An Overview of Epidemiology & Traits of the Human Disease: Monkey Pox Virus

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Abstract: The etiological agent and azoonotic disease known as monkey pox virus (MPXV) is found in wooded territories in West and Central Africa. Fortunately, the virus has recently moved worldwide, causing outbreaks in several non-endemic nations. This publication reviews the virus's ecology, genetics, infection biology, and evolution, as well as the real-time PCR assay and epidemiology. Based on phylogenetic molecular clock analysis, we deduce that the B.1 lineage, which is accountable for the 2022 MPV outbreaks, has been in existence since 2016. [1] The interactions among the host and the virus that modify the pathophysiology, biology, signal transduction, and host immune responses of a virus infection. We discuss the evolving pathophysiology and epidemiology of MPXV and provide an update on the most recent developments in mpox prevention and therapy. Furthermore, this analysis identified. [2]

Key Words: Monkey poxvirus (MPXV), genome, antivirals, epidemiology, virus etc.

1. Introduction: The zoonotic disease known as monkey pox (mpox) is caused by the monkey pox virus (MPXV). This double-stranded DNA (dsDNA) virus is a member of the genus Orthopoxvirus (OPXV) in the Poxviridae family, specifically in the subfamily Chordopoxvirinae [3]. MPXV was first identified in 1958 from crab-eating monkeys (Macaca fascicularis) in Copenhagen (Cop), Denmark. The first recorded human case of MPXV infection occurred in the Democratic Republic of the Congo in 1970 [4]. Monkey pox virus (MPXV) is an emerging zoonotic pathogen with complex epidemiology necessitating rapid diagnosis and distinguishing between clades and subclades. The emerging Clade Ib lacks the genomic region used in the Clade I-specific assay from the Centres for Disease Control and Prevention. We were port an MPXV real-time PCR to specifically detect Clade Ib. The assay demonstrated proficient sensitivity and specificity in 92 samples and can be included along with other TaqMan-based assays to detect MPXV and distinguish between clades and sub clades.[5]. Other members of this genus include Variola virus (VARV), Cowpox virus (CPXV), Vaccinia virus (VACV), Camel pox virus (CMLV), Taterapox virus (TATV), and Ectromelia virus (ECTV).MPXV is divided into Clade I and Clade II, with Clade II sub classified as Clade IIa and IIb [6] Mpox symptoms closely resemble those of smallpox, but the disease is generally milder, typically manifesting as high fever, headache, lymphadenopathy, muscle aches, and rashes [7]. Before 1970, there was no documented report of human MPXV infection, although the virus had previously caused infections in monkeys and apes [8]. Infections in monkeys were reported in laboratory/captive animals and were first identified in captive monkeys in Denmark in 1958. In the Democratic Republic of the Congo (DRC), August 1970, nine months of age. August 1970 witnessed the discovery of the first reported case of human mpox in the Democratic Republic of the Congo (DRC), involving a 9-month-old child. [9]. Nineteen further cases of mpox were found in Liberia, Sierra Leone, and Nigeria between September 1970 and April 1971 [10]. Since then, there have been reports of MPXV in a number of nations. It is endemic in Ivory Coast, Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Sierra Leone, and South Sudan. [11]

