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Review Article

Understanding Monkeypox: Insights into Viral Evolution and Public Health Implications

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I N F O

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A B S T R A C T

Background: The monkeypox virus, or MPXV for short, is a newly discovered zoonotic virus that is linked to the smallpox virus genus and causes human monkeypox, a disease that is closely comparable to smallpox. Scientists first discovered MPXV in laboratory monkeys in 1958. It mostly affects rodents and can spread from human to human or animal to human by respiratory droplets or contact with body fluids. Once limited to rural regions of Central and West Africa, outbreaks have lately shown a troubling worldwide expansion, prompting worries about public health.

Objective: The purpose of this study is to provide an overview of the current preventative and therapeutic techniques for monkeypox virus infection as well as the epidemiology, clinical characteristics, reservoirs, transmission processes, diagnosis, treatment options, and vaccines. Given the virus's potential to cause severe morbidity and its rising occurrence in non-endemic nations, a thorough review is required.

Keywords: Monkeypox, Zoonotic, DNA, Smallpox, Vaccine

Introduction

A zoonotic illness, monkeypox is brought on by the monkeypox virus (MPXV), a member of the Poxviridae family. In addition, Chordopoxvirinae and Entomopoxvirinae are the two subfamilies that comprise Poxviridae.[1] Vertebrates are known to be infected by the Chordopoxvirinae subfamily, which is further divided into 18 genera: Avi poxvirus, Capri poxvirus, Cervi poxvirus, Leporipoxvirus, Ortho poxvirus, Para poxvirus, Sui poxvirus, and Yat poxvirus. Four genera, Alphaentomopoxvirus, Betaentomopoxvirus, Deltaentomopoxvirus, and Gammaentomopoxvirus, make up the Entomopoxvirinae subfamily, which is responsible for infecting invertebrates. The Orthopoxvirus genus now includes 10 species, including monkeypox and variola, or smallpox. Despite being a DNA virus, MPXV lives its whole life cycle in the cytoplasm of the infected cells.[2]

The oval-shaped DNA virus that causes monkeypox, a zoonotic disease, is a member of the Ortho-poxvirus genus, which also contains the smallpox virus.[3] It was initially identified in 1958 by a Danish laboratory following the discovery of a smallpox-like illness in monkeys brought in from Malaysia to aid in the polio vaccine's development. The State Serum Institute of Copenhagen verified that a novel virus, which became popularly known as the monkeypox virus, was the cause of the illness in monkeys. However, the name is misleading. Rats are also infected by the virus.[4]

The first documented clinical instance of human monkeypox

occurred in 1970 in the Democratic Republic of the Congo, affecting a 9-month-old child. At first, the illness only affected people in Central and West Africa.[5] It was formerly suggested that the disease spread to people as a result of people's intimate contact with rats or monkeys that were affected. When Gambian pouched rats were imported for the pet trade and kept with prairie dogs in the USA in 2003, the illness spread, resulting in the first known epidemic of monkeypox outside of Africa.[6] In May and June of 2003, 82 instances were documented; however, none of the sick subjects died. This initial outbreak's specifics in the USA.

Several nations have stepped up their monitoring and testing for monkeypox in individuals arriving from high-risk nations.[7] A vaccination against monkeypox, developed by Bavarian Nordic and authorised by the US Food and Drug Administration (USFDA) in 2019, is now being made available to high-risk contacts of patients in some countries. Another option for therapy is the antiviral medication Tecovirimat, which the USFDA has licensed for the treatment of smallpox and is also showing encouraging results against monkeypox. The smallpox vaccination provides cross-protection against monkeypox equivalent to an 85% degree.[8]

The genetic material of the monkeypox virus is double-stranded DNA (dsDNA), which has a brick-like appearance and ranges in size from 200 to 250 nm in diameter.[9] This allows it to be observed by electron microscopy, with a magnification of about ×10,000. The genetic material of the monkeypox virus is double-stranded DNA (dsDNA), which has a brick-like appearance and ranges in size from 200 to 250 nm in diameter. This allows it to be observed by electron microscopy, with a magnification of about ×10,000. VARVs and the core section of the monkeypox virus genome, which contains structural proteins and necessary enzymes, had 96.3% identity, indicating a high degree of genetic similarity.[10]

The mpox outbreak, formerly known as monkeypox, is continuing strong as of September 2024, and it is having a major impact on people across the world, especially in Africa and some regions of the Americas and Europe. Since 2022, 122 nations have reported over 100,000 cases of mpox, many of which had not previously seen instances. Clade II is the main strain causing the worldwide pandemic, whereas Clade I is still affecting Central and Eastern Africa.[11]

The CDC (Centers for Disease Control and Prevention) has stepped up testing, surveillance, and immunisation efforts in the US to stop future outbreaks. One of the most important strategies for stopping the spread, particularly in high-risk populations, has been to conduct vaccination programmes using the JYNNEOS vaccine. More than 20,000 new cases were recorded in Africa in 2024 alone. The World Health Organisation (WHO) has authorised the MVA-BN vaccination globally, which will assist in boosting access. Equality in vaccination access is a priority for WHO and its international partners, in addition to other public health initiatives aimed at slowing the virus's spread.[12]

The symptoms of mpox, formerly known as monkeypox, might vary, although they usually manifest 7–14 days after exposure, with an incubation period of 5–21 days. Though usually milder, the smallpox signs and symptoms are comparable.[13]

Signs and Symptoms

Common Symptoms

- **Fever:** One of the first signs, often accompanied by chills.
- **Headache:** Intense headaches may occur early in the infection.
- **Muscle Aches:** Myalgia (muscle pain) is common, along with back pain.
- **Swollen Lymph Nodes:** A distinctive feature of mpox compared to smallpox is lymphadenopathy, or swollen lymph nodes, particularly in the neck, armpit, or groin.[14]
- **Fatigue:** General weakness and exhaustion are frequent.

