Wilson et al. Scr Med. 2025 Jan-Feb;56(1):183-97. DOI:10.5937/scriptamed56-52565

CURRENT TOPIC

Overview of Monkeypox Virus

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Abstract

Monkeypox virus (MPXV) is a close relative of the Variola (smallpox) virus, which was formerly prevalent throughout West and Central Africa. Nonetheless, instances have lately been verified outside of Africa in several non-endemic nations. Considering the COVID-19 pandemic, the World Health Organization (WHO) defined the recent monkeypox spread health emergency for the public for global significance on 23 July 2022. This worldwide community may be in danger because of the increased number of confirmed cases. The monkeypox virus (MPXV), the etiologic agent, was isolated from diseased monkeys in 1959, and its pathogenicity in humans was first documented in the 1970s, primarily in Western and Central African endemic countries. But in 2022, this disease shows extreme return at a never-before-seen rate, raising concerns about its communicative expansion in non-endemic areas and its potential for human-to-human transmission. Healthcare professionals, public health regulators and the general people around the world must possess substantial expertise for such relatively unknown viral diseases to mitigate the situation. Here, a thorough and current pathogenesis overview, epidemiology and clinical characteristics, along with monkeypox therapy is presented. This current review also covers future research fields, vaccine advancements and preventive and control methods for this reemerging viral disease that is currently recognised as a global crisis in public health.

Key words: Mpox, monkeypox; Body fluids; Vaccines; Transmission; Zoonoses; *Orthopoxvirus*.

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Citation:
Wilson K, Garima, Goyal R, Chopra H, Chopra S, Dhanawat M. Overview of monkeypox virus. Scr Med. 2025 Jan-Feb;56(1):183-97.

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Received: 3 August 2024
Revision received: 11 September 2024
Accepted: 11 September 2024

Introduction

The monkeypox virus is an *Orthopoxvirus* that causes monkeypox (Mpox), with symptoms similar to smallpox, although less severe.[1,2] Human infection symptoms include fever, enlarged lymph nodes and exhaustion. A rash characterised by macular lesions then develops, commonly on the hands, feet and face and continues for two to five weeks.[3] According to taxonomy, MPXV belongs to the family *Poxviridae*, which consists of 83 species and 22 genera of considerable double-stranded DNA viruses (130–375 kbp). This family is further subdivided into 2 groups: *Chordopoxvirinae*, which has vertebrates as hosts (teleost fish, mammals, crocodiles and birds) and *Entomopoxvirinae*, which has insects as hosts.[4–7] Every genus *Orthopoxvirus* member within the *Chordopoxvirinae* family shows a relation with mammals and phylogenetic investigations have verified the presence of an ancient world-class that includes MPXV alongside several different species, such as *Vaccinia* virus (the origin of contemporary smallpox vaccinations), the

cowpox and the virus variola (the agent causing smallpox).[8] The smallpox-like sickness that caused two outbreaks in a colony of cynomolgus monkeys in Copenhagen in late 1958 caused the monkeypox virus to be identified for the initial time.[9] Before the disease's eruptive phase, which was characterised by a maculopapular rash, no clinical symptoms were observed. Due to the virus's striking resemblance to other known poxviruses, it was given the moniker monkeypox virus. Numerous further monkeypox cases of confined monkeys were recorded in American and Dutch colonies between 1960 and 1968.[10] Even though various infected animals died in this phase of these outbreaks, no monkeypox cases were identified in people, proposing that humans show non-susceptibility for this disease. In 1970, the first recorded case of monkeypox in humans was part of the national smallpox surveillance and eradication campaign in Africa during that point in time.[11]

MPXV has always been classified into two distinct clades: Central and West African. Nevertheless, the current outbreak outside of Africa led to the emergence of a new clade (clade 3). Multiple lineages within clade 3 (B.1, A.1.1, A.1 and A.2) have been characterised since it was first identified, indicating that evolutionary events may have occurred during the current outbreak, allowing the virus to adapt to new hosts in new countries as well as diversify and spread to other geographical areas outside of Africa. According to reports, lineage B.1, which split off from the A.1 lineage during the 2018–2019 outbreak, is strongly linked to the present human monkeypox outbreak. The B.1 lineage segregates in a divergent phylogenetic branch, according to phylogenetic analysis, producing a number of clusters (sub-lineages) that have been found in various geographic locations and indicate continued viral evolution and spread.[12]

According to phylogenetic research conducted in 2021 by Berthet et al, it was found that ten isolates from the Central African Republic (CAR) are closely related to three lineages found in the Democratic Republic of the Congo (DRC). Moreover, the evolutionary pattern demonstrates that they originated in the Congo Basin rainforest block. The most likely explanation is transmissions from wild animals living in the rainforest, as the majority of human index cases in the Central African Republic happened at the northern border of the western and eastern rainforests. Populations will likely interact more and more with wild forest mammals as a result of ecological disruptions brought about by changes in land use, deforestation and the geographic extension of human activity. This will raise the possibility of zoonotic spillover.[13]

Epidemiology of monkeypox virus

The monkeypox virus was discovered in 1958 in a Danish research laboratory when two outbreaks of a pox-like disease occurred in monkey colonies. Consequently, the disease is called "monkeypox," but it is believed that infected people or wild animals like rats can transmit the disease to human beings. However, the virus was isolated from a 9-month-old child in Zaire, which is now known as the Democratic Republic of the Congo (DRC), who was thought to have smallpox sickness in 1970, marking the first known case in humans. Since then, the DRC had a widespread outbreak of monkeypox, which has also spread to numerous other African nations, mainly in West and Central Africa. Between 1970 and 1986, a total of 394 instances of MPXV were documented from the countries of Cameroon, Central African Republic and Zaire in the Congo Basin and 10 cases from Western African nations such as Nigeria, Sierra Leone, Liberia and Côte d'Ivoire.[14]