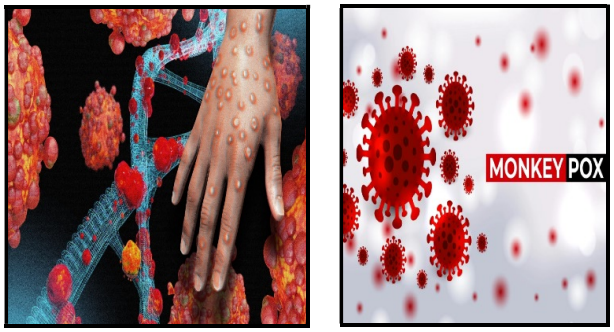


Fig. 1. Monkey Pox Virus

1.1. Genomic characteristics of the human monkey pox virus: Monkey pox virus (MPXV) is a pathogenic virus belonging to the genus *Orthopoxvirus* of the family Poxvirus. It has a double-stranded DNA (dsDNA) genome of approximately 197 kb, housing approximately 223 open reading frames (ORFs), along with variola virus (VARV, also known as smallpox, with humans as its only sensitive host), vaccinia (VACV), camel pox (CMPV), and cowpox (CPXV), all of which are pathogenic for humans and animals [12-14]. These *orthopoxviruses* are immunologically cross-reactive and cross-protective [15]. The 197 kb genome can be divided into three regions: a core region, a left arm, and a right arm containing inverted terminal repeats (ITRs). The core region is highly conserved; is responsible for transcription, replication, and virion assembly machinery; and encodes approximately 181 proteins, while the arms, the variable region, are associated with pathogenicity and host range [16-17]. Recent work has demonstrated that, in addition to single-nucleotide polymorphisms, the variable region is predominantly populated by particular genes, multicopy genes, repetitive sequences, and recombination fragments by in-depth examination of the currently available whole-genome MPXV sequences [18]. Sequence analyses indicate that MPXV is an orthopoxvirus species distinct from VARV, the smallpox virus, and neither a direct ancestor nor a direct descendant of VARV [19].The nucleotide sequences encoding essential enzymes and structural proteins in the central region of the MPXV genome were 96.3% identical to those of VARV but differed in the terminal regions, the places where most of the virulence and host-range genes are located [20]. It was found that the

terminal sections of two variola virus strains, strain India-1967 and strain BSH-75, and the monkey pox virus strain Zaire-96 had 83.5–93.6% amino acid sequence similarity [20]. Less virulent is the African Clade, with a case fatality rate of less than 0.1%.Clade II is further divided into subclades: clade IIa and clade IIb [21]. Neither subclade descends from the other [22]. The order of evolution for the clades is clade I > clade IIa > clade IIb, with clade IIb evolving to become less virulent or adapting to other species, resulting in increased human transmission [23]. The two distinct clades presented a difference of approximately 0.5% in genomic sequence, primarily in the region that encodes important virulence genes, which accounts for the differences in clinical severity [24]. Among them, the strain that caused the global MPXV outbreak in non-endemic areas in 2022 was clade IIb [25]. At present, there are many sub branches of the IIb branch, including the A.1, A.1.1, A.2, A.3, and B.1 sub branches [26].

1.2. Mutations and evolutionary clades: MPXV is divided into two evolutionary clades: (1) Clade I, previously known as the Central African clade or Congo Basin clade, with a high case fatality rate of 1–12 %; and (2) Clade II, once called the West African Clade, which is less virulent, with a lower case fatality rate of <0.1 %. Clade II is further divided into subclades: clade IIa and clade IIb. The genetic differences between Clade I and Clade II are significant and are almost twice as large as the differences between subclades IIa and IIb. Neither subclade descends from the other. The order of evolution for the clades is clade I > clade IIa > clade IIb, with clade IIb evolving to become less virulent or adapting to other species, resulting in increased human transmission .The two distinct clades presented a difference of approximately 0.5 % in genomic sequence, primarily in the region that encodes important virulence genes, which accounts for the differences in clinical severity. Among them, the strain that caused the global MPXV outbreak in no endemic areas in 2022 was clade IIb. At present, there are many sub branches of the IIb branch, including the A.1, A.1.1, A.2, A.3, and B.1 sub branches. Clade I is largely limited to the DRC and is estimated to cause more severe disease and higher mortality than clades IIa and IIb. Since the first imported MPXV case was reported in China in September 2022, the strain sequences reported to the Chinese Centres for Disease Control and Prevention all belong to the IIb branch. Despite this, a number of sequences have been associated with the related A.2 lineage

Survive for months on surfaces such as clothing and bedding, soil, and crusts. However, VARV and VACV are sensitive to heat and can be eliminated in suspension tests within 30 min at temperatures between 55 ◦C and 65 ◦C. MPXV was inactivated in

less than 5 min at 70 ◦C and less than 15 min at 60 ◦C, with no difference between viruses from the West African and Central African clades [27,28]. Common disinfectants such as 70 % ethanol (≤1 min), chlorine-containing disinfectants, 0.2 % peracetic acid (≤10 min), 1–10 % probiotic cleaner (1 h), and ultraviolet light can effectively inactivate vaccinia viruses by at least 4 log10 in suspension tests and on artificially contaminated surfaces, as shown with different types of organic loads [29-31]. Additionally, the addition of hydrogen peroxide, sodium hypochlorite (0.25–2.5 %; 1 min), 2 % glutaraldehyde (10 min), and 0.55 % orthophthalaldehyde (5 min) can effectively inactivate the virus on artificially contaminated surfaces, and hydrogen peroxide (14.4 %) and iodine (0.04–1 %) were effective in suspension tests. Copper (99.9 %) was equally effective against vaccinia virus and MPXV after 3 min An alkaline cleaner (0.9 %) can inactivate the vaccinia virus on stainless steel carriers in 10 min, and UVC light (254 nm) has been shown to inactivate the aerosolized vaccinia virus within 7.6 s and inactive the vaccinia virus within 10 min.Under practical conditions with different types of organic loads (compounds in the blood, respiratory tract and skin lesions), disinfectants with efficacy data obtained via suspension tests are preferred for the inactivation of the MPXV [32].

