

# Mpox: Travel Medicine and Infection Control

## *Mpox; Seyahat Tıbbı ve Enfeksiyon Kontrolü*

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### Abstract

Due to the rapid spread of a new subtype, as well as the increasing number of monkeypox (Mpox) cases seen since 2022, the World Health Organization declared an emergency declaration. To prevent an Mpox outbreak, the risks of infection spread and protecting priority populations must be identified. Mpox virus is mainly transmitted sexually, via skin-to-skin contact, by touching contaminated objects and surfaces, and through airborne droplets and aerosols. Accordingly, men who have sex with men, sex workers, people who are HIV-positive, travelers, and healthcare workers are the main priority groups that are at risk of this virus. Two doses of vaccine are recommended for the risk groups. Moreover, travelers are recommended to receive two doses of vaccine prior to travel, unless contraindicated. Persons with symptoms and rashes suspicious of Mpox are not advised to travel. In healthcare facilities, patients with suspected Mpox should be isolated in single rooms, and healthcare workers should wear full protective equipment. Considering that transmission is possible through indirect contact, health workers should avoid direct contact with patients' belongings, bed linen, and so on.

**Keywords:** Mpox; Mpox virus; Travel medicine; Infection control

**M**onkeypox (Mpox) is a zoonotic disease caused by the MPX virus (MPXV), a member of the genus Orthopoxvirus in the family Poxviridae. It is in the same family as the variola and vaccinia viruses, which cause smallpox. Rodents and primates are the natural hosts of MPXV, whereas humans are incidental hosts.<sup>[1–3]</sup> The natural history of the disease is not fully understood. The virus was first isolated from skin lesions in laboratory monkeys brought from the Democratic Republic of the Congo to Copenhagen, Denmark, in 1958.<sup>[4]</sup>

There are two known subtypes (clades) of the Mpox viruses. On August 12, 2022, the World Health Organization (WHO)

introduced a new clade nomenclature for Mpox viruses:<sup>[5]</sup> Clade one (I) (previously known as the Congo Basin clade or the Central African clade) and Clade (II) (formerly called the West African clade), which is further subdivided into two subclades, namely, Clade IIa and Clade IIb.

Clade II is associated with relatively less severe symptoms and outcomes when compared with Clade I. Nonetheless, Clade IIb has been implicated in the 2022 outbreak, which affected several countries.<sup>[6,7]</sup> As of August 2024, owing to a significant increase in cases, the WHO has declared Mpox a “public health emergency of international concern.” This decision reflects the urgent global spread, particularly the

**Cite this article as:** Eryılmaz Eren E, Çelik İ. Mpox: Travel Medicine and Infection Control. Lokman Hekim Health Sci 2024;4(2):121–130.

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emergence of a more lethal strain in regions including the Democratic Republic of the Congo. This strain has caused higher mortality rates when compared with previous outbreaks, which underscores the immediate need for international cooperation to address this crisis.<sup>[8]</sup>

From 1970 to 2002, numerous human cases of Mpox have been reported in 11 different African countries.<sup>[9–11]</sup> In 2003, the first outbreak of Mpox outside of Africa occurred in the United States.<sup>[11,12]</sup> By May 2022, hundreds of Mpox cases had been reported in over 100 countries, which indicates its global spread. In June 2024, 934 new cases were reported, with 61% originating from Africa, followed by America (19%) and Europe (11%).<sup>[8,12,13]</sup> This global spread emphasizes the critical need for international cooperation to prevent and control the disease. The WHO has declared a public health emergency in response to this worldwide outbreak, highlighting the urgent need for collaboration to address this issue.<sup>[8]</sup>

Poxviruses are known for their remarkable desiccation resistance and ability to tolerate higher temperatures and pH levels when compared with other enveloped viruses. These characteristics contribute to their prolonged survival in the environment. Orthopoxviruses show long-term stability in environmental conditions, as live MPXV can be detected on household surfaces for up to 15 days following surface contamination. Notably, the vaccinia virus, utilized in the smallpox vaccine, is quickly inactivated in wastewater. Although poxviruses are susceptible to commonly used disinfectants, they may be less affected by organic disinfectants when compared with other enveloped viruses.<sup>[14,15]</sup>

This review aims to evaluate the current literature on Mpox and update recommendations for travelers and infection control. Google Scholar, PubMed, and Web of Science were utilized to search the keywords “Mpox, Mpox virus, infection control, and travel” (alone or in combination) from the year 2000. Related articles were selected for review.

