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Monkeypox: A resurgent zoonotic threat in the post-pandemic era

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Abstract

Monkeypox (mpox), once considered a rare zoonotic infection limited to parts of Africa, has re-emerged over the past few years as a significant global health concern. Since the 2022 outbreak, cases have been reported in over 100 countries, with both Clade I and Clade II viruses contributing to sustained human transmission. The disease, caused by the *monkeypox virus* (MPXV), has drawn attention not only for its clinical resemblance to smallpox but also for its potential to spread through close contact and cause complications in vulnerable groups. This review highlights the evolving epidemiology, clinical features, and phylogeny of the virus, along with current strategies for diagnosis, prevention, treatment, and vaccination efforts, antiviral options, and global surveillance challenges. With over 140,000 confirmed cases worldwide as of mid-2025, mpox has exposed gaps in outbreak preparedness, vaccine equity, and public health coordination. Addressing these issues through a One Health approach and integrated global action is key to containing mpox and preventing future zoonotic threats.

Keywords: *Monkeypox virus*, zoonotic disease, *Orthopoxvirus*, surveillance, vaccination

1. Introduction

The global outbreak of *monkeypox* in 2022, now officially referred to as mpox by the World Health Organization (WHO), brought renewed attention to a once-neglected zoonotic disease. This outbreak extended well beyond the historically endemic regions of Central and West Africa, leading to confirmed cases in over 100 countries across all inhabited continents and triggering widespread concern among public health authorities [17, 66, 73].

Mpox is a zoonotic infection caused by the *monkeypox virus* (MPXV), a double-stranded DNA virus classified under the genus *Orthopoxvirus* within the family Poxviridae [70]. It was first isolated in 1958 from cynomolgus monkeys used in research in Denmark [67], and the first human case was identified in 1970 in the Democratic Republic of Congo [51].

Mpox was once considered a rare, self-limiting infection, but this perception has shifted [65]. In the past several decades, sporadic outbreaks have been increasingly reported, both within endemic African regions and in non-endemic countries, often linked to the international trade of exotic pets or human travel. A notable example was the 2003 U.S. outbreak caused by imported rodents from Ghana, which infected pet prairie dogs and subsequently humans [29, 58]. The increased frequency of outbreaks over the last 40 years is thought to result from a combination of factors. One of the most significant is the global cessation of smallpox vaccination, which previously conferred cross-protection against mpox [5, 60]. As a result, a large proportion of the global population, particularly those born after the 1980s, lacks immunity to *Orthopoxviruses*. Other contributing elements include rising human population density, urbanization, climate change, environmental encroachment into wildlife habitats (e.g., deforestation), and increased international mobility, all of which enhance human exposure to infected animals [27, 42].

The world was still recovering from the COVID-19 pandemic when mpox emerged as another threat with pandemic potential. Although human-to-human transmission of mpox is generally less efficient, clusters of infections, especially among close contacts, have shown the virus's ability to spread within specific communities, including vulnerable groups like children, immunocompromised patients, and pregnant women [64, 68].

Moreover, due to its genetic relation to smallpox, effective vaccines and antiviral options are available, though their global access and deployment remain uneven^[43].

Between January 1, 2022, and March 31, 2025, the WHO reported approximately 137,892 confirmed mpox cases across 127 countries, including 315 to 343 deaths^[76]. In response to the resurgence of clade I (Ia/Ib) viruses, particularly in the Democratic Republic of the Congo, the WHO declared a new Public Health Emergency of International Concern (PHEIC) in October 2024^[75]. According to the 53rd WHO multi-country outbreak report released in May 2025, clade I continues to circulate in Central and Eastern Africa, while clade II remains active in 122 countries, underscoring the ongoing global threat. Recent CDC updates (June-July 2025) also highlight travel-associated cases involving clade I and II viruses, including imported infections in India, Australia, and Pakistan. In the United States, the majority of clade II mpox infections have occurred among unvaccinated or partially vaccinated individuals, despite the availability of the JYNNEOS vaccine^[10].

As the epidemiology of mpox continues to evolve, robust surveillance and early detection systems are essential tools to track transmission patterns and prepare for potential surges. With continued sporadic outbreaks reported into 2024 and 2025, healthcare professionals must stay updated on the clinical management, prophylaxis, and infection control practices for mpox^[7, 11, 66]. A coordinated global response will be key not just to containing this disease, but to integrating it into broader frameworks for pandemic preparedness and One Health surveillance. This review provides a comprehensive overview of the *monkeypox virus* with particular focus on its zoonotic importance, evolving epidemiology, and implications for global health security.

2. History of MPOX

The *monkeypox virus* (MPXV) was first identified in 1958, when outbreaks of a pox-like illness were observed among captive monkeys used for research in Denmark. However, its relevance as a human pathogen wasn't recognized until 1970, when the first confirmed human case was diagnosed in a 9-month-old child in the Democratic Republic of the Congo (then Zaire). The child, initially suspected to have smallpox, tested positive for MPXV marking the beginning of documented human mpox cases^[51, 67].

Significant outbreaks followed in Central Africa. One of the earliest large-scale events occurred between February 1996 and May 1997, involving over 170 suspected cases across 13 villages in Katakombé, DRC^[14]. This outbreak was characterized by frequent human-to-human transmission, with epidemiological investigations estimating that more than 70% of cases were likely acquired through contact with infected individuals rather than animals^[39, 74].

