no serious adverse events and no risk of

inadvertent inoculation and autoinoculation. The MVA-BN vaccine is approved in the United States for use against both smallpox and monkeypox. it still requires clinical trials for human efficacy. Among 528 human monkeypox patients in one report. (5%) were given antiviral therapy or vaccinia immune globulin with a favorable response. Tecovirimat (TPOXX or ST246) inhibits the spread of the virus by inhibiting the viral envelope protein VP37, thus blocking the final steps in the viral maturation and its release from infected cells. The CDC-held Emergency Access Investigational New Protocol allows the use of Tecovirimat for non-variola orthopox virus infections such as monkeypox. The protocol also includes an allowance for opening an oral capsule and mixing its contents with liquid or soft food for pediatric patients weighing less than 13 kg. Cidofovir and Brincidofovir work by inhibiting viral DNA polymerase, the latter being more effective in controlling MPV infection.<sup>[33]</sup>



(A) Figure 9. (A) Oral lesions (right tonsil) were visible already at the patient’s first presentation  
 (B) (B-D) Both patients developed 10 to 12 initially vesicular.

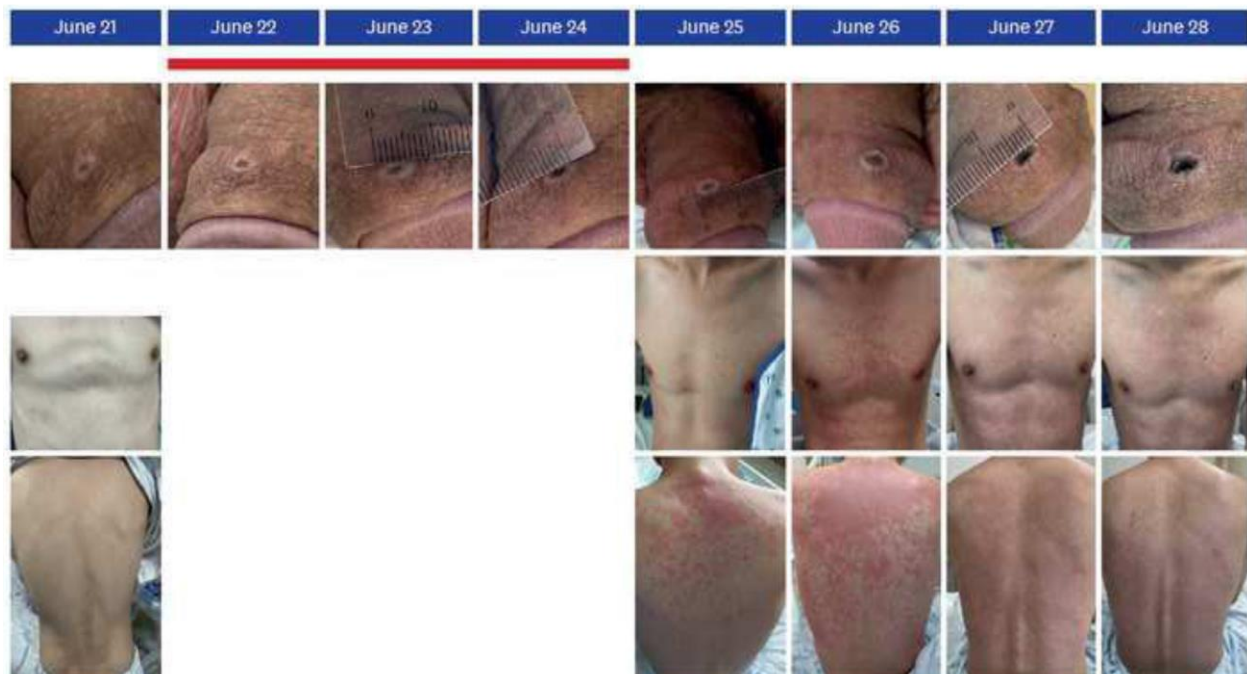


Figure.9.2. Photographs of the penile ulcer and the skin lesions. The red colored line indicates the period of fever ( $\geq 37.5\text{ }^{\circ}\text{C}$ ).

### 10.Prevention:

The disease can be contained by following the basic principles of infection control, which include rapid identification and isolation of the index patient, the use of personal protective equipment (PPE) by health

care workers, and comprehensive contact tracing, which includes secondary case monitoring throughout the incubation period. Hospital systems should ensure that their health providers, particularly clinical staff, are aware of the infection control procedures, especially when dealing with infected patients. Any patient with a fever and disseminated vesicular or pustular rash should be immediately placed on airborne and contact precautions, as these are the classic symptoms of Orthopox virus infections. Vaccines against smallpox are effective in preventing MPX and postexposure prophylaxis. The US Food and Drug Administration has approved the JYNNEOS (Bavarian Nordic) smallpox vaccine to prevent MPX, and the ACAM2000 vaccine can be used off-label for the same purpose. Vaccination of close contacts has successfully limited transmission in previous outbreaks. If a prophylactic vaccine is administered as early as possible after exposure, the infection can be prevented. Vaccinia immune globulin may be an alternative postexposure prophylactic agent when the smallpox vaccine is contraindicated. The Centers for Disease Control and Prevention also recognizes the theoretical risk of airborne transmission and recommends implementing airborne infection control protocols whenever possible. These protocols include using N95 masks and other PPE when providing care or coming into close contact with an infected individual.<sup>[9]</sup>