## Pathophysiology

The pathobiology of human MPXV is similar to smallpox but has a lower reproductive number ( $R_0$ ). MPXV is transmitted through contact with infected animals and via respiratory and person-to-person transmission. The specific receptors for poxviruses are unknown.<sup>[16,17]</sup>

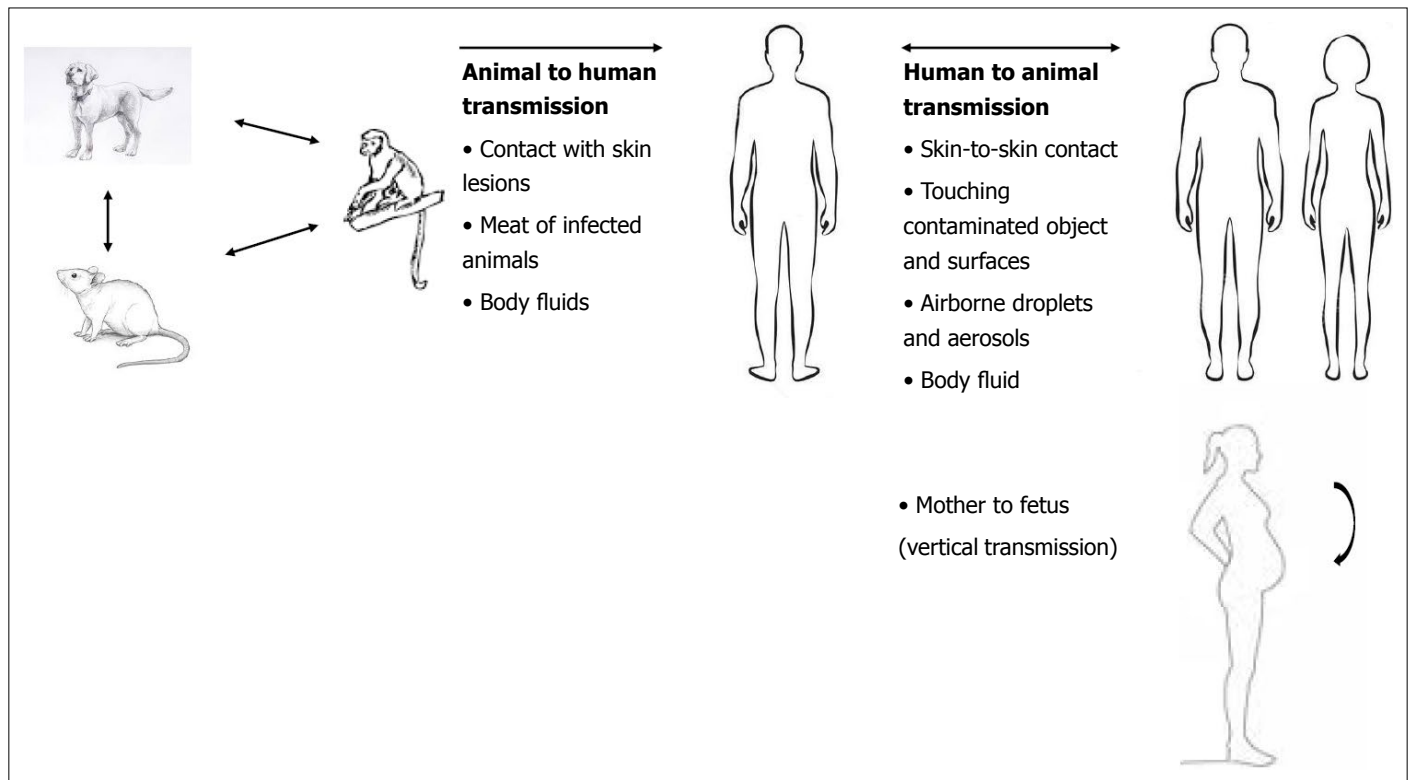
Once inside the host cell, the virus undergoes initial, intermediate, and late replication. After the virus enters the body, it replicates at the entry site and nearby lymph nodes. It then spreads to organs such as the liver and spleen,

