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Clinical manifestations of human monkeypox infection and implications for outbreak strategy

Nishant Johri[a,b,*], Deepanshu Kumar[a,b], Priya Nagar[a,b], Aditya Maurya[a,b], Maheshwari Vengat[c], Parag Jain[d]

[a] Department of Pharmacy Practice, Teerthanker Mahaveer Hospital & Research Centre, Moradabad, Uttar Pradesh, India
[b] Department of Pharmacy Practice, Teerthanker Mahaveer College of Pharmacy, Moradabad, Uttar Pradesh, India
[c] Department of Oncology, Chester Medical School, Chester, United Kingdom
[d] Department of Pharmacology, Chhatrapati Shivaji Institute of Pharmacy, Durg, Chhattisgarh 491001, India

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ABSTRACT

Monkeypox is an orthopoxvirus-based zoonotic illness that causes symptoms similar to smallpox in humans. Health care workers around the world are making it a priority to educate themselves on the many clinical manifestations and treatment options for this virus as public health agencies strive to stop the current outbreak. The infected do not have access to any treatment at this time. However, information obtained from the smallpox pandemic has led researchers to examine vaccinia immune globulin (IVG), tecovirimat, and cidofovir as viable treatments for monkeypox. Moreover, medication like tecovirimat may be given in extreme circumstances, and supportive therapy can help with symptom relief. The European Medicines Agency (EMA) certified tecovirimat as safe and effective against monkeypox in 2022, per the World Health Organization (WHO). As there are now no established guidelines for alleviating these symptoms, the efficacy of these treatments is highly questionable. Some high-profile cases in recent years have cast doubt on the long-held belief that this illness is rare and always resolves itself without treatment. We aimed to conduct this review to get a deeper comprehension of the evolving epidemiology of monkeypox by analysing such factors as the number of confirmed, probable, and potential cases, the median age at presentation, the mortality rate, and the geographic distribution of the disease. This study offers an updated review of monkeypox and the clinical treatments that are currently available as a result of the worldwide epidemics.

Introduction

In 1970, the zoonotic monkeypox virus was first detected in people in the Democratic Republic of the Congo. In Africa, isolated occurrences linked to human contact with wildlife reservoirs have been observed (particularly rodents). Human-to-human transmission is inefficient because secondary spread is low outside Africa [1,2]. Monkeypox has been endemic for decades, but study has been underfunded and underestimated. Since early May 2022, over 3000 instances of monkeypox virus infection have been documented in over 50 nations across five regions, prompting the WHO to name monkeypox a "moderate public health concern" on June 23, 2022. [3]. Monkeypox has no natural host, despite infecting many animal taxa. The virus has only been isolated from a rope squirrel in the DRC and a sooty mangabey in the Ivory Coast [4–8].

Monkeypox (MPX) has a similar clinical presentation to smallpox, but enlarged lymph nodes occur early in the illness, usually with fever. Rash symptoms, including lesions, follow fever and lymphadenopathy by one to three days. Secondary bacterial infections, such as bronchopneumonia, respiratory distress, gastrointestinal involvement, sepsis, dehydration, encephalitis, and corneal infection, can lead to blindness [9,10]. Symptomatic relief and supportive care are used to treat monkeypox virus infections. Vaccination with vaccinia virus (another orthopoxvirus) has been 85% effective against monkeypox [11]. Clinically, monkeypox resembles smallpox. Monkeypox deaths are 10% lower than smallpox [12]. Poxviruses have 130-360 kbp genomes and reproduce in vertebrate or invertebrate cells [13]. Poxviruses do not replicate or express their genomes in the nucleus, relying instead on cellular proteins. Poxviruses rely on virally encoded proteins for cytoplasmic replication [14–19]. Replication and transcription genes are in the middle of the genome, while host interaction genes are at the ends. Orthopoxviruses are larger than other viruses, prompting a quick immune response. Orthopoxviruses resist being eliminated by the host immune system by using virulence gene-expressed compounds as immune modulators [20–23]. These immune response modulating proteins can be split into two classes: intracellular and extracellular. Intracellular and extracellular modulatory proteins regulate the immune response. These modulatory proteins trick the immune system and disseminate viral. These proteins let orthopoxviruses like monkeypox evade the immune system.

* Corresponding author.
E-mail address: nishantjohri22@gmail.com (N. Johri).