Rash

- The hallmark of mpox is a rash that typically appears 1 to 3 days after the fever.
- The rash starts as flat lesions (macules), progressing to raised bumps (papules), then fluid-filled blisters (vesicles), pus-filled lesions (pustules), and finally scabs that eventually fall off.
- It can occur anywhere on the body but often begins on the face and spreads to other areas such as the palms of the hands, soles of the feet, and genital region.[15]
- The number of lesions varies from a few to thousands.

Other Symptoms

- Respiratory symptoms such as a sore throat, cough, or nasal congestion may develop.
- Some patients experience gastrointestinal symptoms like nausea, vomiting, or diarrhoea.[16]

Epidemiology

The first evidence of MPXV was found in 1958 in Asian monkeys (Macaca fascicularis) that had been sent from Singapore to an animal facility in Copenhagen, Denmark, for polio vaccine research. MPXV is divided into two clades: the West African clade and the Congo Basin (Central African) clade. The death rate from the Congo Basin clade is higher than that of the West African clade, with a higher case fatality rate of 10.6% over 3.6%.[17]

In 1980 smallpox eradication, 59 instances were documented between 1970 and 1980, and 338 cases were found in the Democratic Republic of the Congo over a five-year period

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of rigorous surveillance. But recently, instances have been reported from outside of Africa. 53 human cases were recorded in 2003 when prairie dogs in the Midwest of the United States contracted the disease from imported Gambian giant rats from Ghana. This was the first case documented outside of Africa.[18]

The true impact of monkeypox on public health remains uncertain. The smallpox epidemic in 1980: a five-year period of intensive monitoring in the Democratic Republic of the Congo revealed 338 cases out of the 59 cases that had been recorded between 1970 and 1980. Cases have, nonetheless, recently surfaced outside of Africa. When 53 human cases of Gambian giant rats were reported in 2003, the first case outside of Africa occurred in the Midwest of the United States due to prairie dog infection from imported Gambian rats from Ghana. Outside of the Congo Basin and West African areas, the second monkeypox pandemic occurred in Sudan in 2005. Studies indicating both zoonotic and human-to-human transmission were shown in the 122 cases that were reported in Nigeria in 2017. These cases marked the first known diagnoses in39 years.[19]

Global outbreaks are typically associated with individuals who have just returned from endemic areas. As of June 2, 2022, there were over 780 laboratory-confirmed cases from 27 member states that were not endemic to MPXV and had no history of travel to endemic regions. This caused a paradigm change, however, once the World Health Organisation (WHO) announced a new epidemic in May 2022. The genus Ortho-poxvirus, which also contains cowpox (CPX), variola virus (VARV), and vaccinia virus (VACV), is home to the MPXV family of double-stranded DNA viruses. Under an electron microscope, it has distinctive oval or brick-shaped structures that are 200–400 nm in size and have a lipoprotein envelope.[20]

The 6379-bp terminal inverted repetition of the MPXV genome, which has short tandem repeats and a putative telomere resolution sequence, makes it comparable to other viruses in the Ortho poxvirus genus. MPXV can enter the host cell through two different mechanisms: either endosomal uptake via an actin-mediated macro-pinocytosis mechanism or by fusion between ligands on the viral envelope and the host's cell plasma membrane receptors, such as chondroitin sulphate or heparan sulphate, after which parts of the viral envelope quickly disperse in the plasma membrane. The virus then releases enzymes and viral proteins into the cell cytoplasm, which weakens defences against the infection and promotes the expression of early genes, which leads to the manufacture of early proteins, DNA replication, and intermediate transcription factors.[21]

The Central African (Congo Basin) clade and the West African clade are the two phylogenetic clades of MPXV that have been described in the literature. The Central African clade exhibits greater virulence than the West African clade, leading to more severe disease and higher case fatality rates. This is due to differences in genomic structures. Its noteworthy pathogenicity stems from its capacity to impede T cell receptor-mediated T cell activation and obstruct human cell synthesis of inflammatory cytokines like interferon-gamma (IFN-γ) and tissue necrosis factor-alpha (TNF-α). To further enhance its virulence, the Central African clade also has a gene that inhibits complement enzymes, which is an important immune-modulating component. Studies have revealed that the virulence of monkeypox, however, is not associated with the suppression of major histocompatibility complex (MHC) expression or the cellular transportation of MHC molecules.[22]

Reservoirs

The zoonotic disease monkeypox has an unidentified natural reservoir. Numerous studies have been carried out to identify the natural hosts or reservoirs of the monkeypox virus.[23] Two out of the eighteen squirrels examined had antibodies to the virus. The infected squirrel, Funisciurus anerythrus, was the source of the monkeypox virus, which was isolated for the first time from a wild animal. According to other studies, the natural cycle of the monkeypox virus in the Democratic Republic of the Congo may involve squirrels belonging to the genera Funisciurus and Heliosciurus, as well as rodents from the genera Cricetomys, Graphiurus, and Petrodromus, which includes elephant shrews. The monkeypox virus was isolated from a sooty mangabey monkey living in the wild in March 2012. It shared a great deal of similarity with viruses that cause monkeypox in Western Africa, according to its entire genome sequencing. A group of wild-living chimpanzees (Pan troglodytes verus, referred to as chimpanzees) from Taï National Park, Ivory Coast, were found to often exhibit the monkeypox virus. Several examinations have shown that a variety of animal species, mostly rodents and non-human primates, are vulnerable to the virus.[24]

Transmission

The MPXV is propagated by two routes: human-to-human transmission and animal-human (zoonotic) transmission.[25] Direct contact: bites or scratches from an infected animal: or ingestion of an animal host, typically a rodent or a primate, are the ways in which zoonotic transmission takes place. Living in wooded or newly cleared regions, not having received a smallpox vaccine, touching or consuming dead bushmeat or monkeys, and sleeping on the ground (in endemic areas) are risk factors for zoonotic transmission of MPXV. The spread of the infection from person to person can happen through direct contact with respiratory secretions, skin sores, or contaminated clothing and bedding. However, prolonged face-to-face contact