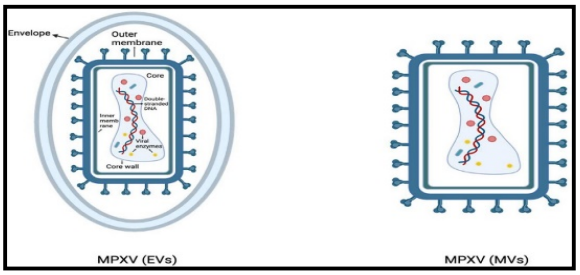
1.3. List of natural MPXV-infected animals and experimental MPXV infected animals.

MPXV Host Range & Reservoir Hosts				
S.N	**Experimental MPXV Infected Animals**	**References**	**Experimental MPXV Infected Animals**	**References**
1	Natural MPXV-Infected Animals	(Alakunle et al., 2020)	Prairie Dog (Cynomysludovicianus)	(Parker and Buller, 2013; Domán et al., 2022)
2	Sooty mangabey monkey (Cercocebusatys)		Mouse (BALB/c and C57BL/6)	(Parker and Buller, 2013; Domán et al., 2022)
3	Gambian-pouched rat (Cricetomysgambianus)		Gambian Pouched Rat (Cricetomysgambianus)	(Parker and Buller, 2013)
4	Rhesus macaques (Macacamulatta)		Crowned monkeys (Cercopithecus ascanius)	
5	Cynomolgus macaque (Macacafascicularis)		Red-tailed monkeys (Cercopithecus pogonias)	
6	Asian Monkeys (M.fascicularis)		White-nosed monkeys (Cercopithecus petaurista)	
7	Southern opossum (Didelphis marsupialis)		Western colobus monkey (Colobus badius)	
8	Sun squirrel (Heliosciurussp.)		Rhesus macaque (Macacamulatta)	
9	African hedgehogs (Atelerixsp.)		Cynomolgus macaque (Macacafascicularis	
10	Jerboas (Jaculussp.)		Thomas's rope Squirrel (Funisciurusanerythrus)	
11	Woodchucks (Marmota monax)		Red-legged sun Squirrel (Heliosciurusrufobrachium)	
12	Shot-tailed opossum (Monodelphisdomestica)		Ribboned rope squirrel (Funisciuruslemniscatus)	
13	Porcupines (Atherurusafricanus)		Thirteen-lined ground Squirrel(Spermophilustridecemlineatus	
14	Giant anteaters (Myrmecophagatridactyla)		Rabbits	
15	Prairie dogs (Cynomysspp.)		Mouse (CAST/EiJ strain)	
16	Elephant shrew (Petrodromustetradactylus)		Cotton rats (Sigmodon sp.)	
17	Domestic pig (Susscrofa)		Eurasia red squirrels (Sciurus vulgaris)	

2. Epidemiological characteristics:

2.1. Mechanisms of viral infection:

Extracellular virions (EVs) EVs are the final product of the viral morphogenetic pathway and have an outer membrane composed of geometrically corrugated lipoproteins. The structure of MPXV consists of an outer membrane, surface tubules, two lateral bodies, and a dumbbell-shaped



nucleoprotein core that contains a large double-stranded linear DNA genome (Fig. 2). Anometers in diameter that produces multiple types of virions: intracellular mature virions (MVs), wrapped virions (WVs), and extracellular virions (EVs). The replication cycle of MPXV occurs in the cytoplasm of the host cell and includes virus entry into the cell, replication, and assembly, after which the virus is ultimately released (as shown in Fig. 3). MPXV encodes one or two proteins for attachment and cell membrane fusion that occur in the plasma membrane or following

Fig. 2. Types of MPXV virions: intracellular mature virions (MVs) and extracellular virions (EVs).

endocytosis. The additional membrane of EVs is discarded prior to entry of the virus [33, 34]. Viral replication involves early and intermediate gene transcription and translation, while viral release involves envelopment through intracellular membranes and budding. For poxviruses, genome uncoating can be divided into two stages: removal of the envelope, allowing early gene expression; and breaching of the core wall, allowing DNA release, replication, and late gene expression, which are prerequisites for replication of most viruses [35,36]. The first stage of uncoating commences almost immediately after infection and involves the removal of the envelope

and release of the cores into the cytoplasm, involving fusion of the viral envelope with the host plasma or endosomal membrane .The second stage of uncoating consists of rupture of the core wall and liberation of the genome, originally defined experimentally as the sensitization of the viral DNA to DNase, which requires RNA and protein synthesis.