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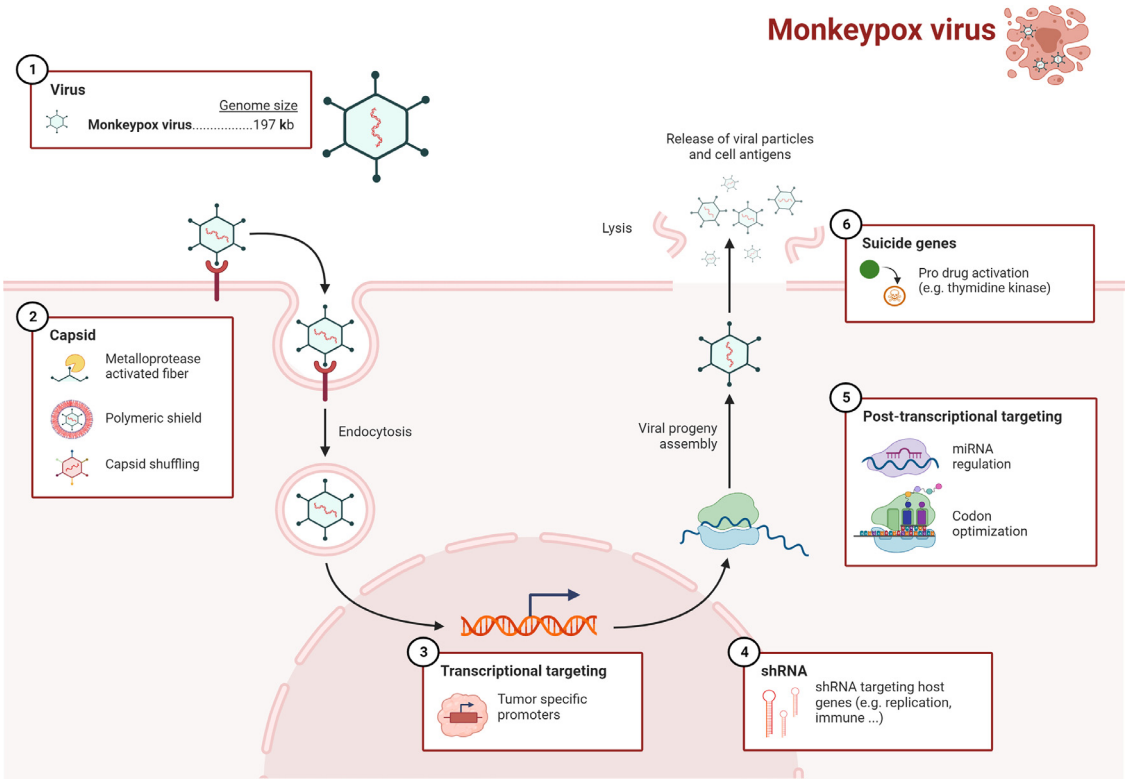

Fig. 1. Cytosolic MPV pathways for the viral life cycle.

MPV can enter through the oropharynx, nose, or skin. The virus multiplies at the injection site, then spreads to lymph nodes. After a brief time of viremia, the virus infects the entire host's body. MPV resembles other orthopoxviruses. MPVs feature an oval or brick-shaped lipoprotein membrane [6]. MPV's double-stranded, linear DNA sequence (197 kb). The DNA virus MPV replicates in the cytoplasm. Virus DNA replication, transcription, and virion assembly require proteins [24]. Poxvirus infection begins with macropinocytosis, endocytosis, and fusion [25] (Fig. 1).

Different poxviruses can reveal the monkeypox virus's reproduction cycle [26]. Guarnier bodies are now called factories. Structures where poxvirus DNA replicates [16,27,28]. In the early stages of infection, each factory manifests as a DNA-containing structure encased in membranes and powered by the host cell's RER. As DNA synthesis continues, these factories will grow and change shape as viral mRNA and host translation factors fill the vacancies.

Epidemiology

Sub-Saharan Africa may have been afflicted by monkeypox for thousands of years, ever since humans first contracted the disease through close contact with diseased primates [29]. Prior to 1970, when the success in eradicating smallpox revealed the persistence of smallpox-like illness in rural areas, monkeypox was not recognised as a separate disease. Research monkeys were used to discover the monkeypox virus for the first time in 1958 at State Serum Institutes in Copenhagen, Denmark, and Africa [30,31]. The number of confirmed cases of monkeypox by the CDC as of July 1, 2022, is at 5783 and has been found in 52 countries throughout the world. The majority of the world's current instances of monkeypox are found in western Europe and other parts of the western hemisphere. On 14 July 2022, Kerala's State Health Minister Veena George reported a suspected imported case, which was later confirmed by the NIV. This marked the beginning of the outbreak in India. India reported the first case of monkeypox in South Asia and was the ninth country in Asia to do so. Ten cases of monkeypox have been confirmed in India; three have been found in Kerala, and five have been found in Delhi. A further eight instances have been recorded; one each in Delhi and Telangana, two in Bihar, and four in Uttar Pradesh.

Table 1
The location of reported or diagnosed cases of monkeypox to WHO from May 13 to June 2, 2022.