There is proof that people have been infected by the neglected tropical pathogen known as the monkeypox virus (MPXV), which is present in several parts of sub-Saharan Africa. Many confirmed cases of human monkeypox were recorded in Nigeria in the years that followed, with 10 cases occurring between 1971 and 1978. The number of human cases of monkeypox documented within the last three decades has increased.[15] In one instance, a boy, nine months old, experienced a fever that was subsequently accompanied by a circular rash a few days later, which is characterised by a rash that primarily affects the arms and legs. Further, his hospitalisation was done at a hospital in Basankusu, DRC, on 1 September 1970. In addition to severe cervical lymph glands, mastectomy (surgery for breast removal) and acute otitis, the patient had additional skin lesions from which the monkeypox virus was cultured. He overcame monkeypox, but measles struck before he could be released, ultimately taking his life.[11] In West African nations, six further cases of monkeypox Individuals were documented between September 1970 and March 1971.

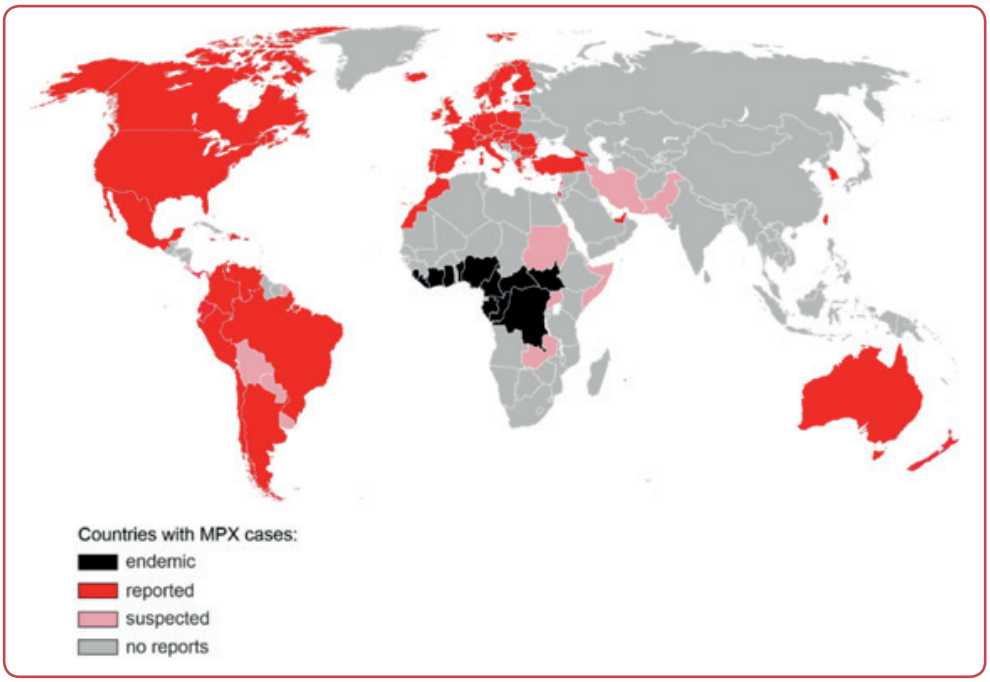

Figure 1: Countries with confirmed (red) or suspected (pink) monkeypox (MPX) cases during the 2022 non-endemic outbreak. Regions, where MPX was endemic prior to 2022, are shown in black. The map includes cases reported until 12 July 2022[8]

The majority of cases were small kids and neither of them received smallpox vaccination.[16] Until 2003, when the initial cases were discovered beyond Africa, monkeypox in humans was still only seen in Africa, with modest outbreaks mainly in the DRC and occasional cases diagnosed in forested Central or West Africa areas.[17, 18] These incidents occurred in the US and were associated with the African sighed rats shipping from Ghana to Texas. The rodents spread the virus to the exotic animal facility's prairie dogs, who infected people, primarily Kids and young people.[19]

Table 1: The characteristic features of classic and new clinical-epidemiologic forms of monkeypox virus

N	Variables	**Classic form** (1970 to present)	**New clinical-epidemiologic form** (2022+)
1	Location	Central and West Africa	Europe, South and North America, Middle East, Australia
2	Epidemiologic features	Sporadic cases and epidemics	The pandemic underway from May 2022
3	Affected population	Children and the young population	Young men who perform sexual activities with other men
4	Transmission	Contact with infected animals and followed by human-to-human transmission	Human-to-human transmission
5	Case fatality rate	1-15 %	0.025 %
6	Viruses	Central and West African variants (Clades 1 and 2, respectively)	West African variant (Clade 3)
7	Symptoms	Lesions on the face and extremities, often associated with axillary or cervical lymphadenopathy	Penile rashes, ulcerative and perianal lesions, proctitis, pharyngitis, vesicular rashes and painful inguinal lymphadenopathy
8	Clinical phase	Incubation, prodromal phase and eruption phase with skin lesions	Incubation, prodromal phase (sometimes absent) and eruption phase with genital lesions

In 2018, five affected patients were discovered: one in Singapore, one in Israel and three in the United Kingdom.[18, 20] Nigerian people were linked with these imported cases, and the country experienced a significant pandemic between 2017 and 2018.[21–23] This illness is still widespread in Africa, with extremely rare instances occurring occasionally in the US and UK.[24, 25] Several cases of monkeypox were discovered in May 2022 in Portugal, Italy and the United Kingdom; these cases primarily involved males who have intercourse with men.[26–28] Health officials quickly determined that this series began a fresh outbreak.[29]

