ISSN 2582 – 6050

Available Online at www.ijpba.info
International Journal of Pharmaceutical & Biological Archives 2022; 13(4):137-144

REVIEW ARTICLE

The Monkeypox Virus: New International Interest in an Old Virus with a New Face

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Received: 07 August 2022; Revised: 25 August 2022; Accepted: 04 September 2022

ABSTRACT

After close contact, the orthopoxvirus-based zoonotic illness known as monkeypox can be spread from people to animals, humans to humans, and humans to humans. Prior smallpox immunization offers some protection against monkeypox. Until this year, when more than 16,000 cases from nonendemic countries were reported, the scientific world was unaware of the slow increase in monkeypox infections in Africa during the previous few decades. Monkeypox has now been deemed a global public health emergency by the World Health Organization. Even though the majority of cases at this time are in guys who have had sex with other men, the largest worry is that the disease may spread to the larger society. A short-lived febrile sickness with lymphadenopathy distinguishes the condition, which is then followed by a centrifugally spreading rash that proceeds through macules, papules, vesicles, and pustule phases. The majority of patients recover within 2–4 weeks. Complications are more likely to occur in children, expectant moms, and immunocompromised individuals. For precise diagnosis, PCR detects viral Deoxyribonucleic acid. Most medical interventions are symptomatic. Due to data gathered during the smallpox pandemic, researchers are currently considering vaccinia immune globulin, tecovirimat, and cidofovir as viable treatments for monkeypox. In addition, supportive counseling can help to lessen symptoms, and in extreme circumstances, medications such tecovirimat may be given. The conventional understanding that this ailment is infrequent and always improves without therapy has been called into question in recent years by a few high-profile cases. This article offers an updated assessment of monkeypox and the available clinical therapies as a result of the extensive epidemics.

Keywords: Congenital transmission, monkeypox, smallpox, vaccines

INTRODUCTION

The monkeypox virus (MPXV) has emerged as a new threat to humanity as the world works to contain the ongoing coronavirus disease 2019 (COVID-19) epidemic. This paragraph aims to assess the existing threat, discuss feasible containment measures, and describe the possible repercussions of the MPXV. The endemic zoonosis illness human MPXV, which only affects Africa's forested regions, has two distinct clades. These clades are the West African and the Congo Basin (Central African) clades.[1] By June 2022, the World Health Organization (WHO) had received reports of at least 48 cases from seven countries in Latin America, which caused public concern due to the virus's potential for sexual transmission, its rapid spread (the majority of cases are in men who have sex with other men [MSMs], or men who have sex with men), or its detection in sexual fluids.[2,3] The uncommon zoonotic disease known as monkeypox is brought on by the Deoxyribonucleic acid (DNA) virus called the MPXV, which belongs

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to the Chordopoxvirinae subfamily and the Orthopoxvirus genus. The illness that became known as "monkeypox" and led to the initial detection of the illness appeared in two outbreaks in colonies of monkeys kept for research in 1958. The phrase "monkeypox" is misleading. Its two genetic subgroups are the West Africa clade and the Congo Basin clade.[4] In 1970, the Democratic Republic of the Congo reported the first case of monkeypox in a human, at a time when smallpox eradication efforts were intensifying.[5,6] Since then, instances of the monkeypox have been reported in several other countries in central and western Africa, including Cameroon, Sierra Leone, and the Central African Republic. The epidemiology of this virus seems to have evolved in recent years.[2] Similar to smallpox, human monkeypox presents clinically. Human monkeypox, on the other hand, is less contagious and frequently goes away on its own compared to smallpox. The disease takes between 6 and 21 days to incubate.[7] Following an invasion phase, patients experience a skin eruption stage during which they experience extreme asthenia, lymphadenopathy, back pain, myalgia, a severe headache, and fever. Human monkeypox can develop into severe instances in children, pregnant women, and those with compromised immune systems. In the medical literature, the case fatality ratio is reported to be between 3% and 6%; MPXV-infected people may experience issues such secondary infections, bronchopneumonia, sepsis, encephalitis, and visual loss.[8,9] DNA orthopoxvirus has also been discovered in a number of internal organs, including the tongue, skin, spleen, thyroid, liver, kidney, and liver.