Countries	Confirmed cases
Argentina	2
Canada	58
Mexico	1
United States of America	19
Morocco	1
United Arab Emirates	8
Austria	1
Belgium	12
Czechia	6
Denmark	2
Finland	2
France	33
Germany	57
Hungary	1
Ireland	4
Israel	2
Italy	20
Malta	1
Netherlands	31
Norway	1
Portugal	138
Slovenia	6
Spain	156
Sweden	4
Switzerland	4
United Kingdom	207
Australia	3

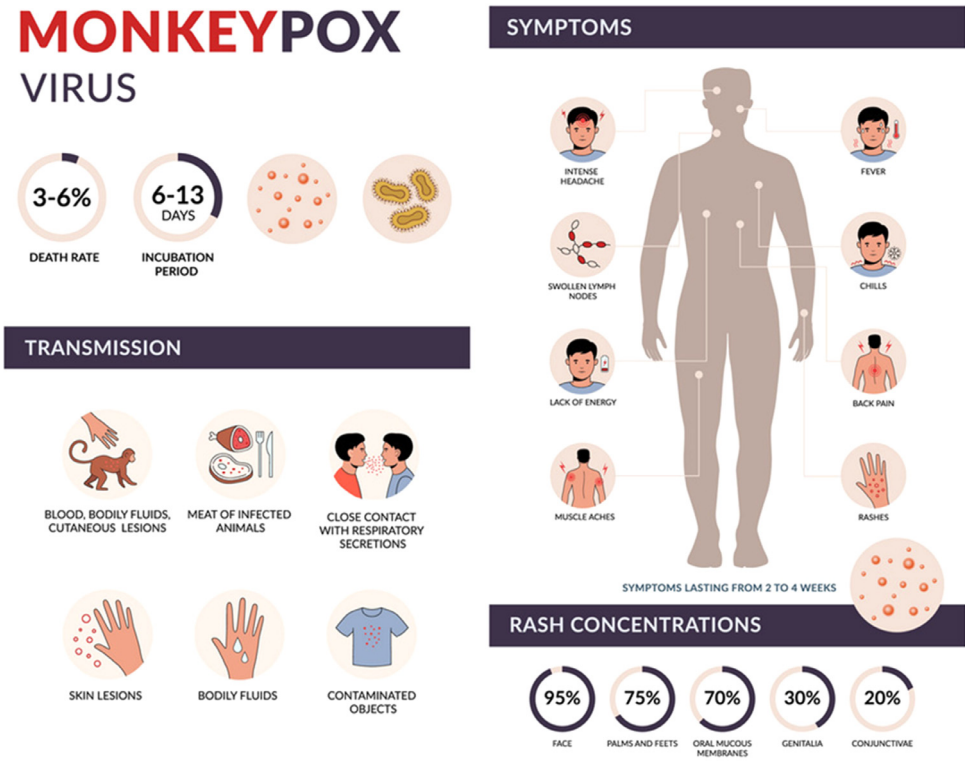

Fig. 2. Schematic representation of human monkeypox transmission modes and symptoms.

An outbreak of monkeypox

As of June 2, 2022, 27 non-endemic countries across four WHO Regions had reported 780 laboratory-confirmed cases to WHO under the International Health Regulations (IHR), or WHO had detected these instances via official public sources. Since the Disease Outbreak News on May 29, when 257 cases were recorded, there has been a +203 percent increase to 523 laboratory-confirmed cases. As of June 2, 2022, there have been no fatalities attributed to the ongoing monkeypox outbreak in non-endemic nations. But reports of new cases and fatalities persist from regions where the disease is common. In non-endemic countries, the location of reported or diagnosed cases of monkeypox to WHO from May 13 to June 2, 2022 is depicted in Fig. 2. The WHO European Region accounted for the vast majority of cases (n = 688; 88%) (20 Countries). Cases have also been reported from the Eastern Mediterranean Region (n = 9), the Western Pacific Region (n = 3), and the Americas Region (n = 80; 10%). India has reported four Monkeypox cases so far, three cases in Kerala and one in Delhi. A youth in Kerala presenting monkeypox-like symptoms died. A high-level inquiry will be conducted into the death of a person with symptoms of monkeypox in Chavakkad Kuranjiyur. The result of the test conducted in a foreign country was positive. He sought treatment in Thrissur. The central government is on an alert even as the count of infections in some other countries has risen.

Re-emergence of monkeypox in both endemic and nonendemic locations has been linked to high-risk sexual behavior, a changing biologic nature of the virus, climatic change, declining immunity after smallpox vaccination, and increasing international travel when COVID-19 travel restrictions were lifted. The recent epidemic of monkey pox virus (MPXV) has now occurred in south east Asia region, the first case of the viral monkey pox disease in India. The two individuals who traveled from the UAE were infected with the virus strain A.2, which is distinct from the one driving the outbreak in Europe, according to an investigation of the first two cases of monkeypox in India by an institute of the Indian Council of Medical Research (ICMR). Major clusters have not been connected to the A.2 strain, which was found in the US last year. The B.1 monkeypox virus is the cause of the present outbreak.

Clinical presentation

People who are male, younger than 15 years old, and who are not resistant to smallpox are more likely to contract monkeypox in a sylvatic setting where monkeypox is prevalent [32–35]. Historically, patients have first had prodromal symptoms as fever, headache, chills, malaise, and lymphadenopathy before finally breaking out in a characteristic rash. Rash manifests initially in the mouth, before spreading to the rest of the face and often the palms and soles. Macules give way to papules, vesicles, pustules, and eventually scabs throughout the progression of each lesion. The number of lesions may vary from 10 and 150, and they may last for as long as 4 weeks. The infective period for a patient with shingles spans from the onset of symptoms (assumed to include prodromal signs prior to the rash's appearance) until the lesions scab over and fall off, at which point a new layer of skin forms. There are multiple hypothesised routes of transmission for the monkeypox virus, all of which include coming into physical contact with an infected animal or human ([36]; Fig. 3). Although domestic rodent infestations and the hunting or preparation of bushmeat from a range of species are known risk factors for human infection, it might be difficult to determine a specific case's exposure to animals.