From 1 January to 12 November 2023, 12,569 suspected mpox cases, including 581 suspected mpox deaths, have been reported in 156 health zones from 22 out of 26 (85 %) provinces in the DRC. This is the uppermost number of yearly cases ever reported, with new cases in geographical regions that had earlier not reported mpox, including Lualaba, Kinshasa and South Kivu. Among these suspected cases, 1106 were tested by real-time polymerase chain reaction (RT-PCR) and 714 were positive for MPXV (positivity rate of 65 %).[30] The characteristic features of the classic and new clinical-epidemiologic forms of monkeypox virus are depicted in Table 1.[31]

Reservoir for monkeypox

Currently, several rodent species from the Gambian pouched rats and tree squirrels found in the tropical rainforests of Central and West Africa are thought to be excellent prospects.[32, 33] It is believed that African apes and monkeys serve as intermediate hosts for the virus.[34] Numerous creatures, including lab animals, are prone to infection when captivity, including rabbits, prairie dogs, rodents and monkeys.[35, 36]

Transmission

The Mpox virus naturally inhabits few rodents and monkeys in Central African regions. Initial infections caused in humans are usually associated with interaction with infected animals, such as eating undercooked meat or encountering bodily fluids, tissues, or mucous membranes. Additionally, animal scratches and bites can transmit the virus.[37] It is thought that direct touch with an infected person's respiratory droplets is how human-to-human transmission happens.[38–40] Moreover, the Mpox virus tends to spread vertically from mothers with the virus to their babies.[41, 42] Unlike earlier outbreaks, this latest Mpox infection was the known epidemic outside of Africa (Figure 1). Previously, a Mpox infection could only be identified by visiting a region where Mpox is prevalent or getting in touch with infected animals.[43–45] Nonetheless, the bulk of the present outbreak's Mpox infections have been linked to intimate sexual interactions rather than travel or contact with infected animals.[46] Male homosexuals or bisexuals have been the victims of Mpox outbreaks in the past two years, according to documented instances (Figure 2). According to a study, 41 % of homosexual or bisexual men who had cases were also jointly infected with the human immunodeficiency virus, accounting for 98 % of cases. There was a case of a twenty-four-year-old transgender woman with HIV experiencing excruciating rash and visible vesiculopapular lesions on her hands, face and genitalia, raising the possibility that she had monkeypox. Consequently, these lesions demonstrate a positive diagnosis of monkeypox, having a CD4 count of 19 cells/uL utilising the polymerase chain reaction (PCR). The drugs given to her for monkeypox were Tecoviri-mat monkeypox and bictegravir-emtricitabine-tenofovir for the therapy of AIDS. Following two weeks of therapy, the patient experiences pain in the left eye, which indicates that the temporal conjunctival injection provided in the infected eye caused the episcleral arteries to enlarge and resulted in a raised papule, indicating PCR-positive monkeypox. An epithelial defect with conjunctival ulcers was seen under higher magnification. Finally, erythromycin ointment was administered to the lesion and within three weeks, the effective patients were cured. As our knowledge of ocular monkeypox advances, it becomes obvious that the symptoms may differ widely, including typical papulovesicular eyelid lesions, conjunctivitis, keratitis, and subconjunctival lumps that, as this patient's case demonstrates, may ulcerate.[47] Furthermore, anal and vaginal regions accounted for 73 % of the lesions that were seen.[48, 49] Mpox takes 7–14 days to incubate and symptoms appear 14–21 days later.[39, 50] Due to the extended incubation time, it might be difficult to diagnose patients accurately, which could delay treatment, exacerbate the illness and spread the virus.[51, 52]

Estimated burden and definition of the reported monkeypox

Based on WHO case definition An individual of any generation presenting since 1 January 2022, having an unresolved severe rash or several severe skin lesions; (2) single or further prodromal signs associated with a monkeypox infection, such as migraines, acute development of fever, lymphadenopathy, fatigue, pain in the back, and asthenia; and (3) the clinical manifestations of acute rash or skin lesions are the standards for possible infection of monkeypox.[53] A person who satisfies the specific criteria of a suspected case and one of its subsequent requirements is considered a possible case: possesses any of the following four circumstances: (1) no previous exposure to smallpox or monkeypox inside the period of 21 days before the start of symptoms; (2) multiple or unidentified sexual partners within the 21 days before the beginning of symptoms; (3) identifiable amounts of antiorthodox virus IgM antibody and a four-fold increase in IgG antibody titre according to acute (up to days 57) and convalescent (days 21 onwards) specimens; or (4) a test result that is positive for orthopoxviral infection. A patient having a sequencing or the polymerase chain reaction test result showing a laboratory-confirmed monkeypox infection was considered a confirmed case.