ETIOLOGY OF MPXV

Infection with MPVX results in monkeypox, a rare illness. The enclosed, linear, virions, brick-shaped double-stranded ds DNA viruses that make up the Poxviridae family can infect a wide range of animals, including birds, reptiles, insects, and mammals. This family is divided into two subfamilies: Chordopoxvirinae and Entomopoxvarinae.[10,11] The MPXV has been able to circulate in wild animals for a long time due to its ability to infect a wide range of species, although sporadic spillover episodes occasionally cause disease in people. Monkeypox disease, which is closely associated with the variola virus, results in a condition that resembles smallpox (smallpox virus). In 1958, monkeys in Denmark were the first animals to carry the virus. The first known human case was an infant in the Democratic Republic of the Congo in 1970. It has a greater case fatality rate and is more lethal.[12] Since the monkeypox (MPX) virus is a DNA virus, it is less likely to often and significantly change its hereditary features.[13] Both monkeypox and benign epidermal monkeypox, a poxviral disease of monkeys caused by the tanapox virus, an antigenically unrelated virus in the genus Yatapoxvirus of the family Poxviridae, must be distinguished from one another. The disease can be transmitted from one person to another as well as from animals to humans by contact with contaminated objects or bodily fluids, by minute droplets, or possibly through the air. Natural reservoirs include nonhuman primates, squirrels, dormice, Gambian pouched rats, monkeys, and other creatures. By getting bitten, scratched, being in close proximity to another person, or eating undercooked animal meat, humans can catch the disease. The three primary routes of human-to-human transmission are by large respiratory droplets, direct contact, and infected fomites.[2,14] Congenital monkeypox can occasionally be brought on by the virus spreading through the placenta. While the role of direct sexual transmission is uncertain, intimate skin and mucosal contact during sex aids in dispersion. Vertical transfer from the mother to the fetus or newborn has also been linked to congenital MPX.[15]

EPIDEMIOLOGY

The affliction known as monkeypox was first identified in people in the hamlet of Basankusu in the Democratic Republic of the Congo in 1970. There was reported to be a second unplanned outbreak of human illness in the DRC/Zaire in 1996–1997.[16] Owners of prairie dogs in the United States experienced a temporary rise in human monkeypox cases in 2003. Unity, Sudan saw a monkeypox outbreak in 2005, and there have been sporadic cases recorded since then.

During an outreach campaign among refugees coming into the Republic of Congo from the Democratic Republic of the Congo in 2009, two instances of monkeypox were discovered and confirmed. A monkeypox outbreak that occurred in the Central African Republic from August to October 2016 resulted in 26 cases and two fatalities. When creating a prognosis, factors including the percentage of virus exposure, host immune response, comorbidities, immunization status, and the seriousness of the repercussions are frequently taken into consideration. Boys and girls are equally likely to have poxvirus infections, and nationality is of no consequence.[10,17] Nearly one-third of the diseases were found to be sub-clinical. The increase in cases was attributed to the civil war, which encouraged the slaughter of squirrels and other woodland animals known to carry monkey pox. There is a chance that the primary reservoir or intermediate hosts of monkey pox will dwindle, which would result in the extinction of the disease. This is a result of better lives brought on by expanding urbanization and the replacement of hunting and trapping with intense agricultural operations.[16,18] On July 14, 2022, India reported its first MPX case; by July 24, 2022, there were four confirmed cases of the virus. Of them, four were men. The final case, from Delhi, had no prior experience travelling abroad, in contrast to the first three, which were all from Kerala. High-risk sexual activity, a changing biologic nature of the virus, climate change, waning immunity following smallpox vaccination, increased international travel following the lifting of COVID-19 travel restrictions, and the discontinuation of smallpox vaccination have all been linked to the resurgence of monkeypox in both endemic and nonendemic areas. According to phylogenetic analysis, the MPX that is causing the current outbreak belongs to clade 3, and is thus connected to the clade 2 viruses that were responsible for the outbreak in Nigeria in 2017–2018 as well as the virus that caused the sporadic case in Maryland, United States of America (USA), in 2021. The genetic sequences of every virus in the current outbreak are closely grouped, which may indicate that the outbreak originated from a single place. Although the majority of those affected to date have been adult homosexual males, it is anticipated that the infection may eventually affect women and children as well as the general population.[16,19] The danger of infection is higher for medical staff. Another issue is the potential for human infection of animals, which might then serve as a recurrent source of disease.