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is typically necessary for transmission by respiratory droplet particles, which increases the risk to healthcare personnel, family members, and other close contacts of active cases. Congenital monkeypox can also result from vertical transmission of the virus from a mother to a foetus. It is yet unknown if monkeypox may be sexually transmitted, even though intimate physical contact is a known risk factor for transmission.[26]

Clinical Features

The self-limiting illness monkeypox has symptoms that last two to four weeks with an eight-day incubation period (4–14 days). Initially, the symptoms are typically non-specific, followed by a viral febrile prodromal phase that is marked by low-grade fever, headache, lethargy, malaise, and backache. Subsequently, 12–16 days following exposure, a vesiculopustular rash appears on the face and trunk, then spreads centrifugally to other body areas such as the palms and soles. Rash lesions go through phases of macular, papular, vesicular, and pustular morphology.[27]

After one to two weeks, the pustules turn into crusts that eventually desquamate. The first symptoms of MPXV infection are like those of smallpox; however, in contrast to smallpox, there is a noticeable characteristic of painful maxillary, cervical, and inguinal lymphadenopathy (1-4 cm), which is observed in 54% of vaccinated individuals and 84% of unprotected patients. The manifestation of lymphadenopathy suggests that MPXV is recognised by the immune system more strongly than variola. Patients with impaired immune systems, prolonged viral particle exposure, and the occurrence of comorbidities such as encephalitis, bronchopneumonia, and corneal infections typically have poorer clinical outcomes. Hypo-hyperpigmentation, scarring, dehydration (due to nausea and vomiting), and a subsequent bacterial infection resulting in septicaemia are other risks.[28]

Laboratory Diagnosis

The monkeypox virus has a new high-throughput molecular testing technique that may shorten detection times and increase capacity. The strain of monkeypox in the present outbreak was identified by whole genome sequencing as well. Furthermore, several additional DNA-based techniques, including recombinase polymerase amplification (RPA), restriction length fragment polymorphism (RFLP), and loop-mediated isothermal amplification (LAMP), have been studied for the purpose of detecting the monkeypox virus.[29]

The enzyme-linked immunosorbent test (ELISA), western blot (WB), and immunohistochemistry (IHC) are further laboratory techniques for identifying monkeypox. In situations when there is no virological material, serologic diagnostic techniques are frequently required to diagnose poxvirus. ELISA is the most often utilised serologic test in most instances. Serological testing for certain IgM and IgG antibodies is frequently used. IgM antibodies develop in response to the rash and peak around two weeks later, then fall and eventually vanish after a year. In contrast, IgG antibodies develop rapidly following the start of the rash, peak in about six weeks, and persist for decades. The immunologic cross-reactivity between the monkeypox virus and other Otho-poxviruses, however, results in a poor specificity. Another technique for identifying the monkeypox virus is electron microscopy observation. Unfortunately, widespread application is challenging because of the time-consuming and expensive sample preparation.[30]

Prevention

Monkeypox and other Ortho-poxvirus infections are successfully prevented by smallpox immunisation, according to studies. It can stop the disease from starting or lessen its severity if given early in the incubation stage. In people who are immunocompromised, there is a chance of serious side effects. Fewer people were protected against monkeypox since smallpox was eradicated in 1980 and immunisation campaigns against the virus were discontinued. In addition to offering an improved safety profile over first- and second-generation smallpox vaccines, next-generation vaccines effectively stimulate antibody production in atopic and immunocompromised patients. These vaccines include ACAM2000 (live vaccinia virus), Modified Vaccinia Ankara (attenuated vaccinia virus), and LC16m8 (attenuated vaccinia virus) with attenuated strains.[31]

Patients in hospitals have to be kept in a negative pressure area with rigorous airborne isolation. Before interacting with these patients until the lesions have crusted and the scabs have gone off, medical professionals should put on properly fitting N95 masks, gloves, and eye protection.[32]

Tecovirimat

The small-molecule viral inhibitor tecovirimat (also called TPOXX, ST-246) works well against Ortho-poxviruses, such as vaccinia virus, camelpox virus, cowpox virus, mousepox virus, variola viruses, and monkeypox virus, both in vitro and in vivo. By keeping viruses from exiting infected cells, tecovirimat, which targets the VP37 protein, restricts the transmission of viruses throughout the body. Tecovirimat does not prevent the manufacture of proteins or DNA, nor does it stop the virus from maturing. Up to cell lysis, the mature virus stays inside the host cell. The antiviral effectiveness of tecovirimat was demonstrated with an EC50 range of 0.01 to 0.07 µM. Numerous investigations have revealed that the VP37 protein is crucial for the encapsulation of intracellular mature viruses with membranes generated from the Golgi apparatus to produce enveloped viruses.[33]

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The 2022 outbreak-causing monkeypox virus lineage is effectively inhibited by tecovirimat when it comes to its in vitro antiviral properties. Additionally, several trials on animals have demonstrated the safety and efficacy of tecovirimat. More than 90% of monkeypox patients who received treatment with tecovirimat (10 mg/kg body weight) for 14 days recovered. By giving tecovirimat orally once a day, it was discovered in a nonhuman primate (NHP) model that NHP were effectively protected against monkeypox virus illness. The treatment group showed significantly lower mortality rates, fewer rashes, lower viral loads, and longer survival times than the vehicle monkeys. Evaluation of tecovirimat's effectiveness against a 65-fold fatal dosage (LD50) of the monkeypox virus in prairie dogs revealed that 75% of infected animals receiving vehicle alone succumbed to infection, but 100% of animals receiving tecovirimat survived the challenge. Tecovirimat's safety and well-tolerance have been shown in several phase 3 clinical trials in the interim.[34]