A projected model was created by Bisanzioa et al using a 50 million-person simulated population that had socioeconomic and demographic traits common to affluent European nations. Without interventions, they calculated that 402 secondary cases might arise from the emergence of 300 cases. In this scenario, the epidemics would have a median length of 37 weeks after 300 cases were introduced.[54] By isolating symptomatic cases and tracing contacts, 68.9 % fewer secondary cases are expected as a consequence. Furthermore, ring vaccination in conjunction with contact tracing would eliminate 86.1 % of secondary cases. This estimate of the burden of monkeypox was consistent with the WHO risk evaluation, which classified present worldwide healthcare administration as moderate.[55]

Clinical manifestations

The average time for monkeypox to incubate was 8.5 days.[56] Monkeypox's prodromal symptoms include adenopathy, fever, chills, throat pain, sneezing, migraines, fatigue and tiredness. Rashes often appear one to three days after the commencement of symptoms. Usually starting on the face, the rash spreads to the palms and soles before becoming more widespread. Additionally, the mouth, genitalia and eyes can develop rashes. These lesions can have a clear or yellowish fluid filling, be flat or slightly elevated and ultimately crust, dry and fall off. There may be a few hundred to several thousand skin lesions. Similar to smallpox, rashes grow in stages between two and four weeks, starting as macules and advancing to

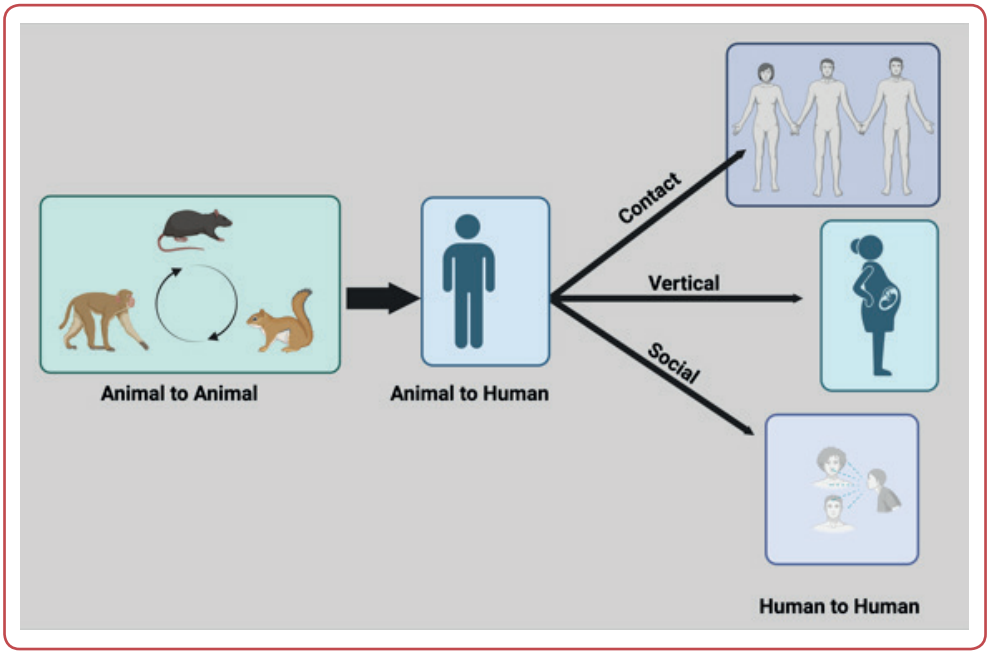

Figure 2: Modes of transmission of monkeypox virus

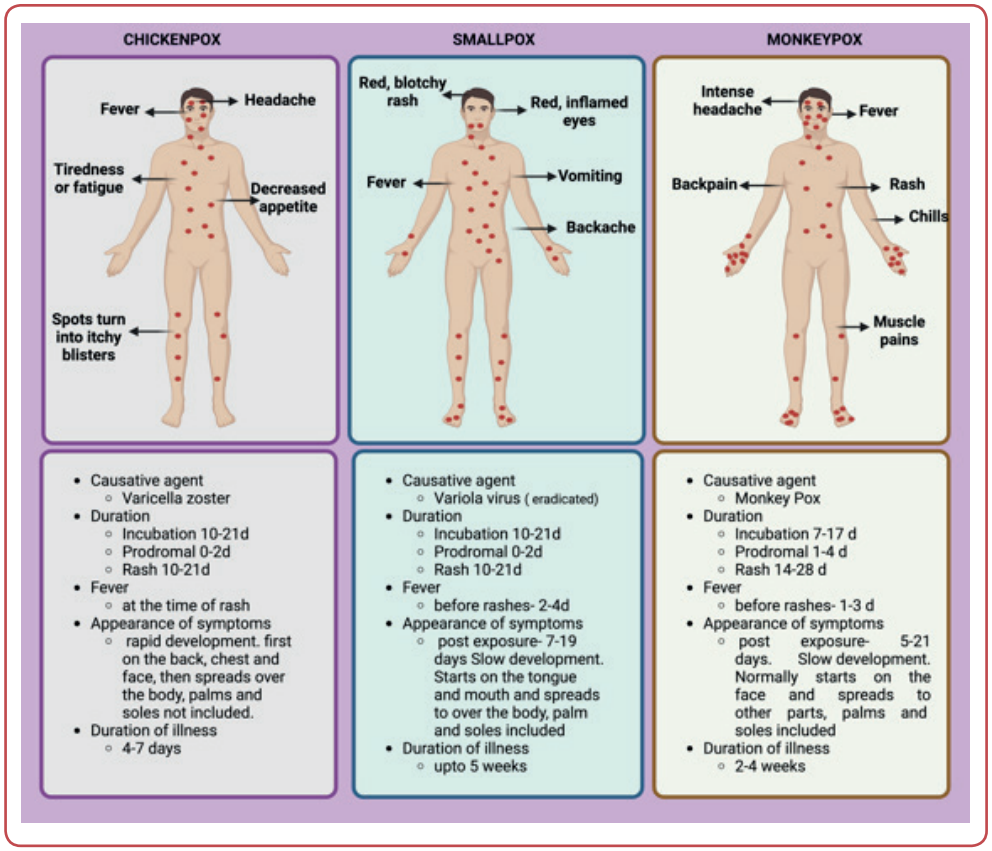

Figure 3: Clinical manifestations of typical chickenpox, smallpox and monkeypox

papules, vesicle pustules and blisters. Skin lesions usually go away on their own after two to four weeks if left untreated. Different from smallpox and chickenpox, these monkeypox dermatology characteristics include lymphadenopathy, aid in the differential diagnosis for medical professionals (Figure 3).[14]