Table 1: Types of smallpox vaccine used in monkeypox

Type of vaccine	Property
ACAM2000-live vaccinia virus	Pricking the skin surface delivers a single dosage, creates a lesion at the injection site, can replicate, not advised for immunocompromised individuals, pregnant women, and those who have atopic dermatitis. Can spread from vaccine to contacts. Cardiac adverse reactions following vaccination have been recorded
Modified vaccinia Ankara (MVA) (Jynneos, Imvanex, Imvamune)	Given subcutaneously in 2 doses, separated by 4 weeks. No lesion at inoculation site. Does not multiply, making it safe for patients with impaired immune systems. A single dose may be provided in times of scarcity
LC16m8 (modified vaccinia virus)-licensed in Japan	Single-dose administration. Less replication ability than ACAM2000, and safer

SIGNS AND SYMPTOMS

Although less severe, monkeypox in humans exhibits the same signs and symptoms as smallpox. Monkeypox starts out with fever, headache, muscle aches, and tiredness as its primary symptoms. The main difference between smallpox and monkeypox symptoms is that smallpox does not result in lymphadenopathy, whereas monkeypox does. The incubation period for monkeypox is normally 7–14 days, although it can last up to 21 days. The infection can be divided into two phases using the invasion time (0–5 days) and the skin eruption time (within 1–3 days after appearance of fever). Period of invasion: A fever, headache, muscle aches, backaches, swollen lymph nodes, chills, and fatigue are the first symptoms of the illness. The patient develops a rash that typically begins on the face before spreading to other parts of the body during the skin eruption period, which lasts for 1–3 days after the fever first appears. The face, hands, and feet's soles are the areas most commonly impacted. It may take 3 weeks before the crusts may be entirely removed.[20,21] The phases of a lesion are rashes, macules, papules, vesicles, pustules, and scabs.

TRANSMISSION

The two possible MPV transmission methods are animal-human transmission and human-human transmission. Respiratory droplets, contact with bodily fluids, contaminated patient settings or objects, and skin lesions from an infected person have all been found to be associated with human-to-human transmission. The MPXV is more likely to pass from person to person because it belongs to the Central African clade and is more virulent than the West African clade.[22] Bed linens and doorknobs may be used as transmission tools since smallpox viruses may survive for a long period outside of the body. Zoonotic transmission can also occur by direct contact with or consumption of one of the natural viral hosts, as well as through direct contact with blood and other bodily fluids, in addition to inoculation through the mucocutaneous lesions of an infected animal. In addition, reports of nosocomial transmission exist. The sex distribution of illnesses in the current outbreak shows a significant bias, with over 95% of cases recorded in young men (under 40 years old).[12,23] Although spread has been seen among MSM, heterosexual relationships should also be considered. Unintentionally, such MPV diffusion across MSM groups may expose a community. According to previously published research, the disease is thought to be transmitted by sexual contact in infected individuals with genital and vaginal lesions. In the Democratic Republic of the Congo, instances are estimated to have increased 20 times between the 1980 s and the middle of the 2000 s.[22]

DIAGNOSIS AND DETECTION

Detection

The most frequent differential diagnosis is chickenpox. Monkeypox is distinguished from chickenpox by a protracted prodromal phase, lymphadenopathy, and centrifugal distribution of the rash. In contrast, chickenpox has a quick prodromal duration, centripetal distribution of the rash, no lymphadenopathy, and a faster pace of rash spread. Other illnesses that can be differently diagnosed as MPX include hand, foot, and mouth disease, measles, infected scabies, drug eruptions, secondary syphilis, and molluscum contagiosum.[24]

