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# Monkey Pox

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## SUMMARY

**Introduction:** The endemic monkeypox virus (MPXV) is a double-stranded DNA virus that is a member of the Orthopoxviral genus of the Poxviridae family. The viruses proliferate quickly and enter the bloodstream, where they cause viremia, which subsequently affects the liver, lungs, genitalia, gastrointestinal tract, and skin, among other organs. Comprehensive knowledge on this subject is essential due to its substantial public health significance.

**Methodology:** Computerized literature search was conducted through PubMed, Scopus and Google Scholar to find literatures using the key words such as monkeypox, clinical features, transmission, diagnosis, vaccine for monkey pox and its prevention.

**Topic:** Because of its significant public health implications, a literature review on this topic is imperative. Thus, the epidemiology, clinical manifestation, transmission, diagnosis procedure, vaccination for prevention complications, and treatment are all discussed in this article.

**Conclusion:** Monkeypox spreads through close contact with an infected person, contaminated materials, or infected animals. It can also be transmitted from mother to child during pregnancy or birth. The disease typically presents with a painful rash, fever, headache, muscle aches, back pain, and swollen lymph nodes. Symptoms can last 2-4 weeks. Vaccines are available for monkeypox, and vaccination is recommended along with other public health interventions. Supportive care is the mainstay of treatment, focusing on managing symptoms such as pain and fever, ensuring proper nutrition and hydration, and preventing secondary infections.

**Keywords:** MPXV; Epidemiology; Transmission; Vaccine; Surveillance

## INTRODUCTION

The endemic monkeypox virus (MPXV) is a double-stranded DNA virus that is a member of the Orthopoxviral genus of the Poxviridae family. After smallpox was eradicated in 1970, MPX first appeared. The cross-protection between smallpox and monkeypox appears to be substantial (>85%), but it is likely most significant in those who have recently had immunization (<10 years). There have been suggestions that older people (over 60) who have received a smallpox vaccination would be somewhat protected. However, more thorough evaluation is required for this. Humans can contract a zoonotic infection from infected animals, such as arboreal and terrestrial rodents (including squirrels), through contact with their blood, bodily fluids, or skin sores. Long-term exposure to MPX causes human-to-human transmission by contact with contaminated objects, infected lesions, or droplet infection [1]. MPX is currently considered a public health emergency of international concern, with over 60,000 cases in more than 95 nonendemic countries globally, as of Sep-

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tember 15, 2022, according to a recent World Health Organization (WHO) proclamation [2-8]. Contact with contaminated fomites, respiratory droplets, bodily fluids, and skin lesions of diseased animals can spread the disease either directly or indirectly. Although they are usually less severe than those of smallpox, the clinical signs of this sickness include a pustular rash along with additional symptoms such adenopathy and maculopapular rash, especially on the palms of the hands and the soles of the feet [9-11]. Potential complications include encephalitis, respiratory distress, bronchopneumonia, gastrointestinal involvement, dehydration, sepsis, and corneal infection with consequent vision loss [12]. The illness has a case fatality rate that ranges from 3% to 6% and presents with symptoms that last for two to four weeks [13].

Although MPX vaccination has historically provided incidental immunity, the therapeutic significance of MPX became evident only after the eradication of smallpox and the subsequent discontinuation of smallpox vaccination efforts [14]. Furthermore, an underestimation of pathogen harm could result from potential misreporting, given that the majority of MPX cases occur in Africa [15]. MPX infects a variety of mammals. However, its native host reservoir remains unclear [16, 17]. Transmission is believed to occur through saliva, touching fluid or surface particles, or respiratory excretions. Another route of viral exposure could be viral shedding through feces [18, 19]. In terms of symptom onset, rash pattern, and dermatitis incidence, MPX shares several characteristics with smallpox. It has a lower death rate than smallpox, though, and is less severe [16]. What distinguishes MPX from smallpox is the early onset of lymph node swelling, which frequently occurs at the onset of fever. One to three days after the onset of fever and lymphadenitis, a rash usually appears, with lesions appearing concurrently and progressing at the same rate. Although they are mostly found in the periphery, in cases of severe illness, they may spread throughout the body. The infection may persist for up to four weeks before resolution [20, 21].