However, the outbreak of monkeypox in 2022 may exhibit unusual characteristics as well, such as (a) a small number of lesions, or perhaps none at all, or in some instances no skin lesions at all; (b) lesions mostly occur in the perianal and genital areas, sometimes with bleeding and anal pain; (c) skin lesions that are limited to the perianal, perineal or vaginal regions; (d) asynchronous lesions, which can be scabs, umbilicated papules with increasing central ulceration, solitary or grouped spots or a combination of these; (e) absence of prodromal signs before a rash appears, such as fever, headache and melancholy.[26, 57]

Virus morphology and genome

The Mpox virus, a member of the Poxviridae family, which is characterised by an oval or brick-like morphology having a diameter between 200 and 250 nm, is the main cause of Mpox.[58, 59] Its ~197 kb genome is composed of linear, double-stranded DNA that codes for roughly 180 different proteins.[60] In addition, the Mpox virus has an ovoid particle containing lipids surrounding a dumbbell-shaped nucleocapsid. The Mpox virus shares several characteristics with other orthopoxviruses, including an extremely protected central core area, varying portions at the ends on both the left and right and a terminal repetition inversion that is tandemly repeated.[61, 62] More than 90 % of the sequences in the Mpox virus's central core region are similar to those of other orthopoxviruses, especially between C10L and A25R in the free reading frame.[63] *Orthopoxvirus* strains and species-specific traits are frequently located in the regions within the genome, which are changeable at both ends. Gaining more knowledge regarding ORFs could help us comprehend the pathophysiology, host predisposition as well as variations in immune-mediated control.[64]The number of polymorphisms involving one nucleotide was greater in the Mpox virus strains that arose in 2022 compared to the previously discovered genome sequences for the virus collected from Nigeria in 2017 and 2018. Throughout time, changes that correspond

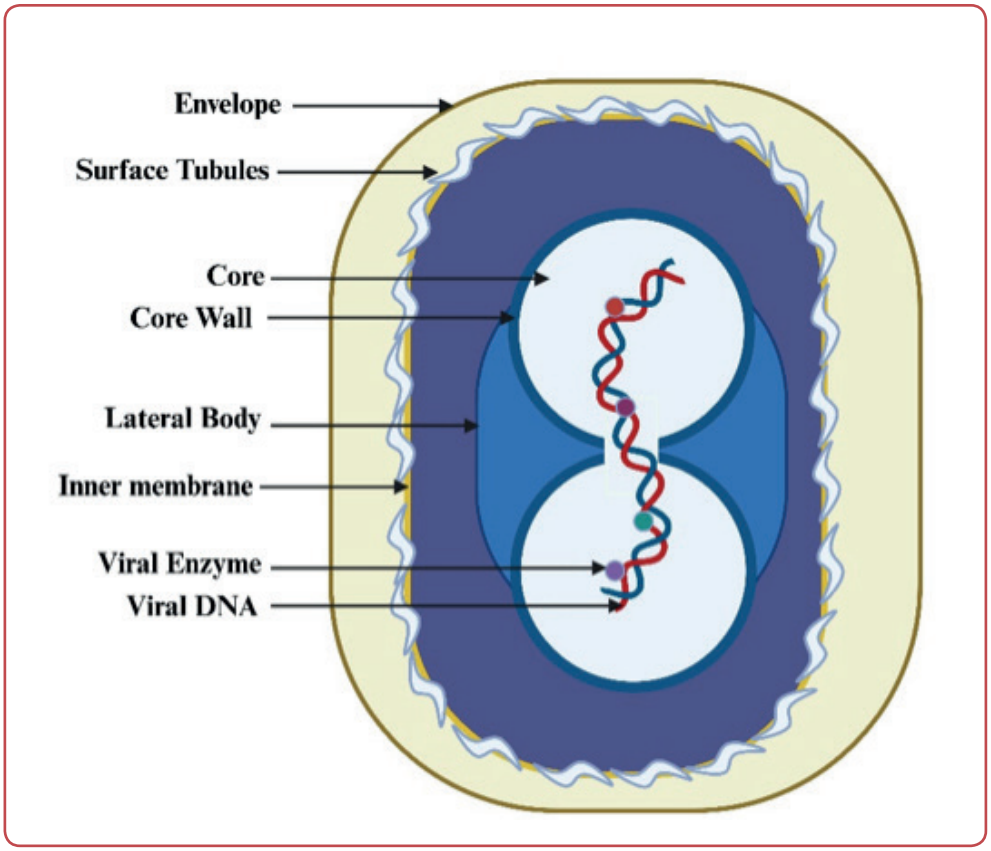

Figure 4: Monkeypox virus morphology

to APOBEC3 activity have steadily gathered. Specimens of the Nigerian A.2 lineage was found, showing the aforementioned lineage has been repeatedly exported to North America although the 2022 outbreak originated in Nigeria and that it kept spreading through interactions between people in Nigeria for nearly a decade prior to its latest export. Lastly, in all A.2 isolates, lineage-defining APOBEC3-style mutation was found that conflicts with gene A46R, that encodes for a viral innate immune modulator. All of these results show that MPXV may vary as time passes in people, including modifications that might fall in line with recognised poxvirus processes.[65, 66] Although the functional significance of these changes is still unknown, the rapid development and increased Mpox virus transmission in non-endemic locations may be explained by this high mutation rate (Figure 4).[67]

