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MINI-REVIEW article

# Advancements and challenges in the medical treatment of monkeypox: A recent focused review

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**Abstract:** Monkeypox, an infectious disease caused by the Orthopoxvirus, was identified in humans in 1970. It has recently emerged as a global health concern due to outbreaks beyond its endemic regions in Central and West Africa. This review examines the current state of medical treatments for monkeypox as of 2024, focusing on antiviral agents, immunotherapies, and supportive care measures. Monkeypox manifests with symptoms including fever, rash, and lymphadenopathy, with severe cases more common in immunocompromised individuals. Antiviral therapies such as tecovirimat and brincidofovir are central to treatment strategies, with tecovirimat demonstrating efficacy in alleviating symptoms and reducing viral shedding. Emerging treatment strategies involve novel lipid-based formulations and combination therapies that integrate antivirals with immune-modulating agents. Supportive care remains essential, involving analgesics and antibiotics for secondary infections, while the MVA-BN vaccine plays a critical role in prevention. Research emphasizes the need for a deeper understanding of viral pathogenesis and host immune responses to improve therapeutic and preventive measures. Despite significant advancements, challenges remain, including potential antiviral resistance, disparities in healthcare access, and the necessity for enhanced diagnostic and surveillance capabilities. This review highlights the imperative for ongoing research, international collaboration, and investment in healthcare infrastructure to advance the management and prevention of monkeypox and to prepare for future outbreaks.

## Introduction

In 1970, the first human case of monkeypox was documented in the Democratic Republic of the Congo. The disease is endemic to various countries in Central and West Africa with occasional outbreaks reported worldwide, raising significant public health concerns. Once overshadowed by smallpox, monkeypox has recently garnered attention due to its rising incidence, particularly in areas where smallpox vaccination has been discontinued following its eradication. The monkeypox virus, similar to the variola virus, causes a disease marked by fever,

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rash, and swollen lymph nodes, though it typically has lower mortality rates. Recent outbreaks of monkeypox in areas outside its usual regions have exposed gaps in global preparedness for emerging infectious diseases. While monkeypox is often self-limiting, the possibility of severe outcomes-especially in immunocompromised individuals the need for effective treatment strategies [1-3].

*Etiology and pathophysiology:* The monkeypox virus is a double-stranded DNA virus within the Orthopoxvirus genus, which also includes smallpox and cowpox viruses It is primarily transmitted to humans through contact with infected animals, such as rodents and primates, but can also spread between people via respiratory droplets, bodily fluids, and contaminated materials. After entering the body, the virus targets epithelial cells, leading to viremia and spreading to lymphoid tissues, where it replicates and causes widespread infection [4]. Pathophysiologically, monkeypox resembles other Orthopoxvirus infections. Following an incubation period of around 7-14 days, the virus causes initial viremia, leading to symptoms such as fever, malaise, and lymphadenopathy. The virus then spreads to the skin, producing a characteristic vesiculopustular rash. The immune response is crucial in managing the infection, involving innate and adaptive mechanisms. Recent studies have identified specific immune response markers associated with disease severity, offering insights into the pathophysiological mechanisms of monkeypox. In severe cases or among immunocompromised individuals, the virus can lead to significant complications, including secondary bacterial infections and potential systemic involvement [5]. Current findings have deepened the comprehension of how the virus interacts with the host's immune system. For example, a recent study has explored the function of T-cell responses in managing viral replication and curbing disease progression. Furthermore, the discovery of biomarkers associated with severe disease outcomes has enhanced the ability to predict and strategize treatments. Progress in genomic sequencing methods has offered a more detailed view of viral genetic variability and its significance for developing treatments and vaccines. These advancements highlight the evolving field of monkeypox research and its influence on clinical practices [6-8].