There is a significant public health concern regarding the prevalence of monkeypox in the Democratic Republic of the Congo (DRC) as a result of the growing population turning to bush meat as their primary source of nutrition and seeking safety in the rainforest. The situation is further exacerbated by declining population immunity, poor living conditions, poverty, inadequate healthcare infrastructure, and low educational attainment. The outbreak in the United States demonstrates the virus's widespread presence outside of Africa [22]. However, its potential impact may bemitigated in regions equipped with advanced healthcare infrastructure. Vaccination against smallpox, which comprises live vaccinia virus, is not advised as a substitute due to the potential danger it presents to members of the population with compromised immune systems and atopic conditions [23]. A literature review on this subject is essential due to its substantial public health significance. Therefore, the aim of this articleis to discuss and outline a brief account of the epidemiology, clinical manifestation, transmission, diagnosis process and vaccination for prevention of complications, and treatment for monkeypox.

## METHODOLOGY

A computerized literature search was conducted through PubMed, Scopus and Google Scholar using the key words such as monkeypox, clinical features, transmission, diagnosis, vaccine for monkey pox and its prevention. This article included case reports, case series, retrospective studies, clinicalguidelines, narrative reviews and online resources. The literature search was done for studies and resources published in English. A total of 91 article were selected and analyzed for inclusion in this review.

## TOPIC

### Geography and epidemiology

The MPXV was first identified in Denmark in 1959 during an epidemic of a disease similar to pox in monkeys. In 1970, the first human case of smallpox was identified in a child in the Democratic Republic of the Congo (DRC) [24, 25]. The two known clades of human MPXV (Central Africa) are found in the Congo and West African Basins. The Congo basin clade, which is associated with higher rates of disease, mortality, and transmission in humans, has primarily affected the Central African countries of the Democratic Republic of the Congo and the Central African Republic [26, 27]. The DRC, the Central African Republic,

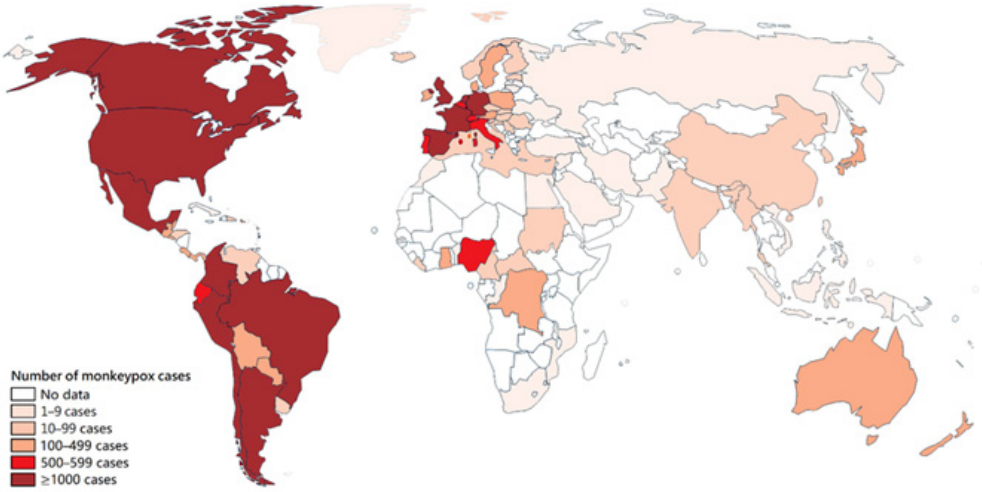


**Figure 1.** Monkeypox prevalence worldwide during 2022-2023 [38]

Nigeria, Cameroon, the Ivory Coast, Liberia, Sierra Leone, South Sudan, and Gabon are the ten African nations with data on human MPX cases [16]. The United Kingdom (UK) confirmed an MPX epidemic on May 6, 2022. The index case was a British national who got the illness in Nigeria, where it is endemic [28]. The WHO has reported 92 confirmed cases and 28 suspected cases with no reported deaths in 13 countries where MPXV had not previously been widely distributed, including the United States, Canada, France, Germany, Sweden, Australia, the Netherlands, Portugal, Spain, Italy, and the United Kingdom [29, 30]. The first infection case in the Middle East was reported by the United Arab Emirates (UAE) on May 2022 [31].For the first time in fifty years, MPX, a disease primarily found in central and western Africa, is now being reported worldwide. Ten confirmed, nine probable, and thirty suspected Human MPX cases were reported in United States in 2005 [32]. Although there were no fatalities during this episode, person-to-person infection has been documented for up to five generations [33]. On March 13, theCongo government publicly declared the outbreak, and children <15 years were most affected [34]. From 2017 to 2018, 101 confirmed cases were reported in 25 states [35]. The disease has been reported to occur in isolated cases on a number of continents, including Europe and Asia, where it is not naturally present. The current epidemic spreads from person to person and is global in possibility. Between May and November 20, 2022, there was a sharp rise in cases—80,328 MPXV-infected cases in 110 different locations worldwide, with 53 fatalities in 15 countries [36, 37]. The epidemiological outbreaks of MPXV are shown in Figure 1.