The life cycle of Mpox virus and the discovery of anti-Mpox virus drugs

Three main steps may be identified in the Mpox viral infection and replication process: 1) invasion of the virus; 2) synthesis and replication of the virus; 3) assembly, maturation and release of the virus (Figure 5).[68] It seems feasible to develop efficient antiviral treatments that combat the Mpox virus by concentrating on every phase of the virus' lifespan. The creation of antiviral medications begins with a detailed comprehension of a virus's lifespan cycle. Extracellular enveloped virions and intracellular mature virions are both distinct infectious viruses that exist in the initial phases of Mpox virus infection.[69] The envelope membrane composition and surface glycoprotein of these virus particles differ; extracellular enveloped virions have a double membrane structure, whereas intracellular mature virions have a single membrane structure. Extracellular wrapped virions enter host cells by membrane fusion, whereas intracellular mature virions are only released during cell lysis, so they enter by endocytosis and immediate fusion.[70]

Intracellular mature virions constitute among the most common virus particles concerning quantity as they lack a lipid membrane, allowing them an additional simple and robust composition.[71] By doing this, they become more resistant to outside harm and may survive longer outside of their host. Nonetheless, the mature intracellular virions' exposed surface

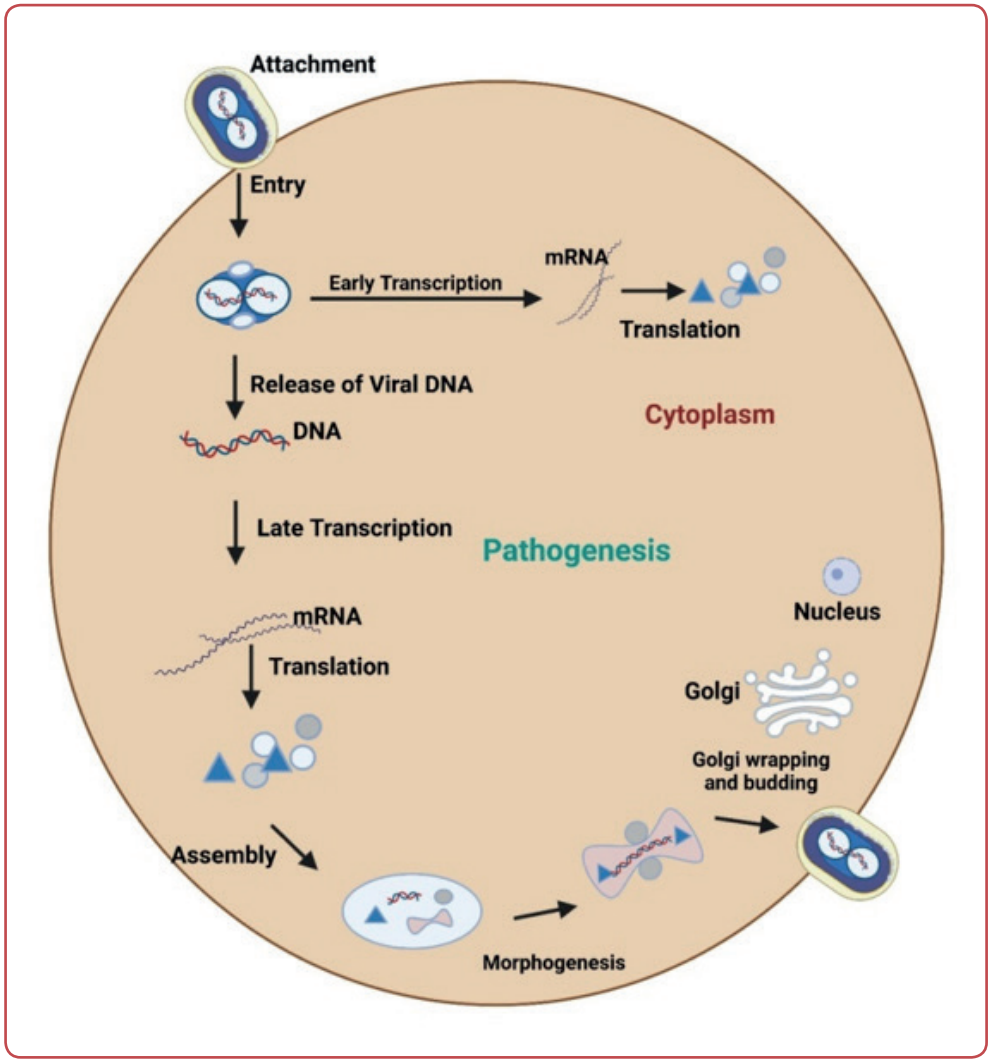

Figure 5: Pathogenesis of monkeypox virus

proteins increase the generation of neutralising antibodies and initiate complement reactions.[72] Furthermore, these exposed surface proteins help immune cells recognise and neutralise the Mpox virus. Extracellular enveloped virions, on the other hand, possess an additional lipid membrane coating which improves intracellular dissemination. The lipid membrane's lipid rafts are a means by which the pox virus can infiltrate host cells and one of the key elements in lipid raft maintenance is cholesterol.[73] A well-known antibiotic for treating fungal infections, amphotericin B, can trap cholesterol within the membranes of host cells, compromising the lipid raft's reliability and possibly preventing the spread of the Mpox virus.