causing clinical signs to appear. Furthermore, spread can lead to lesions on the skin and mucosal areas. Molecular diagnosis is possible from the early spread stage to the formation of pustules. Immunoglobulin M antibodies are detectable from the onset of spread until lesions resolve, and immunoglobulin G antibodies are detectable from the third week of infection for up to a year. Viral shedding can occur when symptoms begin, but the highest risk is during the vesicular and pustular stages.<sup>[18–21]</sup>

## Transmission

During the 2022–2023 Mpox outbreak, sexual contact was the primary mode of transmission in 95%–98% of cases, particularly among men who have sex with men. Close physical contact and respiratory transmission accounted for lower rates of transmission. Transmission through contaminated surfaces and objects also contributed less than 1%. These percentages are based on available epidemiologic data and literature reviews and may vary depending on epidemic dynamics and population characteristics.<sup>[22–26]</sup>

1. Close physical contact: The primary transmission route of MPXV is close physical contact with an infected person. This includes contact with skin lesions, body fluids, and respiratory droplets from an infected person. Activities including sexual contact, kissing, hugging, or any prolonged face-to-face interaction can spread the virus.
2. Skin-to-skin contact MPXV can be spread directly with an infected person's rash, scabs, or body fluids. This contact form is especially important in settings that involve close personal interaction, such as intimate or sexual contact.
3. By touching contaminated objects and surfaces: Transmission can also occur via contact with virus-contaminated objects, fabrics, and surfaces, including clothing, bedding, towels, or utensils used by someone with MPXV. The virus can survive for a long time on these surfaces, so a clean and hygienic environment and regular disinfection must be maintained. These measures can significantly reduce the risk of MPXV transmission, which allows us to take proactive steps to prevent the disease's spread.
4. Airborne droplets and aerosols: Although less common than direct contact, respiratory droplets can spread MPXV. Prolonged face-to-face exposure, especially in confined spaces, increases the risk of transmission by droplets or aerosols.



**Figure 1.** Transmission of the virus (Depicted by the authors).

5. Animal-to-human transmission: MPXV is a zoonotic virus that can be transmitted from animals to humans. This can take place through bites, scratches, or direct contact with the blood, body fluids, or lesions of infected animals, especially rodents and primates.
6. Vertical transmission: Although rare, there is evidence that smallpox can be transmitted from mother to fetus through the placenta, which is known as congenital smallpox. This underscores the importance of protecting vulnerable groups, including pregnant women, from exposure to the virus and the need for proactive measures to prevent such cases (Fig. 1).

In the 2022 Clade II outbreak, there was a high risk of infection through sexual exposure. A contact tracing study found that 66% of sexual contacts were “definitely or probably” infected, whereas only 14% of nonsexual contacts were infected.<sup>[27]</sup> The virus (MPXV) was detected more frequently in skin, anal, and throat samples than in blood, urine, and semen. Replication-competent MPXV was isolated from skin lesions and anorectal specimens and, to a lesser extent, from the oropharyngeal cavity.<sup>[28,29]</sup>

## Symptoms and Clinical Findings of Mpox

The typical incubation period for Mpox is 6–14 days, but it may range from 1 to 21 days. It is shorter in patients with

a history of animal bites or scratches than in those with contact exposure, 9 versus 13 days.<sup>[23,27,30]</sup>