After trials showed that it was safe for people and effective in animals with identical viruses, the FDA approved its initial use in 2018 to treat smallpox. The tecovirimat (600 mg twice daily for two weeks orally) did not produce any negative effects in persons with monkeypox, and the duration of the illness and virus shedding were shortened. Furthermore, data gathered from 25 individuals with a confirmed diagnosis of monkeypox and after they had finished tecovirimat therapy showed that every case had handled the antiviral medication well, with very mild side effects. After 7 days of treatment, 10 patients (or 40%) no longer had any lesions, and 23 out of 25 patients had no discomfort by day 21. The most common side effects of treatment that were recorded were tiredness in 7 patients (28%), nausea in 4 (16%), headaches in 5 (20%), diarrhoea in 2 (8%), and itching in 2 (8%). Furthermore, tecovirimat has been shown to be safe and effective in treating monkeypox in several studies. Patients with monkeypox can now receive tecovirimat therapy from healthcare providers due to an expanded access Investigational New Drug (EA-IND) protocol created by the FDA and CDC. The Centres for Disease Control abstracted data and reported 1001 instances in total that received this antiviral medication. (35)

However, more clinical studies are required to ascertain if this antiviral medication is safe and effective in treating human cases of monkeypox. To assess tecovirimat's safety and efficacy in treating adults and children with confirmed cases of monkeypox, the National Institutes of Health's (NIH) National Institute of Allergy and Infectious Disease (NIAID) will carry out double-blind, randomised controlled research.[36] Meanwhile, NIH/NIAID is investigating the use of tecovirimat as an outpatient treatment for monkeypox in the United States in a phase 3 double-blind, randomised controlled trial through the AIDS Clinical Trials Group. As per the most recent report, various clinical investigations (PALM-007, PLATINUM, WHO/ARNS, and ACTG5418) are being conducted or are scheduled to be conducted to assess the safety and efficacy of tecovirimat in the care of individuals suffering from monkeypox.[37]

Jynneos

Vaccine Type

- Live, non-replicating vaccine.
- Uses a modified Vaccinia Ankara (MVA) virus, which is a type of poxvirus related to smallpox and mpox but is unable to replicate in human cells.[38]

Administration

- Given as two doses, 28 days apart.
- It is administered subcutaneously (under the skin), usually in the upper arm.
- Full protection is generally considered to develop two weeks after the second dose.[39]

Target Groups

Recommended for people at high risk of exposure to mpox, including:

- Individuals exposed to confirmed or suspected mpox cases.[40]
- Healthcare workers handling Ortho-poxviruses.
- Laboratory personnel working with poxviruses.
- Populations at higher risk during outbreaks, such as men who have sex with men (MSM) and others with multiple sexual partners.[41]
- Also used as a preventive measure in certain populations in the event of a bioterrorism threat involving smallpox.[42]

Effectiveness

- JYNNEOS is shown to provide robust protection against both mpox and smallpox, especially when both doses are administered.[43]
- Its effectiveness against mpox is being monitored, but early data suggests that it reduces the severity of the disease in people who are vaccinated after exposure.

Safety

- JYNNEOS is considered safe for a broad range of people, including those with compromised immune systems, HIV, or atopic dermatitis (eczema), unlike some older smallpox vaccines (e.g., ACAM2000), which have more side effects.[44]
- Common side effects include mild reactions at the injection site (redness, swelling) and general fatigue or headache. Serious side effects are rare.

Comparison to ACAM2000

- JYNNEOS is preferred over ACAM2000 for most people because it is safer and has fewer serious side effects.[45]

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- ACAM2000 is a replicating vaccine, meaning it contains a live virus that can reproduce in the body, which makes it less suitable for people with weakened immune systems.[46]

Monkeypox Prevention

The CDC advises against touching your face or hands before eating, using alcohol-containing hand sanitisers before eating, and frequently washing your hands after using the restroom to prevent contracting monkeypox. Additionally, people should avoid close, skin-to-skin contact with anyone who has rashes resembling the disease.[47]

A vaccination to prevent infection with the monkeypox virus does not currently exist. Due to immunological cross-protection across Ortho poxviruses, vaccinations against smallpox (based on the vaccinia virus) were advised for use in the ongoing monkeypox outbreak.[48] According to epidemiological data on human monkeypox gathered in Zaire between 1980 and 1984, individuals who had not had a vaccine in the past had much higher attack rates (7.2% vs. 0.9%) than those who had received one. shown that 30 years after smallpox vaccination operations stopped, the frequency of monkeypox rose sharply in the Democratic Republic of the Congo. Furthermore, the fact that people who received a smallpox vaccination more than 25 years ago are still less likely to have monkeypox suggests that vaccine-induced immunity endures a long time.[49]

A smallpox vaccine may provide cross-immune protection against West African monkeypox for decades after the inoculation, as the US monkeypox outbreak of 2003 showed. Three people who had received a smallpox vaccination decades before and had never had the monkeypox virus were unaware that they would become infected again since they did not exhibit any of the clinical signs of the disease.[50]

According to studies, cross-reactive antibodies that can be produced by Ortho-poxviruses allow first-generation live vaccinia vaccinations to offer around 85% protection against monkeypox infection. ACAM2000 is a live attenuated vaccine that was authorised in the United States in August 2007 to prevent smallpox. It is a second-generation vaccine. Clinical studies and animal models have both shown it to be beneficial.[51]

In order to prevent smallpox and monkeypox disease in 2019, the third-generation vaccine, modified vaccinia Ankara (MVA, JYNNEOS in the US, IMVANEX in the EU, and IMAMUNE in Canada), was approved for use in people 18 years of age or older who were thought to be more susceptible to smallpox or monkeypox infection in the US.[52]