Ever since the SARS outbreak in 2003 and even earlier, experts have realized the grave threat of zoonotic infections rising from the constant remodeling of ecosystems, as per a report issued by the Institute of Medicine back in 2003 as a follow-up to their 1992 report. MPX is one such infection that is portrayed by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) as an emergent disease. Preventing the spread of MPX is a war fought on many fronts: On the ecological front, limiting humans' exposure to suspect host animals must be the first step as available evidence indicates that human-to-human transmission cannot sustain the continuance of an endemic without repeated zoonotic introductions.<sup>[14]</sup>

## 11. Treatment:

Currently, there is no standard-of-care treatment for monkeypox except supportive care. Although smallpox antivirals with poxvirus activity, such as cidofovir, brincidofovir, and tecovirimat, are active against the monkeypox virus, these antivirals would most likely be reserved for the treatment of severe cases or immunocompromised persons. Additionally, vaccinia immune globulin, a hyperimmune globulin licensed by the Food and Drug Administration of the United States (US FDA) for the treatment of certain complications of vaccinia vaccination, may be recommended for severe cases. Monkeypox is usually a self-limiting disease; however, newborns, children, and people with underlying immune deficiencies may be at risk of more serious illness and death. Complications from severe cases of monkeypox include skin, pneumonia, altered sensorium, and eye infections that can lead to loss of vision. A systematic review conducted before the current outbreak reported that the overall CFR was approximately 8.7% but CFR was different in different areas, ranging from 0 to 11%. However, this may be overestimated because surveillance in endemic countries is limited. In the current outbreak, only one death was reported in Nigeria in the second quarter of 2022, and the estimated CFR was only 0.03% (1/ 3413).<sup>[33]</sup> Monkeypox virus is a self-limited disease that needs several weeks for recovery. Infected cases of monkeypox have a fatality rate ranging from 1% to 10%. Monkeypox virus infection does not currently have a proven, safe treatment. However, the Smallpox vaccine, cidofovir, ST-246, and vaccinia immune globulin (VIG) are used to combat a monkeypox outbreak. The US Food and Drug Administration (FDA) has approved the use of cidofovir and tecovirimat drugs for treating smallpox. Although these two approved vaccines are not specific to the monkeypox virus, they are effective against it due to the similarity of the virus to smallpox. Most likely, such medications would only be prescribed for severe cases or in immunocompromised patients, and they would be obtained from a public health department or the CDC.<sup>[14]</sup>

## 11.1. Drugs used in monkeypox:

### 11.1.1. Antiviral treatment for monkeypox:

Certain antiviral agents have been prepared for the unexpected emergence of smallpox, and these drugs have been then approved in the treatment of monkeypox in recent years. Though monkeypox in most patients is mild and self-limited and only needs supportive care, antiviral agents are commonly retained for severe illness occurring in immunocompromised patients, pediatrics, pregnant and breastfeeding women, and for complicated lesions, especially those near the mouth, eyes, or genitals.

### 11.1.2. Tecovirimat:

Tecovirimat (Tpoxx; ST-246) was the first antiviral agent approved for smallpox and monkeypox. Over 300,000 compounds were screened for against orthopox virus, and the best activity was observed in tricyclonone carboxamides, and after testing analogs, the lead candidate, a 4-trifluoromethyl phenol derivative, was initially named ST-246. Tecovirimat inhibits the production of extracellular viruses by interacting with the F13L gene product, which is a phospholipase involved in the formation of a protein complex that catalyzes the envelopment of intracellular mature virus particles.<sup>[34,35]</sup>

### 11.1.3. Brincidofovir:

Brincidofovir (BCV or hexadecyloxypropyl-cidofovir [HDP-CDV]), initially named CMX001, is a lipid conjugate of cidofovir (CDV). The therapeutic efficacy of BCV was shown to be higher than that of CDV due to increased cellular uptake and better conversion to the active form by intracellular enzymes. In contrast to CDV, HDP-CDV is orally active and lacks the nephrotoxicity of CDV. Increased oral bioavailability and increased cellular uptake of BCV are facilitated by its lipid portion, which is responsible for the improved activity profile.<sup>[36]</sup>

## 12. Estimated burden:

Bisanziosa et al. established a projected model based on a simulated population of 50 million people with socioeconomic and demographic characteristics typical of a high-income European country. They estimated that the introduction of 300 cases could result in 402 secondary cases without interventions. The median duration of these outbreaks for this scenario would be 37 (95% CI: 19e121) weeks following the introduction of 300 cases.<sup>[37]</sup> Contact tracing with isolation of symptomatic cases would reduce the number of secondary cases by 68.9%. Moreover, adding ring vaccination to contact tracing would further reduce the number of secondary cases by 86.1%.<sup>[38]</sup> This projection of the monkeypox burden was compatible with the WHO's risk assessment of overall public health risk at a global level as currently moderate.<sup>[39]</sup>

## 13. Conclusion:

Fortunately, and in contrast with SARS-CoV-2, monkeypox is not a novel pathogen and has been markedly less transmissible. However, it is important to act quickly to halt community transmission and avoid the establishment of additional animal reservoirs, potentially leading to further outbreaks. Despite the continuous increase in cases, the spread may be less extensive than in the COVID-19 pandemic. The reason for this is due to the way the monkeypox virus spreads, which is through close contact with bodily fluids, such as saliva from coughing, and FDA-approved drugs, such as cidofovir and tecovirimat. During the last 2 years, scientists, healthcare personnel, and world authorities have coordinated, promptly combating, and curtailing any future epidemic or pandemic. Our preventive strategy can allay apprehensions, anxiety, morbidity, mortality, and resources. Global health systems should develop effective strategies to mitigate the spread of monkeypox. However, precedence should be given to containment efforts that should rely on enhanced case finding, case isolation, contact tracing, and vaccination.

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