To this day, researchers have not determined the precise means by which monkeypox is spread. Bunge et al. [11] describe potential mechanisms of transmission as well as other risk factors for catching monkeypox. Transmission from animals to humans typically occurs by saliva, respiratory excretions, or the exudate from cutaneous or mucosal lesions, but can also occur through direct contact or exposure to infected animals. One possible route of exposure is by feces-borne viruses. Households in places where food is scarce are more likely to resort to hunting and cooking small mammals, putting them at greater risk of contracting monkeypox [37,38]. Unlike animal-to-human transmission, which typically occurs by bites or scratches, human-to-human transmission

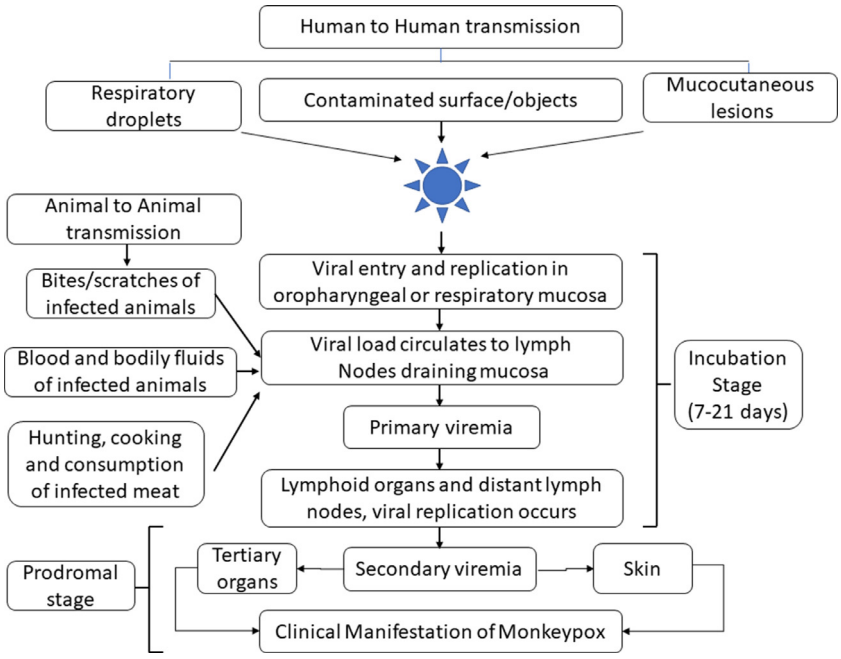

Fig. 3. Proposed Pathogenesis of Monkeypox.

typically occurs through breathing droplets during prolonged face-to-face contact or through contact with lesions of an infected individual. Household members are at danger of contracting a virus if they come into contact with a contaminated object or surface, such as shared beds, a shared home, or utensils used for eating or drinking. It has also been noted that males who have intercourse only with other males are at a higher risk of contracting monkeypox than those who do not [39]. Whether from monkeys to humans or humans to monkeys, the transfer of the virus is the first step in the aetiology and pathophysiology of monkeypox [40].

Rarely, patients with monkeypox develop secondary infections include bacterial superinfections, encephalitis, pneumonitis, and conjunctivitis/keratitis [41,42]. There has been no comprehensive study of when difficulties arise or at what rate. Monkeypox often manifests as a milder illness than smallpox and frequently includes lymphadenopathy, which is uncommon in smallpox. Another difference between monkeypox and smallpox is that monkeypox often has milder symptoms and appears with lymphadenopathy, while smallpox rarely does [43,44]. It's also worth noting that the skin symptoms of monkeypox might be hard to tell apart. Many victims of the ongoing 2022 monkeypox epidemic have presented with non-typical symptoms. The rash, for instance, is always there but may only appear in the vaginal, perigenital, and perianal regions at various times [45]. Moreover, individuals may report with no or little prodromal symptoms, which often start after a rash has appeared in a specific area. As clinicians strive to make an accurate diagnosis for patients and the world works to contain the outbreak, it is essential to take into account a wide range of possible illness manifestations.

Respiratory droplets are the most prevalent route of human-to-human transfer, notwithstanding their rarity. Direct contact with infected mucosa, such as the oropharynx or lungs (Fig. 4); [20,46]), is another route of transmission for monkeypox virus. The monkeypox virus replicates at the site of injection after it has entered the host cell; in human-to-human transmission, this is the respiratory and oropharyngeal mucosa [47]. In primary viremia, the virus is first detected in the blood and then travels to the regional lymph nodes after replication. In secondary viremia, the viral load is carried through the bloodstream to far-flung lymph nodes and organs. The incubation phase encompasses the full time frame, and it normally lasts between seven and fourteen days, with a maximum of twenty-one days. Since no outward signs of monkeypox appear during the incubation period, transmission is prevented at this time. Monkeypox has a distinct prodromal stage that is associated with the onset of symptoms and the appearance of the disease in the clinic [48].