*Clinical presentation:* Monkeypox typically presents with an initial prodrome of fever, headache, myalgia, and lymphadenopathy, followed by a characteristic rash. The rash often begins on the face and spreads centrifugally to other parts of the body, including the palms and soles. It progresses through macular, papular, vesicular, and pustular stages before eventually crusting over. Lesions are often deep-seated and can be painful, with varying degrees of severity depending on the patient’s immune status. Complications of monkeypox can include secondary bacterial infections, bronchopneumonia, sepsis, encephalitis, and corneal infections, which may lead to vision loss. In some instances, the disease can cause severe scarring and keloid formation. The severity of monkeypox is influenced by factors such as age, underlying health conditions, and the presence of immunosuppressive conditions. Recent studies have provided new perspectives on the clinical manifestations of monkeypox. For instance, a clearer understanding of how comorbidities like diabetes and hypertension affect disease severity has emerged, emphasizing the necessity for customized management approaches. Additionally, research has uncovered differences in disease presentation across various demographic groups, which can impact clinical decision-making and patient care. Grasping these details is crucial for enhancing diagnostic precision and treatment effectiveness [2, 5, 9].

*Diagnosis:* The initial diagnosis of monkeypox is primarily based on clinical presentation, with laboratory confirmation supporting the diagnosis. Clinicians should consider monkeypox in patients who present with a vesiculopustular rash, particularly if there is a history of travel to endemic regions or contact with confirmed cases. Polymerase chain reaction (PCR) is considered the gold standard for laboratory diagnosis, as it detects viral DNA in clinical samples such as skin lesions, blood, or respiratory secretions. Serology can detect antibodies

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against the monkeypox virus but is less sensitive and specific compared to PCR, making it more appropriate for retrospective diagnosis. Recent advancements include enhanced PCR techniques, such as real-time PCR, which offer greater sensitivity and specificity. Electron microscopy and viral culture are additional diagnostic methods, though they are less commonly used due to their resource-intensive nature and lengthy processing times. Differential diagnosis involves distinguishing monkeypox from other rash-causing diseases, such as smallpox, chickenpox, and molluscum contagiosum, necessitating a thorough clinical assessment [10, 11]. New diagnostic technologies are enhancing the precision and speed of monkeypox detection. For example, point-of-care PCR tests are being developed to provide rapid results at the site of care, facilitating quick diagnosis during outbreaks without the need for centralized laboratory testing. Additionally, advancements in next-generation sequencing (NGS) offer a detailed understanding of viral genetic variations, which can reveal mutations and inform diagnosis and treatment strategies. These innovations are essential for improving outbreak response by delivering accurate and timely diagnostic information, thereby supporting more effective patient care and targeted public health interventions [10, 12, 13].

## Medical treatment and management

*Antiviral treatment:* The treatment of monkeypox has increasingly incorporated specific antiviral therapies. Tecovirimat (TPOXX) is the primary antiviral used, approved for smallpox and monkeypox due to its activity against Orthopoxviruses. Tecovirimat functions by inhibiting the viral envelope protein, which prevents the spread of the virus. Clinical trials have demonstrated its effectiveness in reducing symptom duration and viral shedding. Brincidofovir is another antiviral that has shown potential in treating monkeypox. Originally developed for smallpox, brincidofovir inhibits viral DNA polymerase, thereby limiting viral replication. Although it is used less frequently than tecovirimat, it serves as an alternative, especially in severe cases or when tecovirimat is contraindicated [14-16]. Recent progress in antiviral therapy is focusing on enhancing drug delivery and effectiveness. For example, lipid-based formulations of antivirals are being explored to improve their efficacy against orthopoxviruses. Scientists are also investigating combination therapies that integrate antivirals with immune modulators to optimize treatment outcomes and address potential drug resistance. These innovative strategies offer promise for more effective management of monkeypox and other viral infections [17, 18].

*Symptomatic treatment:* Supportive care is crucial in managing monkeypox, focusing on symptom relief and complication prevention. Ensuring adequate hydration is essential, particularly for patients with extensive rash and mucosal involvement, to prevent dehydration. Pain management is also a key aspect of care due to the painful nature of the lesions and may include analgesics or more potent pain relief in severe cases. Antibiotics may be used prophylactically or to treat secondary bacterial infections, which are common complications in monkeypox patients. In severe cases, especially those involving respiratory issues or sepsis, intensive care management may be required [19].