The classical presentation of Mpox is characterized by a prodromal phase, followed by a rash associated with lymphadenopathy. The prodromal systemic symptoms include fever, headache, itching, lymphadenopathy, chills or sweats, muscle aches, sore throat, and fatigue. However, systemic symptoms may occur at the same time as the rash. Lymphadenopathy has been suggested as a distinctive sign of Mpox, which sets it apart from smallpox and other viral rash illnesses, including chickenpox. Lymphadenopathy, or swollen lymph nodes, is a hallmark of Mpox and usually occurs in the cervical, axillary, and inguinal regions.<sup>[23,31–33]</sup> The typical rash of Mpox is vesicular/pustular and can appear on all body surfaces; typically, the most affected areas in endemic disease are the face, legs, trunk, arms, palms, genital organs, and soles of the feet. The oral mucosa is involved in 70% of cases; the genitalia, in 30%; and the conjunctiva and cornea, in 20%. The rash lasts between 2 and 4 weeks and has a centralized distribution. Mpox skin lesions progress uniformly from macules to papules, vesicles, pustules, umbilication, crusting, and desquamation; nevertheless, multiple phases may coexist. The number of lesions varies widely, with over 100 lesions noted in almost 50% of individuals. In a recent case series,

the median time from the onset of lesions to the formation of a dry crust was 10 days (interquartile range, 7–13).<sup>[27,33,34]</sup>

Respiratory symptoms may manifest as a sore throat, cough, and nasal congestion. The rash generally emerges 1–3 days after the onset of fever and progresses through various stages, including macules, papules, vesicles, pustules, and crusting. It can be localized or widespread, potentially affecting the palms and soles of the feet. Possible complications include secondary bacterial infections, respiratory distress, encephalitis, and recently reported cardiac issues such as myocarditis and pericarditis. Although the disease typically lasts for 2–4 weeks, severe cases can occur, particularly in immunocompromised individuals, despite that many cases are mild.<sup>[35–37]</sup>

### Laboratory Findings of Mpox

Early diagnosis and treatment of severe symptoms are crucial. Common laboratory findings in patients with Mpox include high transaminase levels, low blood urea nitrogen levels, low serum albumin levels (hypoalbuminemia), high white blood cell count (leucocytosis), and low platelet count (thrombocytopenia). Elevated alanine aminotransferase and aspartate aminotransferase are reliable indicators of a poor prognosis.<sup>[28,32]</sup>

The minimum requirement is that samples suspected of containing MPXV must be carried out in biosafety level-2 facilities. Samples utilized to test for MPXV are typically swabs taken from skin lesions, including vesicles, pustules, and crusts. These samples are collected by gently rubbing a swab on the surface of the lesion to gather enough viral material for testing. The primary diagnostic tests are polymerase chain reaction (PCR) and serology. PCR is considered to be the most reliable method for diagnosing MPXV as it can detect viral DNA with high sensitivity and specificity. Serologic tests can be employed for the detection of antibodies to the Mpox virus, which indicates previous infection, but are less useful for acute diagnosis because of the time required for antibodies to develop. Laboratory biomarkers include viral load, inflammatory markers, and lymphocyte count. Quantitative PCR can measure viral load in lesion samples, potentially correlating with disease severity and stage.<sup>[38–40]</sup> Elevated levels of inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate may be observed, which reflects the systemic inflammatory response. Lymphopenia is common in patients with Mpox, especially in the early stages of the disease.<sup>[32]</sup> Histopathologic examination of skin biopsies may show characteristic findings such as

ballooning degeneration of keratinocytes, necrosis, and eosinophilic intracytoplasmic inclusions (Guarnieri bodies). Although virus culture is not routinely performed because of biosafety concerns, cell culture can isolate the MPXV from clinical specimens and is primarily used for research purposes. Strict protocols are necessary for laboratory personnel to prevent infection acquired in the laboratory, and complete inactivation of the virus is recommended prior to processing samples.<sup>[41–43]</sup>