Several nations have said they are purchasing vaccinations and/or releasing vaccines from national stockpiles to tackle the pandemic in response to the monkeypox outbreak in 2022. These nations include the United States, Spain, Germany, and Scotland. Per CDC releases from May 2022, JYNNEOS is being utilised in the US for pre-exposure vaccination of individuals who may be exposed to Ortho-poxviruses at work.[53]

Immunotherapy in Mpox

Clinical results are negatively impacted by Mpox virus-induced immunopathology, while treatment for the disease may be able to lower the number of severe cases. Potential immunotherapies include immune cells, immunological effector molecules, antibody-based treatments, and modification of cellular signal transmission. Combining immunotherapy and antiviral medications together may be more beneficial to patients' health than using either treatment alone.[54]

Immune globulin and antibodies

Antibody-based therapies are presently being intensively investigated and have demonstrated notable advancements in the treatment of certain infectious disorders. Neutralising antibodies, immune globulin, and convalescent plasma present encouraging alternatives as supplemental therapies in circumstances when antiviral medication efficacy is inadequate in patients with severe conditions. It is noteworthy that people who have received a smallpox vaccination in the past generate stronger neutralising antibodies, which may provide cross-protection against infection with the Mpox virus.[55]

Therefore, for the purpose of treating side effects following smallpox vaccination, certain nations have authorised the intravenous injection of vaccinia immune globulin (VIGIV).[56] VIGIV can be viewed as a preventive measure in vitro (5 mg, incubated with VACV), in vivo (VACV, 400 mg/kg, mice, intravenous), and in one clinical case (6000 U/kg, single-dose intravenous) for individuals with severe T cell functional immunodeficiency due to contraindications to smallpox vaccination. While convalescent plasma (CP) therapy has demonstrated promising results against other infectious viruses, there is now no published research on its application to the management of Mpox infection.[57] proved that Ortho-poxviruses, such as VACV, could be successfully neutralised by monoclonal antibodies (mAbs) that were directed against the particular proteins (A29L and A35R) of the Mpox virus. Additionally, these mAbs had a protective effect in mice, lowering virus titres and lessening lung harm. From the blood cells of human individuals with a history of past Ortho poxvirus vaccination or infection, a substantial number of Ortho poxvirus-specific mAbs were discovered, 16 of which demonstrated neutralising activity against Mpox. Furthermore, mAbs that targeted the A33, L1, A27, or H3 antigens showed the greatest cross-neutralising efficacy against the Mpox and VACV viruses.[58]

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Comparing VACV, 1.2 mg mAbs, intraperitoneal injection, and VIGIV, mice were well protected against lethal dosages of infection by a combination of mAbs with strong neutralising activity, according to in vivo investigations. Even in highly impaired mice with several immunological deficiencies, this protective effect was seen. Consequently, in the development of anti-Mpox medicines, mAbs medications are the most likely to yield successful clinical treatment results as opposed to VIGIV and CP, which have doubtful efficacy.[59]

Immune cells

The mpox virus infects resident immune cells and antigen-presenting cells in the tissues after entering the body through mucous membranes or damaged skin. The typical lymph node swelling seen in Mpox virus infections is subsequently explained by the Mpox virus's fast replication in draining lymph nodes and subsequent dissemination via the lymphatic system. Primarily targeted by viruses, innate immune cells serve as the initial line of defence against viral infections. Monocytes are drawn to the infection site and serve as early targets for viral infection in the early phases of Mpox virus infection. The degree of Mpox virus antigens found in monocytes can be used to gauge the prognosis and severity of an infection.[60]

Natural killer (NK) cells are also essential for producing a strong immune response in the event of an infection with the Mpox virus. Infected people with the Mpox virus have higher numbers of NK cells, but these cells' capacity to migrate, degranulate, and release effector molecules is severely compromised.[61] Patricia's research showed that injecting in vitro expanded natural killer (NK) cells into mice infected with the vaccinia virus led to a considerable extension of the mice's survival time and an increase in the NK cells' release of interferon-γ. T cells are another essential type of immune cell that may control the severity of a disease and have cytotoxic properties. When co-infected with the Mpox virus, individuals with acquired immunodeficiency are more likely to experience severe infections, which frequently need active medical intervention rather than a resolution that occurs on its own.[62]

Additionally, when the Mpox virus is present, those with weakened immune systems are more vulnerable to serious illness and death.[63] Changes also occur in other types of immune cells following Mpox virus infection, including dendritic cells and innate lymphoid cells.[64] For the purpose of better understanding the immune response and creating immunotherapy, it is crucial to comprehend the traits and changes of various immune cells following an infection with the Mpox virus.[65]

Conclusion

MPXV presents with a spectrum of clinical symptoms, most commonly fever, rash, and lymphadenopathy. The virus has an incubation period of 6 to 13 days, followed by a rash that evolves through different stages before crusting. Recent outbreaks have highlighted the virus's ability to spread in close-contact settings, with many cases emerging in urban environments outside Africa. The effectiveness of smallpox vaccines and antiviral treatments such as tecovirimat are discussed as potential interventions.

The monkeypox virus poses a serious threat to public health due to its global expansion. To manage epidemics, heightened awareness, enhanced diagnostic skills, and international cooperation are necessary. Immediate case detection, vaccination, and public health education can all aid in halting the spread of illness. To completely comprehend the mechanics of the virus's propagation, however, especially in non-endemic areas, further study is necessary.