Nucleic Acid Amplification Testing

The main method for locating specific MPXV viral DNA sequences and determining MPXV infection is nucleic acid amplification testing. This is accomplished using real-time or traditional polymerase chain reactions.[25] If a specific MPXV test is not available, the WHO considers a positive polymerase chain reaction result for the orthopoxvirus to be confirmation in nonendemic countries.[26]

Antibody Detection

Using plasma or serum antibodies alone to diagnose a disease is not advised. Samples specific for the MPXV virus can show immunoglobulin (Ig) M and IgG in acute and convalescent stages.[24] After 5 and 8 days of infection, specific IgG and IgE antibodies against MPX can be discovered using an enzyme-linked immunosorbent assay. These, however, are genus-specific and do not discriminate between the many pox viruses. IgG positivity may also be brought on by prior smallpox exposure or immunization.

Electron Microscopy

While MPXV and poxvirus cannot be separated, potential poxvirus in a sample can be identified using electron microscopy. In addition, this method requires pricey facilities and equipment, is very scientific and advanced, and has a poor detection sensitivity. Real-time polymerase chain reaction (RT-PCR), restriction-fragment-length polymorphism, loop-mediated isothermal amplification, and recombinase polymers amplification are a few of the molecular testing (RPA).[27] Using samples from skin lesions, the throat, blood, and urine, a RT-PCR test can accurately diagnose MPX with good sensitivity and specificity. However, these expensive examinations are not actually used in commerce.

Virus Isolation

The recognized technique for identifying infections has been MPXV isolation from clinical samples. However, MPXV testing should only be done in labs that have the right training and containment setup. As a result, this strategy is insufficient for routine diagnostic procedures.[24] It is advised that viral isolation be carried out in P2-level biosafety facilities, while P3-level laboratory standards should be adhered to when it comes to people wearing personal protection equipment.

TREATMENT

The smallpox vaccine, however, can provide defense against the disease. There is no known cure for human monkeypox. Since the widespread immunization campaign was abandoned in the 1980 s, more people are becoming aware that the MPXV exists in the human population.[28]

Cidofovir

Numerous virally generated skin disorders are treated with the powerful antiviral drug cidofovir. It is used topically or intralesionally to treat skin problems brought on by DNA viruses. It is effective against a variety of DNA viruses, including Herpes, adeno, polyoma, papilloma, and poxviruses.[29] Molluscum contagiosum, smallpox, cowpox, monkeypox, camelpox, and other poxviruses have been demonstrated to be susceptible to the inhibitory effects of cidofovir.

Brincidofovir

In June 2021, the FDA authorized brincidofovir for the treatment of smallpox infection. Patients with adenovirus, OPXV, and CMV infections have all previously received treatment with it. A patient who had the smallpox vaccination and was later diagnosed with acute myeloid leukemia received brincidofovir as part of a combination therapy regimen.[30] After receiving induction chemotherapy, the patient experienced increasing vaccineia, for which many medications, including six doses of brincidofovir, were administered. A 17-year-old kidney transplant patient who had disseminated cowpox virus infection was also treated with this medication.[31]

Smallpox Vaccine

The smallpox vaccine successfully guards people against the illness when given before to exposure to monkeypox. The Centers for Disease Control (CDC) recommends that the vaccine be given within 4 days of the date of exposure in order to prevent the disease from developing. Although it will not prevent disease, giving a vaccination between 4 and 14 days after the date of exposure may minimize the severity of the symptoms.[32]

Tecovirimat (ST-246)

Orthopoxvirus-related illnesses can be successfully treated with ST-246. Human clinical trials revealed that the medication was safe, well-tolerated, and had few side effects. Tecovirimati has been granted permission by the U.S. Food and Drug Administration to conduct Phase II trials, which are now being conducted in clinical trials. In phase I trials, tecovirimat generally had a favorable tolerability profile and no serious adverse events.[33,34]

Vaccinia Immune Globulin (VIG)