Diagnosis

The ongoing 2022 outbreak highlights the importance of maintaining a high index of suspicion for monkeypox infection and being familiar with the disease's frequently unusual manifestations [49]. If a doctor suspects monkeypox, he or she will want to know about any recent trips, sexual partners, or anyone they were particularly close to who may have had the disease [50]. Sharing a bed, a meal, and a bathroom Further, this diagnosis should not be ruled out just because the patient has no history of international travel or has no definite reports of intimate contact with someone who has had a rash or who has been diagnosed with monkeypox. It's also important to check the skin for any signs of trouble. In order to properly diagnose a patient who is thought to be suffering from an active case of monkeypox, a skin lesion biopsy is the best course of action. Lesions should be unroofed in order to sample virus-containing fluids adequately, and several specimens should be acquired from at least two different lesions on different areas of the body. While some labs are equipped to perform direct PCR tests for MPXV, others only test for OPXV, which then needs to be confirmed by testing for MPXV at a reference lab. One to two weeks after contracting the monkeypox virus, the typical, nonspecific symptoms appear.

More lesions will appear on the face and extremities than on the trunk and abdomen with a centrifugal distribution. Lesions in the oral cavity might prevent a person from properly consuming food and water. This complication has been observed in 19% of unvaccinated monkeypox patients and is thought to be caused by the substantial skin disturbance caused by the lesions [51–53]. Infected people typically exhibit a highly specific rash pattern.

A rash that is widespread and vesiculopustular in appearance is the defining feature of monkeypox. There are a few stages of the rash itself before the desquamation phase, when the scabs start peeling off [9]. It has been observed that these unique lesions typically manifest in the order, enanthem, macular, papular, then vesicular, and finally pustular. Lesions on the mouth and tongue, known as enanthem, occur before

the rash does. Crusty sores are no longer contagious once fresh skin has emerged. The desquamation process describes this time. Until the desquamation phase, when the crusting produces extreme itching, the lesions are unpleasant at all the stages.

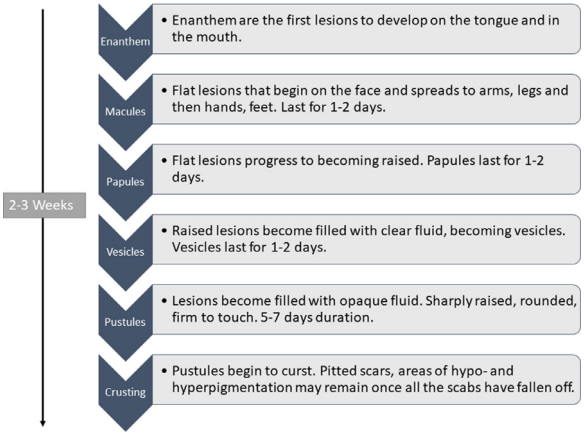

Fig. 4. Stages of the Vesiculo-pustular Rash in Monkeypox Patients.

Furthermore, gastrointestinal symptoms such as vomiting and diarrhoea that appear in the second week of sickness can lead to severe dehydration in an infected person. Complications from monkeypox infections are more common in those who have not been immunised (74% vs. 39.5%). One of the complications of monkeypox infection is bronchopneumonia, however it is more likely in those who are also infected with the influenza virus. Focal lung tissue necrosis, diffuse pulmonary consolidation, and fulminant bronchopneumonia have been repeatedly observed in non-human primates following respiratory challenge at a variety of viral dosages. Patients with severe inflammation and bronchopneumonia may have difficulty breathing and be less motivated to eat and drink.

Clinical management and treatment

Mild symptoms are typical of monkeypox, and most individuals recover without treatment. The Centers for Disease Control and Prevention (CDC) advises that there is presently no cure for monkeypox virus infections. However, the use of vaccinia vaccine, cidofovir, tecovirimat, and vaccinia immune globulin (IVG) is being considered as a potential treatment for monkeypox based on lessons learned during the smallpox epidemic [54]. But antiviral medications currently used to treat smallpox may also be effective against monkeypox. Studies in vitro and in vivo against poxviruses show that the antiviral drug cidofovir (Vistide) is effective. According to the World Health Organization, in 2022 the European Medicines Agency (EMA) approved tecovirimat for use against monkeypox. Since tecovirimat is not yet widely available, its use needs to be tracked closely. Several studies have shown that cidofovir can be used as an antiviral medication by blocking the viral DNA polymerase ([55]; lvarez et al., [56,57]). Several orthopoxviruses, such as variola, vaccinia, cowpox, ectromelia, rabbitpox, and monkeypox, have been shown to be susceptible to tecovirimat's unique effectiveness [58–60].