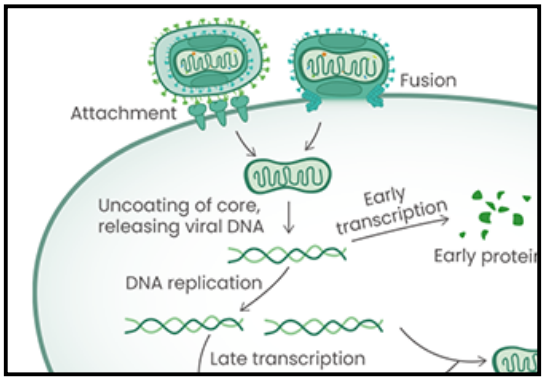


Fig. 3. MPXV replicates in the host cell cytoplasm, from virus entry to release.

2.2. Global epidemiological review:

Between 1970 and 1999, more than 500 mpox patients were documented in Africa. The majority of these cases were reported in the DRC since the first human mpox diagnosis was made in 1970 [37, 38, 39]. From 2001 to 2004, PCR confirmed 51 patients with mpox infection out of 136 suspected cases in the DRC [40]. In 2003, the DRC reported the first human mpox outbreak, involving 11 confirmed and suspected cases, all under 18 years of age, and most of whom were residing in the same hospital. Most of the patients had severe significant symptomatic illness, one death, one secondary complication, and one serious sequelae. Up to six consecutive person-to-person transmissions of MPXV have occurred, making this the longest adequately documented chain of uninterrupted transmission of mpox in humans to date. The novel transmission patterns observed during this outbreak may affect our current view of the ability of this zoonotic virus to adapt to humans [41]. Outside of Africa, the first MPXV outbreak occurred in the USA in 2003; no human-to-human transmission was recorded, and all the cases involved patients who were close to or had contact with excretions and secretions from MPXV-infected prairie dogs [42]. A few cases were reported in Sudan in 2005 [43]. During the 2000–2015 period, the increase in mpox reported in the DRC increased [44]. The sudden outbreak of mpox in several European countries outside Africa and its subsequent rapid spread led the WHO to declare it a Public Health Emergency of International Concern [45]. Since May 2022, a large number of mpox patients have been confirmed in no endemic countries worldwide. As of September 30th, 2023, the WHO has received reports of 91,123 confirmed MPXV cases and 663 probable cases, including 157 deaths from 115 countries and territories. During the global outbreak in 2022, the incidence of mpox in Nigeria was more severe in people with advanced HIV disease and accompanying varicella-zoster virus infection [46]. The ten countries with the highest cumulative number of cases reported are the United States of America (*n* = 30 636), Brazil (*n* = 10 967), Spain (*n* = 7611), France (*n* = 4158), Colombia (*n* = 4090), Mexico (*n* = 4062), Peru (*n* = 3812), the United Kingdom (*n* = 3805), Germany (*n* = 3708), and China (*n* = 1794), replacing Canada among the top ten reporting countries [47]. Together, these countries account for 81.9 % of the cases reported globally.

3. Clinical characteristics:

3.1. Incubation period and susceptible population: The incubation period of MPXV infection is typically between 5 and 21 days, with an average of 6 to 13 days [48, 49]. Infected individuals can spread the disease from the onset of symptoms until the skin rash naturally falls off and new skin forms. Research indicates that some individuals may be contagious 1–4 days before experiencing symptoms. The population is generally susceptible to MPXV infection. According to the Monkey pox Public Protection Guidelines (2023), people at high risk of contracting MPXV include those who live with or have close contact (including sexual contact) with an infected person, such as men who have sex with men (MSM). Additionally, high-risk individuals included those who had been exposed to MPXV infection, such as healthcare workers, children, pregnant women, and individuals with compromised immune systems.