Furthermore, by adjusting cellular cholesterol levels, cholesterol-lowering medications like statins and PCSK9 inhibitors may have antiviral action.[74] The mpox virus binds to injured skin and mucosal membranes because these areas have high glycosaminoglycan concentrations. For host cells, they act as the main attachment receptors. The Mpox virus enters host cells through interactions with glycosaminoglycans through extracellular wrapped virion particles. Marine sulphated polysaccharides are naturally occurring glycosaminoglycan analogues that adhere to the surface of host cells competitively, blocking the Mpox virus's ability to connect and enter. Since the Mpox virus does not yet have specific receptors on the host cell's membrane, several envelope proteins that are essential to the virus's invasion of host cells may make promising targets for the creation of anti-Mpox virus medications. With the help of surface plasmon resonance technology, eight marine sulphated polysaccharides have been examined for their potential for binding the A35R surface protein found in the envelope of the Mpox virus. The results of the study showed that a few

sulphated polysaccharides have anti-Mpox virus activity and competitive binding effects.[75]

In a different investigation, Li et al injected recombinant A35R protein into BALB/c mice and isolated the A35R immune serum, which demonstrated strong neutralising efficacy against two varieties of extracellular wrapped virions of the vaccinia virus.[76] Furthermore, whole-genome sequencing has discovered several intracellular mature virions surface membrane proteins, such as I5L, E8L, and A43R. These proteins may aid in the Mpox virus's entrance into host cells through receptor and membrane fusion. Even though the precise ways in which these proteins interact with the host are not entirely understood, these proteins may be used as targets in the future in the search for an anti-Mpox virus. To fully understand the unique functions of these proteins in Mpox virus infection, more investigation is required.[63] Researchers are currently working to disrupt the viral genome's RNA or DNA synthesis to develop anti-Mpox medications.[77] Chemical substances known as nucleoside analogues are those whose structures resemble those of nucleosides found in nature. By terminating the synthesis of DNA or RNA chains, these medications interrupt the replication process by binding with viral DNA or RNA polymerase competitively. Owing to their capacity to impede viral replication, these medications frequently display extensive antiviral efficacy.[78]

Abundant investigations have been made in the development of pre-stimulated macrophage-like biomimetic nanoparticles based on an aggregation-induced luminescence agent for dual-mode imaging and killing of the Mpox virus. When exposed to an 808 nm laser, the AIE molecule's type I photodynamic and photothermal capabilities can successfully kill the Mpox virus. It is also capable of achieving photothermal imaging and fluorescence of Mpox lesions, allowing for Mpox monitoring. More significantly, this treatment approach efficiently stops the spread of the Mpox virus, which is crucial for averting the Mpox epidemic.[79]

Cidofovir is a non-cyclic monophosphate nucleoside analogue that exhibits robust antiretroviral effects *in vivo* (Mpox virus, 5 mg/kg, intraperitoneal injection; Mpox virus, 5 mg/kg, human, intravenous) as well as *in vitro* (effective concentration half maximal (EC50) = 2.52 µg/mL, Selectivity index (SI) = 15 in human embryonic lung cells).[80] The well-known nucleoside analogue ribavirin prevents the synthesis of viral nucleotides, which in turn prevents viral replication and spread. It is effective against several DNA and RNA viruses, including the Mpox virus, with broad-spectrum antiviral properties.[81] As a result, scientists are actively working on creating new nucleotide analogues, including Sophie et al.'s groundbreaking guanosine analogue KAY-2–41. These analogues show antiviral solid activity against VACV both *in vivo* (VACV-WR, 50 mg/kg, mice, intraperitoneal injection) and *in vitro* (VACV-WR, EC50 = 0.8 µM, SI = 18, in human embryonic lung cells), they continue to work against strains that are resistant to cidofovir.[82]

Finding medications with novel mechanisms of action may be able to address the issue of drug resistance. By preventing the synthesis of actin tails, PA104 inhibited the formation of extracellular virus particles and viral propagation. Its mode of action was not the same as Tecovirimat's. Notably, PA104 has proven to be able to prevent Tecovirimat-resistant VACV strains from replicating *in vitro*.[83]

Vaccination

Only the second and third generations of the smallpox vaccine are now licensed, despite the fact the vaccination went via three generations of medical advancements: The live, nonreplicating vaccination I*mvanex* (also known as *Jynneos or Imvamune*; *Bavarian Nordic*, Hellerup, Denmark) and the replication-competent smallpox vaccine A*CAM2000*.[84] These can be applied in two ways: either after exposure (Ideally, four days after exposure) to enhance outcomes of infection or illness or before contact to protect individuals from infection and disease who are most vulnerable.[85] Live, unattenuated vaccinia virus is used in first-generation vaccinations, such as *Dryvax* from *Wyeth Laboratories* (since merged with *Pfizer*), Madison, NJ, USA. An analysis of surveillance data on monkeypox transmission from person to person in Africa demonstrated its efficacy in preventing the disease.[86]

A significant decrease in the incidence of secondary attacks (7.5 % vs 1.3 %) was linked to vaccination among the 2278 household contacts that took part in the research. Because first-generation vaccinations were produced with unsanitary practices that would prevent them from

being licensed in the modern era, they were discontinued. Replication-competent *ACAM2000* is a second-generation vaccine that was created through a single *Dryvax* clonal viral isolate which showed less neurovirulence in research involving animals.[87, 88] Immunogenicity testing proved that it was not superior to *Dryvax*, and clinical trials showed an identical safety profile.[89] Because *ACAM2000* is contagious, it should not be used for immunocompromised individuals, people with skin disorders, pregnant women, or individuals having underlying cardiac conditions because it can have dangerous side effects, including encephalitis, dermatitis vaccinatum and progressing *vaccinia*.[85] The description of these approved vaccines against the monkeypox virus is depicted in Table 2.