### Complications

Manifestations of MPXV can lead to various complications that affect the skin, respiratory system, eyes, nervous system, gastrointestinal tract, heart, and the body as a whole. Skin complications may result in painful lesions, scarring, and bacterial infections. Respiratory problems may include pneumonia, whereas eye-related issues can lead to vision impairment. Neurological complications may present as confusion or seizures, and gastrointestinal complications may result in dehydration. Cardiac complications may include myopericarditis, whereas systemic complications can lead to sepsis, particularly for individuals with weakened immune systems.<sup>[44–46]</sup> Advanced or untreated HIV and other immunocompromised conditions can remarkably elevate the risk of severe illness and complications.<sup>[47,48]</sup>

### Treatment

Currently, no specific, universally accepted treatment for MPXV exists. However, several therapeutic options that focus primarily on symptom management and prevention of complications are available. Severe or complicated cases may necessitate hospitalization and antiviral medication.<sup>[23,49]</sup>

Treatment is primarily supportive for mild and uncomplicated cases. This includes managing symptoms including fever, pain, and itching. Antipyretics, analgesics, and antihistamines may be utilized to relieve discomfort.<sup>[49]</sup>

No approved therapy for MPXV infections exists. Mild and uncomplicated cases are treated with symptomatic and pain control measures. Severe and complicated cases may require hospitalization and antiviral treatment. This lack of an approved therapy underscores the need for further research and development and the urgency of finding effective treatments for this disease.<sup>[27,35]</sup>

Tecovirimat is highly active against orthopoxviruses, including MPXV. It was approved as an antiviral against smallpox in 2018 and has shown effectiveness against MPXV in animal models. Nonetheless, there is no definitive

evidence of its efficacy in treating MPXV infection in humans, and studies have shown inconsistent results.<sup>[50,51]</sup> Recent studies report that tecovirimat may not be more effective than placebo against the Clade I virus.<sup>[52]</sup>

Brincidofovir, an FDA-approved prodrug of cidofovir, is used to treat human smallpox. Although it has not been proven effective in treating MPXV in humans, it has shown efficacy against orthopoxviruses *in vitro* and animal studies. Brincidofovir should be considered in cases where tecovirimat is contraindicated or be combined with tecovirimat in cases of severe or progressive immunosuppression.<sup>[53–55]</sup>

VIGIV is approved by the FDA for treating complications from vaccinia vaccination but can be considered for use during MPXV outbreaks, particularly in individuals with severe immunodeficiencies. It is not explicitly approved for MPXV treatment but is employed as an adjunctive therapy in severe cases.<sup>[56,57]</sup>

## Vaccination

In 1980, smallpox was eradicated worldwide mainly because of the successful vaccination campaign using the vaccinia virus. The smallpox vaccine provides protection against smallpox and most other diseases caused by members of the Orthopoxvirus family. Two vaccines are available for smallpox and MPXV prevention, namely, the replication-deficient modified vaccinia Ankara (MVA) vaccine and the replication-competent smallpox vaccine (ACAM2000). The MVA vaccine (JYNNEOS in the United States, IMVANEX in the European Union, and IMVAMUNE in Canada) is derived from a highly attenuated, non-replicating smallpox virus. Individuals at higher risk are recommended to receive two doses 4 weeks apart. The MVA vaccine is safe for patients with compromised immune systems.<sup>[56,58–60]</sup>

Individuals at higher risk, such as those with a history of sexually transmitted infections, those with multiple sexual partners, or men who have sex with men and their partners, should receive two doses of the vaccine. Travelers to high-risk areas, particularly healthcare workers, should also be vaccinated.<sup>[56]</sup>

Despite the availability of vaccines like JYNNEOS (MVA) and ACAM2000, significant disparities remain in vaccine distribution, particularly in African countries. Global health experts call for more substantial equity in the distribution of vaccines and treatments, emphasizing the importance of ensuring that all regions, especially those with limited resources, access these critical tools.<sup>[61–64]</sup>

Postexposure prophylaxis (PEP) should be administered within 4 days of exposure to prevent disease onset. Symptoms may be reduced if given between 4 and 14 days of exposure, but the disease may not be entirely prevented. Vaccination is recommended if you have been exposed to MPXV and have not received a smallpox vaccination in the past 3 years.<sup>[56,65]</sup>