## Transmission

The primary mode of MPX transmission from

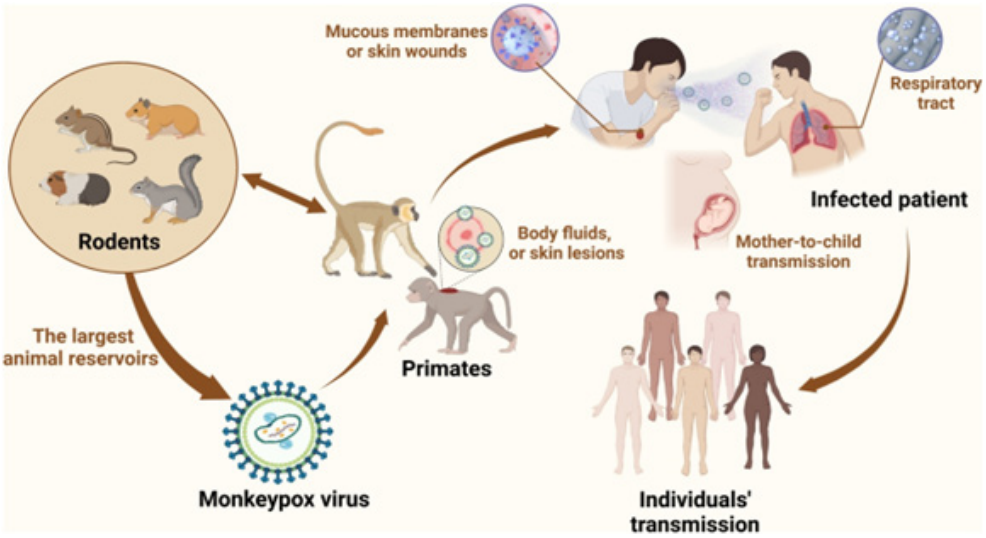


**Figure 2.** Ways of transmission for MPXV, copyright from Niu et al [42]

animal to human is through bodily fluids from infected animals. Squirrels, rats, and monkeys are among the many animal species that have been found to carry MPX, and rodents being the most likely reservoirs [39]. During the current global outbreak, human-to-human transmission of MPX has become more prominent since mid-2022, as the majority of cases in the USA and Europe were unrelated to animal exposure or travel to sub-Saharan Africa. Human-to-human transmission primarily occurs through bodily secretions or skin sore contact, which may be brought on by prolonged, non-sexual close intimate contact or direct sexual contact [39]. A vast majority of cases reported from the non-endemic countries were noted in men who have had sex with men, though any form of intimate contact is a known risk [40]. There have also been reports of viral transmission through respiratory secretions and contact with infected materials (such as clothing and bed linens) or fomites, through respiratory spread requires prolonged face-to-face contact [41]. The overall rates of transmission remain unknown, but it is possible for the virus to spread from mother to fetus through the placenta (vertical transmission) or through close contact during childbirth, which can result in congenital disease.Few methods of transmission are shown in Figure 2.

## Clinical features

Clinical manifestations occur after an incubation period of 3 to 34 days with a mean incubation period of 13 days [43]. Systemic illness is the hallmark of the early stage of illness, also referred to as the invasion phase or prodromal phase. This includes headache, arthritis, myalgia, fever, malaise, sweating, and lymphadenopathy [44, 45]. Over 90% of patients exhibited significant lymphadenopathy 1-2 days prior to the rash, which is a crucial difference between smallpox and human MPX. Both unilateral and bilateral presentations are possible, and it may impact the lymph nodes in the submandibular, cervical, postauricular, axillary, or inguinal regions [46]. These lesions have a diameter of roughly 0.5 cm, yet some of them have the potential to double in size and enlarge to 1 cm [47]. The initial week following the appearance of the rash marks the inception of the infectious phase [48]. The rash progresses through multiple phases, starting with macules, papules, vesicles, and pustules, and ends with crusts and scabs that separate as the skin heals. The rash may progress through multiple phases. Erythema and/or skin darkening are typically seen around individual lesions. It's possible that the removed scab is much smaller than the initial lesion. There is also a chance of vaginal, conjunctival, and pharyngeal mucosal inflammation [16, 49-53]. Furthermore, compared to chickenpox, MPX infections are more likely to afflict the palms and feet soles. Differentiating between the two infections can also be aided by epidemiological trends. Being an animal-borne disease, MPX can spread from humans to other humans or from animals to other animals. Conversely, only humans can contract chickenpox, and only people can infect one another. Moreover, compared to MPX, chickenpox has a significantly higher chance of causing a second infection. Adults are more likely to have MPX, but young children are primarily affected by varicella [54, 55]. Table 1 lists every typical clinical symptom and indication linked to MPXV.