*Vaccination:* Vaccination is a key element of monkeypox management, providing preventive and therapeutic benefits. The MVA-BN (Imvamune/Imvanex) vaccine, a third-generation smallpox vaccine, is currently preferred due to its improved safety profile compared to older vaccines. It is especially recommended for healthcare workers, laboratory personnel, and individuals with potential exposure to monkeypox. ACAM2000, an older smallpox vaccine, remains effective but is associated with a higher risk of adverse effects, which limits its use to high-risk populations. Recent studies have shown that MVA-BN offers strong protection with fewer side effects, underscoring its benefits for broader vaccination strategies [20, 21]. Current vaccine development efforts focus on enhancing efficacy and safety. Researchers are exploring mRNA-based vaccines and other advanced platforms

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to provide longer-lasting immunity with fewer side effects. These innovations aim to streamline vaccine administration and improve global distribution, which is crucial for effectively managing monkeypox outbreaks. [20-22].

## Recent advances and ongoing research

Recent progress in monkeypox research has led to notable advancements in treatment and prevention strategies. Tecovirimat and brincidofovir remain the primary antiviral treatments, although ongoing studies are evaluating their effectiveness across various populations and viral strains. Scientists are investigating combination therapies that combine antivirals with immunomodulators to enhance treatment efficacy and mitigate the risk of resistance [14, 15]. New research is centered on developing novel antiviral agents and optimizing existing ones. Lipid-based antiviral formulations are demonstrating potential for improving drug delivery and efficacy. Additionally, monoclonal antibodies targeting specific viral proteins are being explored for their potential to provide targeted and effective treatment [17, 18]. Vaccine development is progressing with a focus on creating vaccines that provide longer-lasting immunity and fewer side effects. While the MVA-BN vaccine is currently the most advanced, scientists are investigating mRNA-based vaccines and other innovative platforms. These emerging vaccines aim to offer broader protection and enable more efficient distribution during outbreaks [20, 21]. Understanding the genetic diversity of the virus and the mechanisms of the immune response is essential for developing effective treatments and vaccines. Genomic studies are illuminating viral mutations and their impacts on disease severity and treatment outcomes. This information is vital for tailoring interventions and ensuring effective management of monkeypox [6, 13].

## Challenges in treatment and management

Despite progress, several challenges remain in the treatment and management of monkeypox. A major concern is the potential for antiviral resistance, which could diminish the effectiveness of current therapies. Monitoring resistance patterns and developing new antiviral agents are essential to addressing this issue. Another challenge is ensuring equitable access to treatments and vaccines, particularly in low-resource settings where monkeypox is most prevalent. Global collaboration and investment in healthcare infrastructure are essential for improving access to care and supporting effective outbreak response efforts [23, 24]. Public health strategies also encounter difficulties with early detection and rapid response. Enhancing diagnostic capabilities and improving surveillance systems are essential for the prompt identification and management of monkeypox cases. Addressing these challenges necessitates a comprehensive approach that includes continued research, investment in healthcare infrastructure, and international cooperation. By addressing these issues, it can improve monkeypox management and strengthen global preparedness for future outbreaks [23-25].

*Conclusion:* The management of monkeypox has seen significant advancements over the recent years, with notable improvements in antiviral therapies, vaccination strategies, and supportive care. Ongoing research continues to deepen our understanding of the virus and to develop more effective treatments and vaccines. Nonetheless, challenges persist, including the risk of antiviral resistance, equitable access to treatments, and the need for enhanced diagnostic and surveillance systems. Addressing these issues requires a collaborative approach, involving sustained research, investment in healthcare infrastructure, and international cooperation. Looking ahead, the insights gained from managing monkeypox will be crucial in preparing for future outbreaks of emerging infectious diseases. Harnessing advances in science and technology can improve patient outcomes and bolster global public health responses.

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