## Vaccination for MPXV

Vaccination is crucial in controlling the spread of MPXV, particularly in populations at high risk of exposure. The vaccines primarily utilized for MPXV are based on those developed for smallpox, as viruses cause both diseases in the Orthopoxvirus family.<sup>[56,66,67]</sup>

The MVA vaccine has brand names, including JYNNEOS (USA), IMVANEX (EU), and IMVAMUNE (Canada). The MVA vaccine is a nonreplicating live virus vaccine that provides cross-protection against smallpox and MPXV and is considered safer than previous smallpox vaccines, especially for immunocompromised individuals. It is typically administered in two doses 4 weeks apart and has been shown to provide strong immunity.<sup>[56,68]</sup>

The ACAM2000 vaccine is a replication-competent live vaccinia vaccine originally developed for smallpox. It can also protect against smallpox, but because it is a live, replicating virus, it carries a higher risk of side effects, especially in immunocompromised individuals. This vaccine is administered as a single dose by pricking (making multiple punctures in the skin), like the old smallpox vaccines.<sup>[56,69]</sup>

Vaccination is recommended for people at high risk of exposure to MPXV. These include healthcare workers, laboratory personnel working with orthopoxviruses, and men who have sex with men, especially those with multiple sexual partners or known contact with infected individuals.<sup>[70]</sup>

PEP involves vaccinating people exposed to the MPXV and is most effective if the vaccine is given within 4 days of exposure. It can reduce the severity of symptoms if given between 4 and 14 days after exposure. The MVA and ACAM2000 vaccines have been shown to induce strong immune responses against MPXV. Even in people with compromised immune systems, the MVA vaccine, particularly, is well tolerated and effective. The MVA vaccine has a favorable safety profile, with fewer side effects than the older smallpox vaccines. ACAM2000 is effective but has a higher risk of side effects, including myocarditis and pericarditis, especially in people with heart disease or a weakened immune system.<sup>[56,65,66]</sup>

## Travel Recommendations

MPXV is spread through close and prolonged physical contact and sexual transmission. Two doses of the MPXV vaccine should be received before travel unless contraindicated. Avoid close contact with people who have symptoms of Mpox and touching lesions and objects used by a person with Mpox. The CDC strongly recommends vaccination for people who have been exposed to MPXV or who are at high risk for exposure.<sup>[56,71,72]</sup>

Patients suspected of having an Mpox rash or blisters should not travel and should remain in isolation until all symptoms are gone, the rash has healed, and the scabs have fallen off. MPXV travel recommendations for August 2024 include general advice, pretravel precautions, travel precautions, and posttravel precautions.

General advice includes avoiding nonessential travel to areas with active MPXV outbreaks, particularly the Democratic Republic of the Congo and neighboring countries with MPXV Clade I outbreaks. Vaccination of high-risk individuals, including healthcare and laboratory workers and travelers to endemic areas, should be ensured. Before travel, up-to-date information and personalized advice should be obtained from travel health clinics, vaccines should be checked to ensure they are up to date, and comprehensive medical insurance should be obtained to cover medical evacuation and treatment for MPXV. While traveling, avoid contact with wild animals and exotic pets that may be reservoirs for the virus, practice strict hygiene such as frequent hand washing with soap and water or alcohol-based hand sanitizers, and avoid close contact with people who have symptoms of Mpox. After travel, symptoms of Mpox should be monitored for 21 days after returning from an endemic area, and if symptoms develop, seek medical attention immediately and inform healthcare providers of recent travel.<sup>[56]</sup>

## Infection Control

Clear infection control measures are essential to prevent human-to-human transmission, which is the primary means of outbreak spread. Minimizing the spread of the disease within the community and reducing the risk of hospital-acquired outbreaks and transmission to healthcare workers (HCWs) is crucial. MPXV transmission occurs through physical contact, sexual contact, indirect contact, inhalation of aerosols or droplets, and percutaneous injury.<sup>[17]</sup> Air samples taken from rooms of patients wearing N95 masks showed high levels of the virus, suggesting that airborne transmission is possible, although not yet proven.<sup>[73]</sup>