## Diagnosis

Samples from surface lesions and/or skin materials such crusts, swabs, and exudates would be suitable [64]. Multiple site samples are used

**Table 1.** Clinical manifestations of the Monkey pox virus

| Systems involved | Symptoms |
|---|---|
| Gastrointestinal | Diarrhea, Nausea, Vomiting [56] |
| Upper respiratory | Runny nose, Sore throat [56] |
| Lower respiratory | Wheeze, Cough, Respiratory Distress [56] |
| General respiratory | Symptoms from both the upper and lower respiratory systems together [56] |
| Systemic | Lymphadenopathy, Back Pain, Headache, Chills, Abdominal Ache, Muscle Ache [56,57] |
| Genitals | Rash [58], Infectious sore [59] |
| Brain | Encephalitis and Headache [60], |
| Eyes | keratitis and Corneal ulceration [61] |
| Skin mucous membranes | Rash, Spots, Papules, Blisters and Pustules [62], Ulcerative or necrotic lesions [63] |

to aid in the diagnosis. It is also necessary to push the swabs firmly against the lesion in order to obtain a decent sample. The CDC (center for diseases control) advises clinicians to take two samples from every patient in order to guarantee a precise diagnosis. Specimens must be refrigerated (2–8°C) or frozen (-20°C or less) within an hour after collecting [64]. Several diagnostic methods are being used in detection of MPXV infection elaborated here and listed in Table 2.

Nucleic acid detection

PCR is now the most sensitive and specific method for detecting nucleic acids [65]. Targets selected for PCR amplification include the complement binding proteins C3L, F3L, and N3R; the extracellular envelope protein gene (B6R); the 16 DNA polymerase gene (E9L); and the DNA dependent RNA polymerase subunit 18 (RPO18) gene [66]. In RT-PCR tests, the genes E9L and B6R together showed 100% specificity for monkeypox [67]. Contact tracing, testing, and immunizing those exposed are advised after a positive test. If the RT PCR comes back negative, the other tests mentioned below can be done [68]. The gold standard for differentiating MPXV is whole genome sequencing, [69] although its application is limited, particularly in underdeveloped nations [67]. In recent outbreak, MPXV's genomicsequencing reveals that it originates from the West AfricanClade [70, 71]. Between 2018 and 2019, an average of 50 mutations in single-nucleotide (SNPs) have been discovered in comparison to the viral genome [66].

Electron microscopy

MPXV shares a similar morphology with the other orthopox viruses. Thus, electron microscopy is unable to support the MPXV diagnosis. In epidemics, it is also not very helpful because of the time commitment, high cost, and complicated sample preparation requirements [66].

Serological testing

IgM antibodies can typically be detected five days after infection using the enzyme-linked immunosorbent assay, and eight days after infection, IgG antibodies can be detected using ELISA [66]. Nevertheless, the specificity is inadequate because MPXV and other orthopox viruses display antigenic cross reactivity [72, 73].

Viral isolation and culture

This method can confirm the diagnosis by growing the virus and subsequently using it to classify different viral species. However, it has limitations: bacterial contamination can interfere with results, and the process can take several days. Due to these challenges, monkeypox culture-based testing is rarely performed in diagnostic or clinical laboratories [74].

In conclusion, DNA-based testing methods like PCR with subsequent sequencing are the most precise methods for detecting and categorizing orthopoxviruses [75]. Serological testing for MPXV antigens is difficult because of the close antigenic relationships among the orthopoxviruses' surface antigens. Currently available serological techniques include a haemagglutination-inhibition assay using chicken erythrocytes and a virus-neutralizing test using hyper-immune reference sera [76].