3.2. Signs and symptoms: The initial symptoms of MPXV infection include fever, muscle pains, and sore throat, followed by an itchy or painful rash, headache, swollen lymph nodes, and fatigue [50] (Fig. 4). Some individuals with MPXV may also experience oropharyngeal lesions such as oral ulcers and tonsillitis; ocular symptoms, including conjunctivitis and blepharitis; and upper respiratory symptoms, including cough are also commonly observed in lymphadenopathy, including enlarged cervical or submaxillary lymph nodes and generalized lymphadenopathy [51]. The rash and mucous rash typically appear after the fever has subsided, and in some cases, they may precede systemic symptoms [52]. Rashage usually occurs through several stages, such as macules, papules, blisters, pustules, scabbing, and scab shedding Different forms of rash may exist simultaneously and may be accompanied by obvious itching and pain. It can involve the oral and pharyngeal mucosa, anus, genitals, conjunctiva, and cornea [53]. After the scab falls off, it can cause red spot pigmentation or even scarring, which can persist for several years [54]. A study from

Germany indicated that the clinical picture of MPXV infection did not differ between MSM with and without human immunodeficiency virus (HIV) infection [55].

3.3. MPXV infection course, complications and sequelae: MPXV typically lasts for 2–4 weeks but can persist longer in people with weakened immune systems. MPXV infection is a self-limiting disease, and most cases of symptoms resolve on their own. However, severe cases can lead to death, especially in children, pregnant women, and people with low immunity. The specific etiologies and pathologies leading to death are still unknown. Complications of MPXV infections include neurological manifestations, ocular infection, bronchopneumonia, and sepsis [54] and include superinfected skin lesions, paronychia, cellulitis, anal and digestive involvement, and angina with dysphagia [55]. Cardiovascular manifestations in MPXV infection have also gained increasing recognition as significant complications, including myocarditis, viral pericarditis, heart failure, and arrhythmias, can occur, leading to adverse effects on an individual's health and quality of life [56]. In addition, new complications, including paraphimosis, whitlow, proctitis, and perianal lesions, have been reported [57-61]. MPXV has been found to access the.

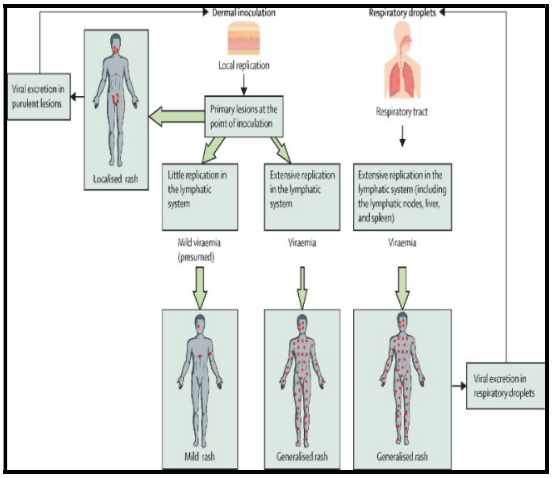


Fig. 4. The whole progression of mpox infection

3.4 Treatment and prevention of MPXV infection

Treatment for MPXV infection typically involves supportive care, antivirals, and intravenous vaccinia immune globulin (VIGIV). Since the majority of cases are mild and self-limiting, supportive care is often sufficient [62] need for medication and instead require only.

3.5. Symptomatic supportive treatment: This includes a range of active care procedures, pain management, ensuring adequate hydration and nutrition, and protecting vulnerable areas such as the eyes and genitals. Additionally, it is important to prevent and treat secondary bacterial infections and other complications while improving overall care For those experiencing severe pain due to MPXV infection, treatment options include oral pain relievers such as acetaminophen, ibuprofen, lidocaine gel, metamizole, and oral laxatives for severe anal pain. Topical analgesia, such as rectal suppositories containing emollients or steroids, may also be helpful. In severe cases, opioids may be used Replenishing fluids and nutrient replacement are needed when the patient has gastrointestinal symptoms, including vomiting and diarrhoea.

3.6. Antiviral drugs and intravenous (intravenous) treatment of vaccinia immune globulin (VIGIV): Several antiviral drugs, such as tecovirimat, brincidofovir, and cidofovir, may be effective at treating MPXV infections. However, the efficacy of these drugs has not been fully established, despite human dosing studies being conducted [63] Tecovirimat (TPOXX, ST-246) is an inhibitor of the *orthopoxvirus.*