To some extent, other antiviral treatment medicines have also demonstrated efficacy against Orthopoxviruses. Among these is the modified cidofovir medication CMX-001. It has been shown to be active against Orthopoxvirus species, including Monkeypox [52,61], and it does so without causing the same level of nephrotoxicity as cidofovir. In addition to ST-246 (Tecovirimat), another promising antiviral impact is seen with TPOXX, which is effective against a wide range of Orthopoxviruses. In doing so, it prevents the virus from escaping the cell. When treating MPV infections, doctors in endemic regions might weigh the benefits and risks of using these medications based on the individual patients they are caring for.

According to current CDC recommendations, this medication may be used to treat individuals with severe cases of monkeypox; however, the drug's therapeutic efficacy in such cases is uncertain. Adults and children alike can take the antiviral drug tecovirimat (ST-246) to combat the effects of smallpox. Because this antiviral medication has been given the go light by the FDA, it can be utilised to treat an outbreak of monkeypox. The injectable form of tecovirimat (200 mg capsule) is taken orally. Complications from vaccinating against vaccinia, such as vaccinia eczema, severe generalised vaccinia, and vaccinia-induced infections, can be treated with an intravenous infusion of vaccinia immune globulin (VIGIV). During an epidemic, VIGIV can be utilised to treat patients with monkeypox. The Food and Medication Administration has approved the antiviral drug bricindofovir (Tembexa) for the treatment of human smallpox illness in both adults and children. To combat monkeypox, the Centers for Disease Control and Prevention (CDC) is working on an Expanded Access Investigational New Drug (EA-IND) for Brincidofovir. Supportive and symptomatic therapy has been identified as the foundation for controlling a monkeypox virus infection, notwithstanding the indicated treatment strategies. A glimpse of the range of supportive therapy options available to people experiencing symptoms is shown in Table 1. There is no definitive cure for monkeypox; at most, symptoms can be managed and consequences can be avoided. After the 2003 monkeypox outbreak in the United States and the continued appearance of cases around the world, more study is needed before a therapy or vaccine can be developed [62,63]. Possible sustaining treatment is listed in Table 2.

Tecovirimat

The FDA has approved tecovirimat (trade names TPOXX and ST-246) for the treatment of human smallpox illness caused by the Variola virus in both adults and children. The FDA has not cleared it for use against monkeypox or any other orthopoxvirus diseases. Therefore, tecovirimat can be used for primary or early empiric therapy of non-variola orthopoxvirus infections, such as monkeypox, in adults and children of all ages thanks to a non-research extended access Investigational New Drug (EA-IND) protocol held by the CDC.Early administration of tecovirimat has been found in animal trials to reduce mortality from orthopoxvirus infections. Blood medication levels and a few case studies have been the only indicators of effectiveness in humans. Patients infected with the Monkeypox virus and treated with tecovirimat show promise for reducing sickness and viral shedding, according to a case series [41]. Tecovirimat can be taken by mouth as a 200mg capsule, or injected intravenously (IV). Taking a drug in pill form, eating a big, fatty meal at the same time will increase your body's ability to absorb the medicine. For patients with severe renal impairment (CrCl 30mL/min), IV tecovirimat is contraindicated. There is still the possibility of oral formulation for this group of people. Because of immature renal tubular function, IV tecovirimat should be administered with caution in patients with moderate (CrCl 30-49 mL/min) or mild (CrCl 50-80 mL/min) renal impairment, as well as paediatric patients younger than 2 years of age.

Vaccinia Immune Globulin Intravenous (VIGIV)

The Food and Drug Administration has approved VIGIV for the treatment of vaccinia-related side effects like eczema vaccinatum, progressive vaccinia, severe generalised vaccinia, vaccinia infections in people with skin conditions, and aberrant infections induced by the vaccinia virus (except in cases of isolated keratitis). The Centers for Disease Control and Prevention (CDC) has an expanded access protocol that authorises the use of VIGIV to treat orthopoxviruses (such as monkeypox) during an outbreak. There is a lack of information regarding the efficacy of VIG in the treatment of monkeypox virus infection. There is no evidence

Table 2
Potential treatment option for Monkeypox infection.

Drugs	Mechanism of action	Side effects	Refs.
Brincidofovir	Cidofovir lipid-conjugate prodrug	diarrhoea, Abdominal pain, nausea, increased bilirubin and vomiting	[69]
Cidofovir	Competitive inhibition of DNA polymerase prevents viral DNA synthesis	Nephrotoxicity; neutropenia; decreased intraocular pressure, nausea, vomiting	[68]
Tecovirimat	Blocks VP37 activity, which in turn blocks viral replication and spread within the host organism by preventing the production of infectious virions that can be discharged from infected cells.	Abdominal pain, headache, nausea, swelling at the infusion site, vomiting	[70]
VIGIV	Smallpox vaccine recipient's pooled plasma with antibodies specific to OPXV provides passive protection.	Hypersensitivity reactions	[71]

that VIG is effective against monkeypox, and it is unclear whether people with a severe monkeypox infection will benefit from treatment with VIG. Although, in extreme cases, doctors might consider using it. If a patient have severe T-cell immunodeficiency and have been exposed to monkeypox virus, but he/she cannot get vaccinated against smallpox, then a physician may want to consider getting VIG as a prophylactic measure.