**Prevention and treatment**

Individuals who were vaccinated against smallpox exhibit protection from MPXV. The smallpox vaccine can be given up to two weeks after exposure, but it is currently advised for post-exposure prophylaxis, usually within four days of exposure. Additionally, pre-exposure prophylaxis may be given to high-risk individuals, such as healthcare professionals [77]. Individuals with monkey pox rash should avoid close, skin-to-skin contact. To avoid contracting MPXV, the CDC advises using an

**Table 2.** Diagnostic methods for MPX

| Test | Characteristics |
|---|---|
| PCR | High specificity and sensitivity identifies the genes of viruses. |
| Serology | Antibodies against the MPX viral genes are detected. Lack of specificity as a result of antigenic cross-reaction. |
| Viral culture | It is possible to cultivate live viruses and able to validate the diagnosis |
| Electron microscopy | Highly expensive and usually not employed |
| Immunochemistry | Detects orthopoxvirus-specific antigens |

| Vaccine | Vaccine type | Route of administration | Injection volume | Timing | Main complications | Reference |
|---|---|---|---|---|---|---|
| ACAM2000 | 2nd generation | Percutaneous | 0.0025 ml | Single dose | Cardiac complications like myocarditis, pericarditis | [74] |
| JYNNEOS | 3rd generation | Subcutaneous | 0.1-0.5 ml | 4 weeks interval | Reactions at injected site | [74] |

**Table 3.** ACAM2000 and JYNNEOS vaccine

alcohol-based hand sanitizer or washing your hands before touching your face, eating, or using the restroom. Patients with monkeypox should be isolated in separate rooms and, if receiving medical treatment, should cover their skin lesions with masks and gowns. Protecting the eyes is essential, as MPXV can cause severe complications, including blindness in extreme cases [78]. It is important to adhere to isolation protocols until every lesion has separated, crusted, and a new layer of healthy skin has grown underneath. Healthcare professionals should wear full protective gear when working with these patients. People who are ill but not very serious can be kept apart at home [79]. Both air borne and contact precautions should be taken by medical personnel and those in their vicinity to prevent illness. The health of both people and animals is at risk when exotic animals are brought in as pets because they introduce microbes that are not indigenous to the area. Animals exhibiting respiratory symptoms, mucocutaneous sores, rhinorrhea, eye discharge, or possibly lymphadenopathy should be kept apart from other animals right away, especially if they are infected or have come in close contact with them. Avoiding contact, especially through bites, scratches, or exposure to bodily fluids—is crucial [80].

The care of MPX needs to be fully optimized to help relieve symptoms, prevent complications, and stop long-term effects. Patients should receive fluids to keep their nutritional status at a reasonable level. Additionally, those with bacterial infections should receive appropriate treatment [81]. The MPX and smallpox viruses are genetically similar. Antiviral drugs and vaccines to protect against smallpox also prevent and treat MPX infections [82]. The European Medicines Agency has granted tecovirimat a license to treat MPX and has approved it as an antiviral medication for smallpox [83]. Initially, tecovirimat was used for severe MPX or a high risk of developing a serious illness. This addresses those with compromised immune systems. Tecovirimat may be able to prevent or lessen severe MPX that impacts the anus, throat, genitalia, and eyes. It may be beneficial for short-term issues like scarring, pain, inflammation, and abscesses. It is taken orally twice a day for two weeks or intravenously [84]. Brincidofovir, approved for smallpox treatment, is effective against poxviruses and other double-stranded DNA viruses. It stops the MPXV from spreading by stopping the polymerase-mediated synthesis of DNA. It is given to patients in two doses. Due to the risk of harming the embryo and fetus, brincidofovir is not recommended for pregnant women. People who could have children should not try to get pregnant and use effective birth control during treatment and for at least two months after the last dose [85, 86]. Cidofovir is another antiviral that targets DNA polymerase, effectively inhibiting MPXV replication and combating poxviruses [86]. The original purpose of Vaccinia Immunoglobulin Intravenous (VIGIV) was to treat side effects following smallpox vaccination. Since it is currently off label, the CDC has an improved access protocol that permits the use of VIGIV to treat orthopoxviral infections, like MPXV, during an epidemic. Despite the paucity of data on its efficacy, a recent case report demonstrated that VIGIV is effective against MPXV when used in conjunction with tecovirimat [87].

