

## Monkeypox: A Contemporary Review for Healthcare Professionals

Shah Md. Sarwer Jahan<sup>1</sup>, SM Nurun Nabi<sup>2</sup>

1. Professor  
Department of Medicine  
Rangpur Medical College  
Mobile: 01712787838  
E-mail: jahansarwer@gmail.com
2. Senior consultant  
Department of Pediatrics  
Rangpur Medical College



The recent monkeypox outbreak in many countries is the largest in history to occur outside of Africa. Monkeypox is an emerging zoonotic disease having significant epidemic potential because of the increasing occurrence of human outbreaks in recent years.<sup>1,2</sup> As public health entities work to contain the current outbreak, healthcare professionals globally are aiming to become familiar with the various clinical presentations as previously observed and the management of this infection. We present in this review an updated overview of monkeypox for healthcare professionals in the context of the ongoing outbreaks. In 2022, outbreak of monkeypox in both endemic and non-endemic regions has generated significant international interest. This once-neglected zoonotic virus was endemic to West and Central Africa, monkeypox virus was first identified in 1958<sup>3</sup> and first in human case was reported in 1970 in the Democratic Republic of Congo.<sup>4</sup> Over the past 50 years, sporadic outbreaks have been reported mainly in African countries, with several thousands of human reported being infected to date. The cumulative effects of deforestation, population growth, encroachment on animal reservoir habitats, increasing human movement, and enhanced global interconnectedness have made this possibility more real in the last 20 years.<sup>5</sup> With recent increasing case numbers being reported in many countries, it is important for clinicians everywhere

to update their knowledge of this zoonotic infection, including its prevention, clinical management, prophylaxis, and basics of infection control, to understand the broader implications of the current outbreak.<sup>6-8</sup>

Monkeypox belongs to the Poxviridae family, the Chordopoxvirinae subfamily, and the genus Orthopoxvirus, has a wide range of potential host organisms, which has allowed it to circulate in wild animals including birds, reptiles, insects and mammals for a prolonged period of time while sporadically causing human disease through spillover events.<sup>9-10</sup>

Monkeypox is endemic in the tropical rainforest regions of Central and West African countries, specially Cameroon, Central African Republic, Democratic Republic of the Congo (DRC), Cote d'Ivoire, Gabon, Liberia, Nigeria, Republic of the Congo and Sierra Leone. Most cases arise sporadically or occur in the context of localized outbreaks.<sup>6-8</sup>

Cases outside endemic countries are typically linked to international travel or importation of animals infected with MPXV. Before the recent outbreak, cases outside of Africa had previously been reported in the United States, United Kingdom (UK), Israel, and Singapore. The Central African clade and the West African clade are the 2 distinct genetic clades of the MPXV. Infection with the West African clade typically results in a more self-limited disease, with case-fatality rates estimated to be approximately 3-6%, whereas the Central African (Congo Basin) clade has historically been associated with higher transmissibility and higher case-fatality rate about 10%. The definitive animal reservoir of MPXV has not been identified. Transmission between animal-to-human occurs via bites and scratches from infected animals, also preparation and handling of infected animal products (bushmeat) may also result in transmission. Human-to-human transmission is thought to occur via direct skin-to-skin contact with lesions on the skin, through indirect contact with contaminated fomites, such as bedding or clothing and through respiratory secretions containing live virus.

Historically, patients have usually presented with prodromal symptoms, including fever, headaches,

chills, malaise, and lymphadenopathy, followed by development of a characteristic rash. The rash begins as a macule and then progresses to papules, vesicles, pustules, and scabs and usually starts in the mouth, and then spreads to the face and extremities, including the palms and soles. Pain can be prominent, but it is not universally present, and pruritus can occur at the healing stage. Unlike chickenpox, skin lesions due to monkeypox tend to be similar in size, 10 to 150 in number, typically present at the same stage and can persist for up to 4 weeks. Patients are infectious from the time symptoms start (presumed to include prodromal symptoms before the appearance of the rash) until the lesions scab and fall off, with a new layer of skin being formed. In rare instances, complications can occur, such as bacterial super infection, encephalitis, pneumonitis, and conjunctivitis/keratitis. The timeframe for developing complications and their rates have not been systematically determined. In the current 2022 outbreak, many patients presented with atypical features, like characteristic rash was limited to the genital, perigenital, and perianal areas and present at different stages of development and sometimes patients presented with only mild or absent prodromal symptoms, which may begin after onset of a localized rash.<sup>11</sup>

When there is clinical suspicion, clinicians should ask about travel and sexual history and any history of close contacts (include sleeping in the same room, drinking or eating from the same container, living in the same residence, etc.) with people with a similar rash or suspected or confirmed monkeypox infection. More importantly, absence of travel history or history of close contact with a rash or with suspected or confirmed monkeypox infection should not exclude the possibility of this diagnosis. A thorough skin examination should also be performed. The optimal diagnostic procedure for a patient with suspected active monkeypox infection is to obtain more than 1 specimen from 2 separate skin lesions on different parts of the body, and lesions should be unroofed to adequately sample virus containing secretions and then send for molecular testing by PCR. Cell culture provides virus strains for further characterization, but it is restricted to accredited biosafety level 3 reference laboratories. Serological testing can potentially be helpful in epidemiologic investigations, retrospective diagnosis of past infections, and diagnosis of

late clinical manifestations, such as encephalitis.<sup>12</sup>

The mainstay of clinical management for typical monkeypox infection is supportive care includes maintenance of adequate fluid balance as there is possibility of increased insensible fluid losses from the skin, decreased oral intake, and vomiting or diarrhea. Other measures such as hemodynamic support, supplemental oxygen, or other respiratory support and treatment of bacterial super infections of skin lesions should be considered where indicated.<sup>13</sup>

At the present time, there is no specific treatment approved for monkeypox virus infection. However, there are some antiviral agents that have activity against MPXV, including cidofovir, brincidofovir (a lipid-conjugate prodrug of cidofovir), and tecovirimat. In addition to antiviral agents, intravenous vaccinia immune globulin (VIGIV), which is licensed for the treatment of complications from smallpox (vaccinia) vaccination, may be authorized for use to treat monkeypox and other pox viruses during an outbreak.<sup>14</sup>

Contact tracing is crucial for controlling the spread of monkeypox. Types of contact are face-to-face contact, direct physical contact (including sexual contact), and contact with contaminated fomites such as bedding or other objects with shared use. In the healthcare setting, anyone who has had contact with the patient of monkeypox (staff, roommates, visitors) should be identified. If someone is exposed to a person with monkeypox, they should be monitored for symptoms like fever, chills, rash, and lymphadenopathy for 21 days after the last exposure and offered vaccination as PEP were appropriate.<sup>13</sup>

The ongoing global outbreak of monkeypox is one of the largest in history, with chains of transmission occurring in multiple countries and occurring outside of regions where monkeypox is known to be endemic. With the world still in a global pandemic caused by another emerging zoonotic virus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) the current situation with monkeypox, although serious, is different. It is less likely that the ongoing monkeypox outbreaks will lead to a global pandemic on the scale of COVID-19. MPXV is not a novel virus, and there is experience from previous outbreaks regarding how to prevent propagation of the infection. More importantly, the transmission of monkeypox is also substantially different from that of SARS-CoV-2.

However, monkeypox is new to many clinicians, who understandably do not have extensive experience in diagnosing or treating cases of the disease. Now is the high time to adopt a global approach that addresses this problem definitively not only in wealthy countries but also, critically, in the endemic countries that have been responding to monkeypox for decades.

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