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References

1. Kabuga AI, El Zowalaty ME. A review of the monkeypox virus and a recent outbreak of skin rash disease in Nigeria. Journal of medical virology. 2019 Apr;91(4):533-40. [Google Scholar] [Pubmed]
2. Karagoz A, Tombuloglu H, Alsaeed M, Tombuloglu G, AlRubaish AA, Mahmoud A, Smajlović S, Ćordić S, Rabaan AA, Alsuhaimi E. Monkeypox (mpox) virus: Classification, origin, transmission, genome organization, antiviral drugs, and molecular diagnosis. Journal of infection and public health. 2023 Apr 1;16(4):531-41. [Google Scholar] [Pubmed]
3. Panchal V, Gajera V, Desai T, Parekh D. A Review on Monkeypox. [Google Scholar]
4. Stefano JS, e Silva LR, Kalinke C, de Oliveira PR, Crapnell RD, Brazaca LC, Bonacin JA, Campuzano S, Banks CE, Janegitz BC. Human monkeypox virus: Detection methods and perspectives for diagnostics. TrAC Trends in Analytical Chemistry. 2023 Oct 1;167:117226. [Google Scholar]
5. Hassan AO, Omojola TE, Adeyemo AT, Obeagu EI. An update on Monkey pox in Africa. [Google Scholar]

6. Hill K. A one health perspective on a recent outbreak of monkeypox. [Google Scholar]
7. Zardi EM, Chello C. Human monkeypox—A global public health emergency. International journal of environmental research and public health. 2022 Dec 14;19(24):16781. [Google Scholar] [Pubmed]
8. Liu H, Wang W, Zhang Y, Wang F, Duan J, Huang T, Huang X, Zhang T. Global perspectives on smallpox vaccine against monkeypox: a comprehensive meta-analysis and systematic review of effectiveness, protection, safety and cross-immunogenicity. Emerging Microbes & Infections. 2024 Dec 31;13(1):2387442. [Google Scholar] [Pubmed]
9. Huang Y, Mu L, Wang W. Monkeypox: epidemiology, pathogenesis, treatment and prevention. Signal transduction and targeted therapy. 2022 Nov 2;7(1):1-22. [Google Scholar] [Pubmed]
10. MARTIN JW. SMALLPOX AND RELATED ORTHOPOXVIRUSES [Internet]. [Google Scholar]
11. Aden D, Zaheer S, Kumar R, Ranga S. Monkeypox (Mpox) outbreak during COVID-19 pandemic—Past and the future. Journal of medical virology. 2023 Apr;95(4):e28701. [Google Scholar] [Pubmed]
12. Jecker NS. Achieving global vaccine equity: The case for an international pandemic treaty. The Yale Journal of Biology and Medicine. 2022 Jun 30;95(2):271. [Google Scholar] [Pubmed]
13. Pan D, Nazareth J, Sze S, Martin CA, Decker J, Fletcher E, Déirdre Hollingsworth T, Barer MR, Pareek M, Tang JW. Transmission of monkeypox/mpox virus: a narrative review of environmental, viral, host, and population factors in relation to the 2022 international outbreak. Journal of Medical Virology. 2023 Feb;95(2):e28534. [Google Scholar] [Pubmed]
14. Bętkowska A, Maciejewska M, Adrian P, Szymański K, Czuwara J, Olszewska M, Rudnicka L. Key features of mpox and its new presentations. Dermatology Review/Przeglad Dermatologiczny. 2023 Mar 1;110(2). [Google Scholar]
15. Quain R, editor. A Dictionary of Medicine: Including General Pathology, General Therapeutics, Hygiene, and the Diseases Peculiar to Women and Children. Longmans, Green, and Company; 1882. [Google Scholar]
16. Makic MB. Management of nausea, vomiting, and diarrhea during critical illness. AACN advanced critical care. 2011 Jul 1;22(3):265-74. [Google Scholar] [Pubmed]
17. Parker S, Buller RM. A review of experimental and natural infections of animals with monkeypox virus between 1958 and 2012. Future virology. 2013 Feb 1;8(2):129-57. [Google Scholar] [Pubmed]
18. Hasan S, Saeed S. Monkeypox disease: an emerging public health concern in the shadow of COVID-19 pandemic: an update. Tropical medicine and infectious disease. 2022 Oct 3;7(10):283. [Google Scholar] [Pubmed]
19. Hussain N, Ashraf MH, Arooj R, Arif I, Haqqi R. An overview of Monkeypox Virus: Molecular Biology, Epidemiology, Pathogenesis, Treatment and Prevention Strategies. [Google Scholar]
20. Heymann DL, Rodier GR. Hot spots in a wired world: WHO surveillance of emerging and re-emerging infectious diseases. The Lancet infectious diseases. 2001 Dec 1;1(5):345-53. [Google Scholar] [Pubmed]
21. Sun Y, Nie W, Tian D, Ye Q. Human monkeypox virus: Epidemiologic review and research progress in diagnosis and treatment. Journal of Clinical Virology. 2024 Feb 28:105662. [Google Scholar] [Pubmed]
22. Nakazawa Y, Mauldin MR, Emerson GL, Reynolds MG, Lash RR, Gao J, Zhao H, Li Y, Muyembe JJ, Mbala Kingebeni P, Wemakoy O. A phylogeographic investigation of African monkeypox. Viruses. 2015 Apr 22;7(4):2168-84. [Google Scholar] [Pubmed]
23. Di Giulio DB, Eckburg PB. Human monkeypox: an emerging zoonosis. The Lancet infectious diseases. 2004 Jan 1;4(1):15-25. [Google Scholar] [Pubmed]
24. Devaux CA, Mediannikov O, Medkour H, Raoult D. Infectious disease risk across the growing human-non human primate interface: a review of the evidence. Frontiers in public health. 2019 Nov 5;7:305. [Google Scholar] [Pubmed]
25. Martínez-Fernández DE, Fernández-Quezada D, Casillas-Muñoz FA, Carrillo-Ballesteros FJ, Ortega-Prieto AM, Jimenez-Guardeño JM, Regla-Nava JA. Human Monkeypox: a comprehensive overview of epidemiology, pathogenesis, diagnosis, treatment, and prevention strategies. Pathogens. 2023 Jul 18;12(7):947. [Google Scholar] [Pubmed]
26. Najimudeen M, Chen HW, Jamaluddin NA, Myint MH, Marzo RR. Monkeypox in pregnancy: susceptibility, maternal and fetal outcomes, and one health concept. International Journal of Maternal and Child Health and AIDS. 2022 Aug 30;11(2):e594. [Google Scholar] [Pubmed]
27. Alharbi S, Almarkhi A, Alharbi T, Shabekni A, Almalki A, Aljohani R, Albalawi N, Miralam R, Hawsawi A, Alshaikhi A, Assiri S. Epidemiology, Clinical Manifestations, and Diagnosis of Monkeypox. [Google Scholar]
28. Khattak S, Rauf MA, Ali Y, Yousaf MT, Liu Z, Wu DD, Ji XY. The monkeypox diagnosis, treatments and prevention: a review. Frontiers in cellular and infection microbiology. 2023 Feb 6;12:1088471. [Google Scholar] [Pubmed]
29. Isabel S, Eshaghi A, Duvvuri VR, Gubbay JB, Cronin K, Li A, Hasso M, Clark ST, Hopkins JP, Patel SN, Braukmann TW. Targeted amplification-based whole genome sequencing of Monkeypox virus in clinical specimens.