**Vaccination for MPX**

In the United States, two vaccines (JYNNEOS and ACAM2000) are specifically administered to individuals at risk of exposure to orthopoxviruses (Table 3). These vaccines are used as pre-exposure prophylaxis (PrEP), a preventive measure for those who may be at higher risk, such as workers in laboratories, research facilities, and public health or healthcare services. The modified Ankara vaccine (MVA) is the basis for the JYNNEOS vaccine, which is currently unavailable [88]. According to research, it is very effective, offering about 85% protection against MPX. Two doses, of 0.5 mL each, are required for the administration of this vaccine. Subcutaneous injections are used to adminis-

ter these doses four weeks apart [89]. Within the European Union, this product is referred to as Imvanex, whereas in Canada, it is known as Imvamune. The ACAM2000 smallpox vaccine is manufactured using live vaccinia virus obtained from the New York City Board of Health in the United States. Emergent BioSolutions collaborated with CDC [90] to create it. Dryvax is renowned for providing immunogenic protection to around 95% of individuals who take it. In 2008, ACAM2000 replaced Dryvax in the national strategic stockpile. Unfortunately, the production of Dryvax has been discontinued.

Usually, patients recover without the need for medical intervention. Those who have gastrointestinal symptoms (like vomiting or diarrhea) will require oral or intravenous rehydration to minimize gastrointestinal fluid losses [91]. Vaccinia immunoglobulin has received FDA approval for the treatment of certain vaccine-related side effects [91].

## CONCLUSION

Once confined to Africa, monkeypox (MPX) has now become a global health issue. MPXV can spread from person to person, particularly among person who have sex with other infected person, as well as from infected animals to humans. The clinical signs and symptoms of smallpox and MPX are comparable.Clinical signs do not prove that MPXV is present. It is best to use laboratory techniques for confirmation, including histology, immunology, microscopy, and molecular approaches. Most of the current knowledge about MPX comes from reports of individual cases or localized outbreaks, often gathered through passive and sporadic surveillance. However, these sources do not provide a complete picture of the disease. There is an urgent need to strengthen public health infrastructure and surveillance systems to improve data collection, prevention, preparedness, and response for MPX and other emerging or re-emerging diseases with pandemic potential. Tecovirimat, Cidofovir, and Brincidofovir are just a few of the antiviral medications that have been approved for the treatment of smallpox based on model studies. However, the effectiveness of these medications has not been fully determined, necessitating further research on these treatments in humans. Furthermore, a number of factors, including past vaccination history, baseline health, and co-occurring conditions or comorbidities, can influence the prognosis of monkeypox. Consequently, the most logical approach is to create customized treatments for every patient based on their risk of developing a serious illness.

## CONFLICT OF INTEREST

The author declares no conflict of interest.

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# Majmunske boginje

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## KRATAK SADRŽAJ

**Uvod:** Virus majmunskih boginja (MPXV) je dvolančani DNK virus koji pripada rodu Orthopoxvirusa porodice Poxviridae. Osnovne karakteristike ovog virusa su da se brzo razmnožava i ulazi u krvotok. Posledično nastala viremija dovodi do oštećenja kože i vitalnih organa.. Postojeća znanja o ovoj temi je potrebno unaprediti zbog velikog javnozdravstvenog značaja.
**Metodologija:** Pretraživanje elektronskih baza stručne i naučne literature (PubMed, Scopus i Google Scholar) u cilju pronalaženja relevantnih istraživanja, a prema ključnim rečima virus majmunskih boginja, način prenošenja, klinička slika, prevencija, dijagnostika i lečenje majmunskih boginja.
**Tema:** U cilju unapređenja postojećih znanja o virusu i bolesti majmunskih boginja, autori ovog rada su pregledom naučne literature obuhvatili epidemiološke karakteristike, kliničku sliku, dijagnostičke procedure i načine prevencije i lečenja majmunskih boginja.
**Zaključak:** Majmunske boginje se prenose neposrednim kontaktom sa zaraženom osobom, kontaminiranim materijalima ili zaraženim životinjama. Postoji mogućnost i prenošenja sa majke na dete tokom trudnoće ili porođaja. Bolest se obično manifestuje bolnim osipom, groznicom, glavoboljom, bolovima u mišićima, bolovima u leđima i uvećanim limfnim čvorovima. Simptomi mogu trajati 2-4 nedelje. U slučaju majmunskih boginja vakcinacija je specifična mera prevencije. Neke zemlje imaju ili razvijaju strategije za vakcinaciju lica koja mogu biti izložena visokom riziku od zaražavanja, kao što su laboratorijski radnici, timovi za brzo reagovanje i zdravstveni radnici. Osnovno lečenje čini simptomatska terapija kao i prevencija sekundarnih infekcija.

**Ključne reči:** MPXV, epidemiologija, prenos, vakcina, nadzor

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