Cidofovir (also known as Vistide)

Antiviral cidofovir has been given the green light by the Food and Drug Administration (FDA) to treat cytomegalovirus (CMV) retinitis in people with AIDS (AIDS). The efficacy of Cidofovir in the treatment of monkeypox in humans is unknown. Animal and in vitro tests have shown its efficacy against orthopoxviruses. For the treatment of orthopoxviruses (such as monkeypox), the CDC has an expanded access protocol that allows for the use of stockpiled Cidofovir. In cases of severe monkeypox infection, it is unclear whether Cidofovir would be beneficial, but it could be tried. Compared to Cidofovir, Brincidofovir's safety profile may be preferable. Brincidofovir has been used with no increased risk of renal toxicity or other adverse events when treating cytomegalovirus infections, compared to Cidofovir.

Brincidofovir (also known as CMX001 or Tembexa)

On June 4, 2021, the Food and Drug Administration (FDA) approved brincidofovir, an antiviral medicine used to treat human smallpox disease in adults, children, and newborns. Brincidofovir's efficacy in treating human instances of monkeypox is not known. Animal and in vitro tests have shown its efficacy against orthopoxviruses. An EA-IND for Brincidofovir as a therapy for monkeypox is currently being developed by the CDC. Unfortunately, Brincidofovir cannot be purchased over the SNS at this time. The CDC's Emergency Operations Center is the place for state and territorial health departments to go when they need monkeypox medication.

Vaccines and immunization

Despite recent approval in several nations, there remains a severe shortage of the monkeypox vaccine. Some nations may have stocks of smallpox vaccination that may be used if recommended by authorities there. Some countries may make vaccines available through national authorities, albeit in low quantities. Cross-protection against other orthomyxoviruses is possible after an OPXV infection. Protection against monkeypox sickness and infection is not provided by any currently available vaccinations [64,65]. Potential vaccinations against MPXV use vaccines derived from the Vaccinia virus, which were originally designed to combat smallpox. Secondary attacks were 9.28% more common among unvaccinated household contacts of people with MPXV illness compared to 1.31% among vaccinated contacts in research done in the DRC in the late 1980s. The results indicated that earlier protection from smallpox vaccination against monkeypox was almost 85%. The only OPXV vaccination available in the United States prior to 2019 was ACAM2000. The OPXV genus, which includes the virus used to create ACAM2000, is known as Vaccinia virus. As a result of being capable of replication, ACAM2000 carries the potential for major adverse outcomes (e.g. progressive vaccinia, eczema vaccinatum, and myopericarditis). Vaccinia can also spread from a person to another by touching the immunisation site.

Monkeypox and pregnancy

Women who are pregnant or breastfeeding are not necessarily barred from treatment with tecovirimat if it is determined to be safe to do so following a thorough clinical assessment and discussion of risks/benefits with the patient utilising a shared decision-making process. Human data are needed to determine whether or not tecovirimat poses a risk of fetotoxicity, affects milk production, and/or is present in human milk, and what effects it may have on breastfed children. In animal investigations, tecovirimat was found in small concentrations in milk, but it was not teratogenic. No clinical studies have been conducted in juvenile populations, but tecovirimat has been administered in a kid as young as 28 months with no reported side effects. Because of theoretical concerns that renal immaturity in young paediatric patients may result in greater exposure of hydroxypropyl—cyclodextrin, a component in IV tecovirimat, monitoring of renal function is recommended in kids younger than 2 years of age. Extremely high doses of hydroxypropyl—cyclodextrin have been linked to nephrotoxicity in animal experiments.

Case fatality rate of monkeypox

The World Health Organization (WHO) reports that the case fatality ratio for monkeypox has traditionally fluctuated from 0 to 11%, with the rate being greater in youngsters. Recent case fatality rates have hovered between 3% and 6%. An official with the health ministry's National Centre for Disease Control stated that while the government was taking all necessary measures to prevent a significant breakout of the disease in India, the situation was currently under control. The death rate from monkeypox this year is extremely low, with even Dr. Jayadevan noting this fact. Noting that 98% of cases are male and that 36%-41% of officially published case series in 2022 were HIV positive, he emphasised the lack of data from these cases to prescribe particular preventive actions for death beyond what is already known about preventing and treating the disease.

Foresight scanning: future directions of clinical and pharmaceutical research

Current outbreaks of monkeypox in several countries in 2022 are the largest of their kind outside of Africa. For decades, monkeypox has been recognised as an urgent public health concern as an emerging zoonotic disease with high epidemic potential due to the increasing frequency with which it has been transmitted to humans. Monkeypox has been a global threat ever since the first human case was discovered in the Democratic Republic of the Congo (DRC) in 1970. The illness has since spread throughout the remainder of Africa, particularly West and Central Africa. Occasional occurrences and isolated outbreaks related with travel or the import of animals infected with the virus have also been documented from non-endemic locations. The average age of patients seeking medical attention has increased from 4 in the 1970s to 21 in the 2010s. (2010–2019). Overall, 8.7% of people died from the disease,

Table 3
Symptoms/Complications and potential supportive treatment.