Microbiology Spectrum. 2024 Jan 11;12(1):e02979-23. [Google Scholar] [Pubmed]
30. Dubois ME, Slifka MK. Retrospective analysis of monkeypox infection. Emerging infectious diseases. 2008 Apr;14(4):592. [Google Scholar] [Pubmed]
31. Ghaseminia M. Preventing monkeypox outbreaks: Focus on diagnosis, care, treatment, and vaccination. Journal of clinical and translational science. 2023 Jan;7(1):e60. [Google Scholar] [Pubmed]
32. Kellogg CC, Marshall C. Pathology for the Physical Therapist Assistant-E-Book: Pathology for the Physical Therapist Assistant-E-Book. Elsevier Health Sciences; 2016 Nov 29. [Google Scholar]
33. Wang J, Shahed-Al-Mahmud M, Chen A, Li K, Tan H, Joyce R. An overview of antivirals against monkeypox virus and other orthopoxviruses. Journal of medicinal chemistry. 2023 Mar 24;66(7):4468-90. [Google Scholar] [Pubmed]
34. Hutson CL, Kondas AV, Mauldin MR, Doty JB, Grossi IM, Morgan CN, Ostergaard SD, Hughes CM, Nakazawa Y, Kling C, Martin BE. Pharmacokinetics and efficacy of a potential smallpox therapeutic, brincidofovir, in a lethal monkeypox virus animal model. MSphere. 2021 Feb 24;6(1):10-128. [Google Scholar] [Pubmed]
35. Grosenbach DW, Honeychurch K, Rose EA, Chinsangaram J, Frimm A, Maiti B, Lovejoy C, Meara I, Long P, Hruby DE. Oral tecovirimat for the treatment of smallpox. New England Journal of Medicine. 2018 Jul 5;379(1):44-53. [Google Scholar] [Pubmed]
36. Chakraborty S, Chandran D, Mohapatra RK, Alagawany M, El-Shall NA, Sharma AK, Chakraborty C, Dhama K. Clinical management, antiviral drugs and immunotherapeutics for treating monkeypox. An update on current knowledge and futuristic prospects. International Journal of Surgery. 2022 Sep 1;105:106847. [Google Scholar] [Pubmed]
37. Chenchula S, Ghanta MK, Chavan M, Amerneni KC, Padmavathi R, Gupta R. Novel Clinical Manifestations of Human Monkeypox Virus Infection and Current Therapeutic and Preventive Strategies: A Systematic Review. medRxiv. 2023 Jan 7:2023-01. [Google Scholar] [Pubmed]
38. Sutter G. A vital gene for modified vaccinia virus Ankara replication in human cells. Proceedings of the National Academy of Sciences. 2020 Mar 24;117(12):6289-91. [Google Scholar] [Pubmed]
39. Kester KE, Cummings JF, Ockenhouse CF, Nielsen R, Hall BT, Gordon DM, Schwenk RJ, Krzych U, Holland CA, Richmond G, Dowler MG. Phase 2a trial of 0, 1, and 3 month and 0, 7, and 28 day immunization schedules of malaria vaccine RTS, S/AS02 in malaria-naive adults at the Walter Reed Army Institute of Research. Vaccine. 2008 Apr 24;26(18):2191-202. [Google Scholar] [Pubmed]
40. Amer F, Khalil HE, Elahmady M, ElBadawy NE, Zahran WA, Abdelnasser M, Rodríguez-Morales AJ, Wegdan AA, Tash RM. Mpox: Risks and approaches to prevention. Journal of infection and public health. 2023 Jun 1;16(6):901-10. [Google Scholar] [Pubmed]
41. Oliver SE, Mbaeyi SA. A review of global epidemiology and response to meningococcal disease outbreaks among men who have sex with men, 2001–2018. Current Epidemiology Reports. 2018 Dec;5:321-30. [Google Scholar]
42. Guharoy R, Panzik R, Noviasky JA, Krenzelok EP, Blair DC. Smallpox: clinical features, prevention, and management. Annals of Pharmacotherapy. 2004 Mar;38(3):440-7. [Google Scholar] [Pubmed]
43. Natami M, Gorgzadeh A, Gholipour A, Fatemi SN, Firouzeh N, Zokaei M, Mohammed Ali SH, Kheradjoo H, Sedighi S, Gholizadeh O, Kalavi S. RETRACTED ARTICLE: An overview on mRNA-based vaccines to prevent monkeypox infection. Journal of nanobiotechnology. 2024 Mar 1;22(1):86. [Google Scholar] [Pubmed]
44. Cices A, Prasad S, Akselrad M, Sells N, Woods K, Silverberg NB, Camins B. Mpox update: clinical presentation, vaccination guidance, and management. Cutis. 2023 Apr 1;111(4):197-202. [Google Scholar] [Pubmed]
45. Meo SA, Al-Masri AA, Klonoff DC, Alshahrani AN, Al-Khlaiwi T. Comparison of biological, pharmacological characteristics, indications, contraindications and adverse effects of JYNNEOS and ACAM2000 monkeypox vaccines. Vaccines. 2022 Nov 21;10(11):1971. [Google Scholar] [Pubmed]
46. Abdelaal A, Reda A, Lashin BI, Katamesh BE, Brakat AM, Al-Manaseer BM, Kaur S, Asija A, Patel NK, Basnyat S, Rabaan AA. Preventing the next pandemic: is live vaccine efficacious against monkeypox, or is there a need for killed virus and mRNA vaccines?. Vaccines. 2022 Aug 29;10(9):1419. [Google Scholar] [Pubmed]
47. Mabry TD. Infection Control: The critical need to wash your dirty hands. Page Publishing Inc; 2019 Apr 4. [Google Scholar]
48. Gieryńska M, Szulc-Dąbrowska L, Struzik J, Gregorczyk-Zboroch KP, Mielcarska MB, Toka FN, Schollenberger A, Biernacka Z. Orthopoxvirus zoonoses—do we still remember and are ready to fight?. Pathogens. 2023 Feb 21;12(3):363. [Google Scholar] [Pubmed]
49. Reynolds MG, Damon IK. Outbreaks of human monkeypox after cessation of smallpox vaccination. Trends in microbiology. 2012 Feb 1;20(2):80-7. [Google Scholar] [Pubmed]
50. Bano R, Jamil M, Kashif M, Qasim M, Khan M, Ali M, Jabeen N, Ahmad S, Naz R. The Zoonotic Disease Human Monkey Pox: An Insights into Epidemiological, Clinical, and Preventative Features. Pakistan Journal of Medical & Health Sciences. 2022 Jul 26;16(05):1289. [Google Scholar]