The tecovirimat small-molecule virus inhibitor (also referred to as *TPOXX, ST-246*) works effectively in both *in vitro* and *in vivo* against orthopoxviruses, including vaccinia virus, camelpox virus, cowpox virus, mousepox virus, variola viruses and monkeypox virus.[91] By keeping viruses from exiting infected cells, tecovirimat inhibits the spread of viruses inside the human body by targeting the VP37 protein.[92] 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. Strong antiviral efficacy was demonstrated by tecovirimat, with an EC50 range of 0.01 to 0.07µM.[93, 94] Numerous investigations have revealed that the VP37 protein is crucial for encasing intracellular mature viruses inside the membrane produced through the Golgi apparatus to create enveloped viruses.[95, 96]

An FDA-approved drug called vaccine immune globulin administered intravenously is employed to treat side effects following smallpox vaccines, including progressive *vaccinia*, *dermatitis vaccinatum*, severe generalised *vaccinia* and aberrant infections (excluding isolated keratitis) triggered by the vaccinia virus. A sterile solution known as vaccine immune globulin is composed of high titers of IgG antibodies produced by individuals in good health who were earlier immunised against the live *vaccinia* virus.[97] In an outbreak, the administration of *vaccinia* immune globulin for the treatment of monkeypox is approved by the CDC. According to several research studies, individuals treated for *Orthopoxvirus* infection got intravenous vaccination immune globulin.[98, 99] Nevertheless, information regarding the efficiency of vaccination towards monkeypox virus infection is lacking. For extreme circumstances, doctors might think about utilising it. After exposure to the monkeypox virus, smallpox immunisation is not recommended for individuals with a significant impairment in T cell function, for whom the vaccinia immune globulin is also appropriate for prophylactic usage.

The altered, replication-deficient vaccine Ankara is the source of *Imvanex*, a third-generation vaccination. Although results about the clinical efficacy of monkeypox in humans remain awaited, the vaccine produces significant humoral and cellular immune responses in a non-human primate model, in addition to clinical defence against severe diseases and death rates.[100] Overall peak neutralising antibody titres in human volunteers following two doses of a modified vaccinia Ankara vaccination outcomes are comparable to those after one single *ACAM2000* dosage. However, no severe side effects were observed throughout clinical studies.[101] However, one study reported lower levels of neutralising antibodies specific to monkeypox.[102] These vaccines can be given to immunocompromised people and have an enhanced safety profile because of their attenuated pheno-

Table 2: Description of approved vaccines for the management of monkeypox virus[90]

Variables	*ACAM2000*	*IMVANEX (JYNNEOS)*
Recommended population	18 years or older	18 years or older
Route of administration	Percutaneous (scarification) using multiple puncture technique	Subcutaneous injection (preferred deltoid muscle)
Dosage	Single dose (0.0025 mL)	2 dose-regimen (0.5 mL) given 4 weeks apart
Local complications	Pain, erythema, swelling, pruritus	Pain, swelling, redness, induration, itching
Systemic complications	Fatigue, feeling hot, malaise, rigors, decreased exercise tolerance	Myalgia, fatigue, headache, chills, nausea
Use in children < 18 years of age	Not recommended	Only for post-exposure prophylaxis (given subcutaneously)
Booster dose	Every 3 years for high-risk population	

type. The modified third-generation *vaccinia* Ankara vaccinations are administered subcutaneously in two dosages, approximately four weeks apart. However, with a lack of vaccination supply, several nations have approved intradermal administration in people older than 18, which necessitates one-fifth of the subcutaneous route's volume.[103, 104]

Intradermal delivery is supported by extrapolations with other infections in which it increases immunogenicity and phase 2 trials showing similar antibody responses for the two modified vaccinia Ankara administration routes.[105] Some nations have started using intradermal single-dose delivery to reach greater populations. Men who have intercourse with other men are most likely to contract monkeypox, hence vaccination campaigns targeting them have received the greatest attention in recently impacted nations. Vaccines are mostly given in North America and Europe, but vaccines are not yet available in African nations. Despite the emphasis placed on increasing vaccine coverage in African nations by global alliances like GAVI, the Vaccine Alliance, or The Global Fund to Fight AIDS, Tuberculosis and Malaria, high-income countries have thus far controlled the supply of vaccines.[106]

Conclusion

Viruses are well-known microbes that can seriously infect humans. Since pox viruses may infect birds, insects, mammals and reptiles, they are not a novel threat. Monkeypox, or mpox, is reemerging, which raises serious concerns about global health and may be a sign of a future pandemic. Recent data indicates that the comeback of this virus might have been facilitated by a decrease in human immunity. Since samples from the excreta have been found to contain monkeypox viral DNA, it is crucial to raise knowledge of health hygiene in underdeveloped nations to stop the virus from spreading. All facets of society should also be extensively informed about pandemics and related illnesses, as well as how to treat them. The public health community has to prioritise efforts to stop the spread of mpox and acknowledge the growing risk it poses. To prevent the spread of the disease from person to person, healthcare professionals caring for afflicted people need to be extremely cautious. The urgent necessity of the hour is the development and distribution of vaccinations and antiviral drugs specifically targeted against MPXV. It is advised to have the smallpox vaccination as a preventative measure against monkeypox. Monkeypox containment and response tactics, such as immunisation and education, are essential for reducing the disease's transmission and effects. Sustaining public health and averting future outbreaks will need ongoing study and international collaboration.

Ethics

This study was a secondary analysis based on the currently existing data and did not directly involve with human participants or experimental animals. Therefore, the ethics approval was not required in this paper.

Acknowledgement

Authors are thankful to their parent institutions for the facilities.

Conflicts of interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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