According to CDC guidelines, all confirmed and suspected cases of MPXV must be isolated upon admission. Patients with symptoms such as fever and skin lesions, or those who have visited endemic regions or had contact with confirmed cases, should be placed in single rooms. Strict contact and droplet precautions must be implemented. Hand hygiene is the most critical precaution and must be applied without exception. Medical nonsterile gloves should be worn before contact with patients, lesions, or their environment.<sup>[56]</sup>

HCWs caring for these patients must wear a face mask that covers the nose and mouth, with FFP2 masks recommended by the CDC and other authorities. A gown or sheet should cover patients' exposed areas with rashes or lesions. To prevent needle-stick injuries, used syringes, especially those that have come into contact with lesions, should not be capped and must be disposed of in appropriate waste containers. HCWs should be monitored for signs of acute illness, such as fever or cough, for 14 days.<sup>[56]</sup>

## Infection Control Measures for Mpox in Healthcare Settings

The isolation measures for patients with Mpox differ in healthcare and community settings. In healthcare settings, suspected or confirmed Mpox patients should be placed in a single room with a private bathroom. Airborne infection isolation rooms should be in use, especially for procedures where aerosols are generated. Healthcare workers should wear appropriate personal protective equipment (PPE), including N95 respirators, gloves, gowns, and eye protection (goggles or face shields). The number of visitors should be limited, and they must wear appropriate PPE where necessary. Hand hygiene should be maintained using soap and water or alcohol-based hand rub before and after patient contact, after removing gloves, and after touching potentially contaminated surfaces. Environmental cleaning and disinfection should include regular cleaning and disinfection of surfaces and equipment in the patient room using EPA-registered disinfectants that are effective against enveloped viruses. After patient discharge or transfer, thorough room cleaning and disinfection should be done. According to local biohazard regulations, waste management should include disposing of PPE and patient care materials. Contaminated linen and textiles should be handled with minimal agitation, and standard precautions should be taken during laundering. Patient transport should be limited to essential medical purposes, and if transport is required, ensure that the patient is wearing a surgical mask and that lesions are covered. HCWs should receive regular

training in infection control practices and the correct use of PPE. Patients and their families should be educated about infection control measures and the importance of adhering to them. In community settings, mildly ill patients should be advised to stay at home and avoid contact until all lesions have scabbed and fallen off. Patients should use a separate bedroom and bathroom if possible. Hand hygiene should include frequent washing with soap and water or using alcohol-based hand rubs. When coughing or sneezing, patients should cover their mouth and nose with a handkerchief or elbow. Household cleaning should include regular cleaning and disinfection of high-touch surfaces and common areas with disinfectants. Personal items such as individual items, towels, bedding, or equipment should not be shared with others in the home.<sup>[56,74]</sup>

## Conclusion

Owing to the increasing number of cases, there is a possibility for an Mpx epidemic. Vaccination is recommended for risk groups. MPXV is transmitted mainly through sexual contact, skin contact, touching contaminated objects and surfaces, and airborne droplets and aerosols. Infection control measures for MPXV in healthcare settings include patient isolation, use of PPE, hand hygiene, environmental cleaning, waste management, and staff training. In community settings, home isolation, hygiene practices, and regular cleaning are essential to prevent the spread of the virus. To minimize transmission and protect HCWs and the community, these measures must be adhered to.

**Ethics Committee Approval:** Not applicable. This article is a review.

**Authorship Contributions:** Concept: EEE, İÇ; Design: EEE, İÇ; Supervision: EEE, İÇ; Fundings: EEE, İÇ; Materials: EEE, İÇ; Data Collection or Processing: EEE, İÇ; Analysis or Interpretation: EEE, İÇ; Literature Search: EEE, İÇ; Writing: EEE, İÇ; Critical Review: EEE, İÇ.

**Informed Consent:** Not applicable.

**Conflict of Interest:** None declared.

**Use of AI for Writing Assistance:** Not declared.

**Financial Disclosure:** The authors declared that this study received no financial support.

**Peer-review:** Externally peer-reviewed.

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