3.7. Monkey pox vaccines: Smallpox vaccination was stopped 35 years ago after the disease was eradicated. As a result, a large portion of the world population now has no immunity to smallpox or any other zoonotic orthopoxvirus infections. However, vaccinations against smallpox can provide long-term cross-protective antiviral immunity against other related viruses, such as MPXV, which can last for decades [64, 65]. Currently, four smallpox vaccines have been designed and approved for emergency use against MPXV infections. These include the Aventis Pasteur Smallpox Vaccine (APSV), which is a strong live vaccine, as well as two attenuated live vaccines, LC16m8 and the modified Ankara–Bavaria Nordic (MVA–BN) vaccine. The first-generation vaccine is no longer in use [66, 67]. The Aventis Pasteur Smallpox Vaccine (APSV), also known as "WetVax," is an animal reaction vaccine that involves inoculating untreated vaccinia virus onto the skin of large animals, such as cattle, and liquid formulation of a calf-lymph-origin replication-competent vaccinia virus vaccine. It may be used under IND or emergency use authorization (EUA) in situations where licensed vaccines are unavailable or contraindicated to prevent smallpox [68]. Sanofi Pasteur Biologics developed ACAM2000, which is a second-generation smallpox vaccine. It is a live attenuated vaccinia strain with replication competence and was primarily reserved in the USA for emergency use against VARV before the 2022 MPXV outbreak [69]. However, this vaccine does carry significant risks of adverse reactions such as myocarditis, pericarditis, ocular complications, and even blindness in certain individuals. Active immunization against smallpox disease is indicated for individuals at high risk for VARV infection but is not suitable for people with congenital or acquired immune deficiency disorders; infants; children; pregnant individuals; or those with eczema or other skin diseases

[70]. LC16m8 (Kaketsuken) is a third-generation smallpox vaccine that has been licensed in Japan. It is made using a live, highly attenuated, replicating version of the vaccinia virus, which is derived from the Lister strain. The vaccine was first used in the 1970s, after which its neurotoxicity has been significantly reduced [71]. It is also highly immunogenic, suggesting that it can provide robust cellular and humoral immunity as well as long-term immune memory in animal models after just one dose [72, 74].

Discussion: Human MPXV infections in recent decades have been primarily associated with zoonotic spill over episodes that have short estimated human-to-human transmission chains, primarily within or connected to endemic countries [9–11]. The monkeypox virus belongs to two different genomic clades: Clade I (previously known as the Congo Basin strain), which is endemic to Central Africa, and Clade II (previously known as the West African strain), which has a history of being enzootic in West Africa. Due to the paucity of standardized investigations, meaningful estimates are unavailable for Clade I, despite the fact that far higher case fatality rates have been recorded.

Conclusion: Despite being present for more than 50 years, nothing is known about the virological profile of MPXV or the features of the disease it produces. The reservoir host of MPXV, the viral, host, and environmental factors that control the virus maintenance in the wild, animal-to-animal transmission, zoonotic transmission, and reverse spill over are among the specific mysteries that still need to be resolved. With a fatality rate of 5-8 percent, MPXV is a virus that can spread from animals to people and create a sickness resembling smallpox. Despite a lengthy period of dormancy, human mpox has lately surfaced again. It was possible that the mpox epidemiology had altered due to the rise in confirmed cases in no endemic locations. Globally, public health is threatened by MPXV, and effective prevention and treatment of this disease are crucial. The number of confirmed cases of mpox is increasing rapidly worldwide, especially in the U.S. To limit the further spread of the virus, awareness and diagnostic ability need to be increased for the treatment of the mpox epidemic, especially among public health the development of rapid, sensitive, and efficient detection technology is important for controlling and preventing further spread of the disease. Additionally, we need to increase the stock of relevant vaccines and antiviral drugs, vaccinate high-risk groups, and accelerate the development of safe and effective monkey pox vaccines and therapeutics. These measures are crucial for strengthening the immune protection of the general population and preventing current outbreaks. Tracking the transmission dynamics of MPXV and predicting the emergence of its rapidly evolving pathogens requires genomic surveillance. This information can aid in the development of timely control and prevention measures. A global collaboration is needed to conduct clinical investigations and test the efficacy and safety of MPXV vaccines, as well as antiviral drugs. By identifying and informing genomic changes in the virus, we can better prepare for potential outbreaks and protect public health. This review summarizes the current global prevalence of MPXV transmission, and while infection rates are declining rapidly, new diagnostics, antiviral treatments, and vaccines must be accelerated to ensure that the global world is ready for the reappearance of the monkey pox virus. The WHO has declared that MPXV is not as strongly contagious as other viruses but can still affect anyone who comes into contact with infected humans or animals. This review concludes that additional novel target-based antivirals for this disease need to be developed and that highly effective and safe MPXV vaccines need to be developed to control possible future global infections.

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