Symptom/Complication	Supportive Treatment
Respiratory distress	Prophylactic oral and IV antibiotics, nebulizer therapy, non-invasive ventilation (ex. CPAP)
Sepsis	Antibiotics orally and intravenously, oxygen therapy, corticosteroids, and insulin
Ulcers	Rehydration with oral and intravenous fluids, antiemetic and antidiarrheal drugs by mouth and injection
Fever	Treatment of fever with antipyretics and/or ventilation and/or cooling
Superinfection skin	Advanced wound care, including antibiotics (both orally and intravenously), incision and drainage, and techniques like negative pressure wound therapy
Inflammation	Medication for pain and inflammation, either orally or intravenously
Corneal infection	Eye drops containing corticosteroids and antimicrobials
Skin problems	Treatment involving the use of occlusive dressings made of moist materials in order to hasten epithelialization and re-epithelialization

but this varied widely by clade: in Central Africa, it was 10.6% (95% CI: 8.4%- 13.3%), whereas in West Africa, it was 3.6% (95% CI: 1.7%-6.8%).

Over the past 50 years, there have been reports of several thousand cases in humans, most of which have originated in Africa. Despite its name, the monkeypox virus has no connection to monkeys. It's unclear where monkeypox first appeared. Nonetheless, a number of rodents and other small mammals have been proposed as potential viral carriers. The unusual symptoms, such as vaginal, perigenital, and perianal lesions, point to the importance of sexual contact [66]. The potential for sexual transmission of monkeypox is now under investigation. The virus has been isolated from patient semen at extremely low concentrations in Italy [45] and Germany [67]. Until more is known about the role of sexual transmission, public health experts in the UK recommend abstinence during active infection and for up to 8 weeks after recovery. Preventative vaccination of gay/bisexual and other men who have sex with men (MSM) and vaccination of close contacts of case patients (ring-vaccination) as postexposure prophylaxis is being promoted in some countries in an effort to contain the outbreak (PEP). The present global outbreak is one of the greatest ever recorded because monkeypox is spreading in many countries outside of its typical range. Due to its extremely long incubation period and the low index of suspicion initially held by clinicians unfamiliar with the virus, MPXV may have gone unnoticed for some time despite its potential to cause local transmission leading to substantial clusters.

The early stages of the coronavirus disease 2019 (COVID-19) pandemic have been compared to the multi-country monkeypox outbreaks that occurred when the world was still in a global pandemic caused by another new zoonotic virus, severe acute respiratory syndrome coronavirus 2. (SARS-CoV-2). The current situation with monkeypox is serious but also unprecedented. The current outbreaks of monkeypox are not expected to result in a global pandemic comparable to that caused by COVID-19. We know what to do to contain an MPXV outbreak since we've done it before. The transmission of monkeypox is strikingly dissimilar to that of SARS-CoV-2. Because monkeypox is very uncommon, however, many medical professionals lack experience diagnosing and treating the condition. It is crucial to understand the current outbreak in order to allocate the available resources effectively. Deploying screening methods in healthcare settings and maintaining a high index of suspicion using shifting clinical case definitions can help find people and contain the outbreak. Isolating suspected and confirmed cases, strictly monitoring their contacts, and vaccination individuals who have received high-risk exposures are all necessary steps to take immediately in order to reduce the spread of the disease and safeguard healthcare staff at high risk of exposure. Given its wide range of potential hosts, monkeypox has the potential to spread beyond Africa if the current outbreak is allowed to persist.

As with the early days of the HIV/AIDS pandemic, a clustering of cases among the gay/bisexual and other MSM community has regrettably led to unacceptable stigmatisation of this population. When it comes to fighting back against the stigma and discrimination that have arisen as a result of HIV and other contagious diseases, the infectious illness community has been at the forefront. A similar approach is expected of us in dealing with the ongoing pandemic. Although we will be allocating resources to identify patients in social networks at higher risk for exposure, the foundation of our work should be supportive and nonjudgmental public health messaging. As scientists, we have a responsibility to remind the public and our colleagues that infectious viruses do not care about race, gender, or sexual orientation when infecting humans.

Conclusion

Healthcare workers all over the world are attempting to familiarise themselves with the varied clinical manifestations and management of this infection as public health bodies seek to contain the current outbreak. In light of the continuous global outbreaks, we give in this study an up-to-date summary of monkeypox for healthcare professionals. The Centers for Disease Control and Prevention (CDC) advises that there is presently no cure for monkeypox virus infections. The use of vaccinia vaccine, cidofovir, tecovirimat, and vaccinia immune globulin (IVG) is being considered as a potential treatment for monkeypox based on lessons learned during the smallpox epidemic. Cidofovir works by blocking the viral DNA polymerase. To some extent, other antiviral treatment medicines have also demonstrated efficacy against Orthopoxviruses. As efforts to detect more cases increase in the coming months, we will learn more about the scope of this outbreak. Timely, preventative action will be essential for keeping it under control. For a long time, experts have voiced concerns that monkeypox could become a major international health crisis (Table 3).

Declaration of Competing Interest

The authors declared no conflict of interest.

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