To make VIG, the blood of people who have received the smallpox vaccine is gathered (VIG). Types of smallpox vaccine used in monkeypox are listed in Table 1. In case they develop antibodies in response to the smallpox vaccine, these individuals are separated from one another and purified.[31,35]

PREVENTION

Whether the infection is suspected or proven, a patient with monkeypox should be kept in an isolation room. It is not required to handle air differently. The door should ideally remain closed (if safe to do so). There ought to be a separate bathroom in the space. Standard precautions should be taken for anyone who fear they have monkeypox. Avoid using portable fans, dry

dusting, sweeping, or vacuuming because these activities could re-suspension dried blemishes debris. Moving the patient outside the room should only be done when it is strictly medically required. A sheet or robe should be used to cover any exposed skin lesions if the patient is transferred from one room to another while wearing source control that fits appropriately (such as a surgical mask).[36] Intubation, exudation, and any other procedures that can spread oral secretions should be performed in a space dedicated for the isolation of airborne infections. Up until all lesions have crusted, the crusts have separated, and a fresh layer of healthy skin has formed underneath, it is crucial to practice isolation precautions. Patients with mild diseases who are isolated at home can follow the same recommendations. Medical personnel should wear PPE, which consists of a gown, gloves, eye protection (such as goggles or a face shield that covers the front and sides of the face), and a N95/FFP2 or higher respirator, while entering a patient's room. The right measures should be taken when managing waste (i.e., handling, storage, treatment, and disposal of soiled PPE, and patient dressings). Soiled laundry, including bedding, towels, and personal clothing, should be handled according to best practices to prevent contact with any lesion-causing materials that may be on the laundry. Never handle soiled clothes in a way that could potentially spread infectious material; instead, enclose it gently and as quickly as you can in an appropriate laundry bag. Medical personnel and patients in healthcare facilities who have been exposed to monkeypox should be kept apart and under close surveillance for 21 days after the last exposure.[37] Smallpox vaccinations are no longer being given because the illness was declared eliminated in 1980. The proportion of cohorts that have not gotten the vaccine is growing, and the vaccine's protection might eventually wane. As a result, the susceptible population is growing globally, perhaps establishing the ideal conditions for MPXV infection. In the USA, the use of the ACAM2000 and JYNNEOS (sometimes called imvamune or imvanex) vaccines to prevent MPXV is permitted. The live attenuated virus vaccination JYNNEOS has been granted approval by the US FDA for those individuals who are at risk of contracting the poxvirus. However, ACAM2000 no longer has a license in the EU because of its harmful side effects. These two vaccinations have primarily been used to immunize people who are in close proximity to those who have been diagnosed with monkeypox.[38]

CONCLUSION

The MPXV is now creating alarm on a global basis after sporadic cases were confirmed in areas of the western hemisphere. It is essential to keep a safe distance from one another and keep an eye on any encounters because the most common means for human-to-human transmission to happen are through respiratory droplets or direct touch with the mucocutaneous lesions of an infected person. Monkeypox cases in persons in their mid-20 s are now recognized. This may explain why smallpox vaccination in elderly individuals results in a loss of cross-immunity. This virus replicates within the cytoplasm and moves to the adjacent lymph nodes as it develops into a primary viremia. Infection with monkeypox is also associated with encephalopathy, bronchopneumonia, dehydration, respiratory distress, and other side effects. The most worrisome adverse effect is corneal scarring, which might cause vision loss. It is essential to be able to provide the appropriate supportive therapy in order to ensure that the risk of these consequences can be minimized to the greatest extent possible. According to the CDC and prevention, there is presently no cure for MPXV infections (CDC). The use of the vaccinia vaccine, cidofovir, tecovirimat, and IVG is being investigated as a potential cure for monkeypox on the basis of the knowledge obtained from the smallpox pandemic. Cidofovir works by limiting the viral DNA polymerase. To keep it under control, quick, preventative action will be needed. For years, experts have expressed concern that monkeypox could become a severe global health catastrophe.

SOURCES OF FUNDING

None.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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