ISSN: 0019-5138
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51. Gan LL. Pathogenesis of orthopoxvirus (OPXV) infection in common CM and identification of immune correlates after vaccination with differently attenuated vaccines (Doctoral dissertation, Georg-August-Universität Göttingen). [Google Scholar]
52. Ara R, Rahman T, Nath R, Islam AK, Haque MM, Rahman MF, Nabi MH, Hawlader MD. Vaccine approach for human monkeypox over the years and current recommendations to prevent the outbreak: a rapid review. medRxiv. 2022 Sep 29:2022-09. [Google Scholar]
53. Kavey RE, Kavey A. Viral pandemics: from smallpox to Covid-19. Routledge; 2020 Sep 28. [Google Scholar]
54. Casadevall A. Antibody-based therapies for emerging infectious diseases. Emerging infectious diseases. 1996 Jul;2(3):200. [Google Scholar] [Pubmed]
55. Tan Z. Virus-Like Particle Qβ as Immunogenic Carrier for Antiviral and Antibacterial Vaccines. Michigan State University; 2024. [Google Scholar]
56. Wittek R. Vaccinia immune globulin: current policies, preparedness, and product safety and efficacy. International journal of infectious diseases. 2006 May 1;10(3):193-201. [Google Scholar] [Pubmed]
57. Rejeki MS, Sarnadi N, Wihastuti R, Fazharyasti V, Samin WY, Yudhaputri FA, Johar E, Nurainy N, Bachtiar NS, Muljono DH. Convalescent plasma therapy in patients with moderate-to-severe COVID-19: A study from Indonesia for clinical research in low-and middle-income countries. EClinicalMedicine. 2021 Jun 1;36. [Google Scholar] [Pubmed]
58. Noy-Porat T, Tamir H, Alcalay R, Rosenfeld R, Epstein E, Cherry L, Achdout H, Erez N, Politi B, Yahalom-Ronen Y, Weiss S. Generation of recombinant mAbs to vaccinia virus displaying high affinity and potent neutralization. Microbiology Spectrum. 2023 Oct 17;11(5):e01598-23. [Google Scholar] [Pubmed]
59. Ali SI, Salama A. Natural Immunomodulatory Agents as a Complementary Therapy for Poxviruses. Poxviruses. 2024 May 28:337-54. [Google Scholar] [Pubmed]
60. Dwivedi S, Singh V, Agrawal R, Misra R, Sadashiv, Fatima G, Abidi A, Misra S. Human monkeypox virus and host immunity: new challenges in diagnostics and treatment strategies. Poxviruses. 2024 May 28:219-37. [Google Scholar] [Pubmed]
61. Parnian R, Heydarifard F, Mousavi FS, Heydarifard Z, Zandi M. Innate immune response to monkeypox virus infection: mechanisms and immune escape. Journal of Innate Immunity. 2024 May 27;16(1):413-24. [Google Scholar] [Pubmed]
62. Mmerem JI, Johnson SM, Iroezindu MO. Monkeypox and chickenpox co-infection in a person living with Human Immunodeficiency Virus. The Journal of Infection in Developing Countries. 2024 Jul 29;18(07):1152-6. [Google Scholar] [Pubmed]
63. Reda A, Dhama K. Mpox impact on different organ systems: complications, mechanisms, and management. Reviews in Medical Virology. 2023 Jul;33(4):e2443. [Google Scholar] [Pubmed]
64. Melo-Silva CR, Sigal LJ. Innate and adaptive immune responses that control lymph-borne viruses in the draining lymph node. Cellular & Molecular Immunology. 2024 Sep;21(9):999-1007. [Google Scholar] [Pubmed]
65. Saghazadeh A, Rezaei N. Insights on Mpox virus infection immunopathogenesis. Reviews in medical virology. 2023 Mar;33(2):e2426. [Google Scholar] [Pubmed]

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