The disease gained international attention on May 24, 2003, when mpox was identified in the United States for the first time. A 3-year-old girl in Wisconsin developed fever and cellulitis after being bitten by a pet prairie dog. Subsequent investigations linked the case to a shipment of African rodents imported from Ghana, which had been housed with the infected prairie dog. The outbreak ultimately affected 47 confirmed human cases across six U.S. states, Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin and was attributed to animal-to-human transmission via contact with exotic pets^[8, 58, 62, 70].

After sporadic reports in the 2000s, a major resurgence occurred in Nigeria in 2017, where more than 200 confirmed and suspected cases were reported. This marked the largest outbreak in West Africa since the 1970s and demonstrated both zoonotic and human-to-human transmission pathways^[73, 77].

The global landscape shifted dramatically in May 2022, when an imported case of mpox was detected in the United Kingdom in a traveler returning from Nigeria. Within weeks, mpox was reported in multiple non-endemic countries across Europe, the Americas, and Asia. On July 23, 2022, the World Health Organization officially declared the outbreak a Public Health Emergency of International Concern (PHEIC) its highest level of alert^[73]. By October 2022, more than 90 non-endemic countries had reported cases, with 77,000+ confirmed infections and several related deaths^[59]. The situation continued to evolve through 2023 and 2024, with cases becoming sporadic but persistent in certain regions. In October 2024, the WHO declared a second PHEIC, this time focused on the Democratic Republic of the Congo, due to a large outbreak involving the more virulent Clade I (formerly Congo Basin lineage). This clade was responsible for sustained transmission and increased mortality, prompting urgent global attention^[71].

As of March 31, 2025, WHO reports indicate that over 137,000 confirmed cases of mpox have been recorded worldwide since 2022, across 127 countries, with 315 to 343 reported deaths. The 53rd WHO situation report (May 2025) notes continued Clade II activity globally, alongside Clade I endemic transmission in Central and Eastern Africa, reinforcing mpox's status as a resurgent zoonotic threat with pandemic potential^[9, 10, 72].

3. Phylogeny of MPOX Virus

The *monkeypox virus* (MPXV) is a member of the genus *Orthopoxvirus* in the family *Poxviridae*, which includes several other notable viruses like variola virus (the cause of smallpox), cowpox virus, and vaccinia virus. All members of this genus are large, double-stranded DNA viruses that infect a wide range of vertebrate hosts, including mammals, birds, reptiles, and insects^[34, 48].

MPXV is part of the *Chordopoxvirinae* subfamily and has evolved a broad host range, allowing it to persist in wild animal populations, particularly rodents and occasionally spill over into humans^[66]. A defining feature of *Orthopoxviruses* is their strong immunological cross-reactivity: infection or vaccination with one virus in the group often provides some degree of protection against others^[18, 64].

Monkeypox virus (MPXV) has a wide range of potential host organisms, which has allowed it to circulate in wild animals for a prolonged period of time while sporadically causing human disease through spill-over events^[66]. *Orthopoxviruses* (OPXV) exhibit immunological cross-reactivity and cross-protection, and infection with any member of the genus confers some protection from infection with any other members of the same genus^[18, 63].

Under electron microscopy, MPXV appears as a brick-shaped or ovoid particle, measuring around 200-250 nm in size. Its surface is covered with tubular filaments, and it contains a characteristic biconcave core^[65]. The MPXV genome is a linear, double-stranded DNA molecule of ~197 kilobases, encoding approximately 200 genes. Core "housekeeping" genes are located centrally in the genome

and are well conserved across *Orthopoxviruses*, while genes involved in host interaction and immune evasion are found near the terminal regions and tend to be more variable [28, 78]. Phylogenetic studies have shown that MPXV exists in two major genetic clades, each with distinct geographic and clinical features:

- Clade I (previously called the Congo Basin clade), which is more virulent and transmissible
- Clade II (West African clade), further subdivided into Clade IIa and Clade IIb, which are less severe in humans [30, 44].

The strain responsible for the 2022-2025 global outbreak is classified as Clade IIb, sometimes referred to as human MPXV (hMPXV). Genomic surveillance shows that this sub-lineage likely diverged from West African strains but has acquired adaptations favouring increased human-to-human transmission [66, 75].

Importantly, many of the genes in the MPXV genome are non-essential for viral replication in vitro but play crucial roles in modulating host immune responses in vivo, often acting as virulence factors [28, 48]. The virus replicates

entirely in the cytoplasm of host cells, an unusual trait for DNA viruses, using complex viral machinery to complete its life cycle [48]. Entry into host cells is facilitated by interactions between the viral envelope and glycosaminoglycans (GAGs) on the host cell surface, although the exact receptors remain partially undefined [21, 48]. Once inside, the virus produces both intracellular mature virions (IMVs) and extracellular enveloped virions (EEVs), enabling efficient spread within and between hosts.

There is some evolutionary evidence suggesting that variola virus (smallpox) may have originated from a rodent *poxvirus* several thousand years ago, highlighting the long-standing potential of *Orthopoxviruses* to adapt and emerge as human pathogens [16]. With global smallpox vaccination discontinued in the 1980s, a large segment of the population now lacks pre-existing immunity to these viruses, increasing vulnerability to infections like mpox [60, 63]. This genetic plasticity, combined with increased human-animal interaction, underscores the risk of future adaptive mutations that could enhance the transmissibility or severity of MPXV in humans.

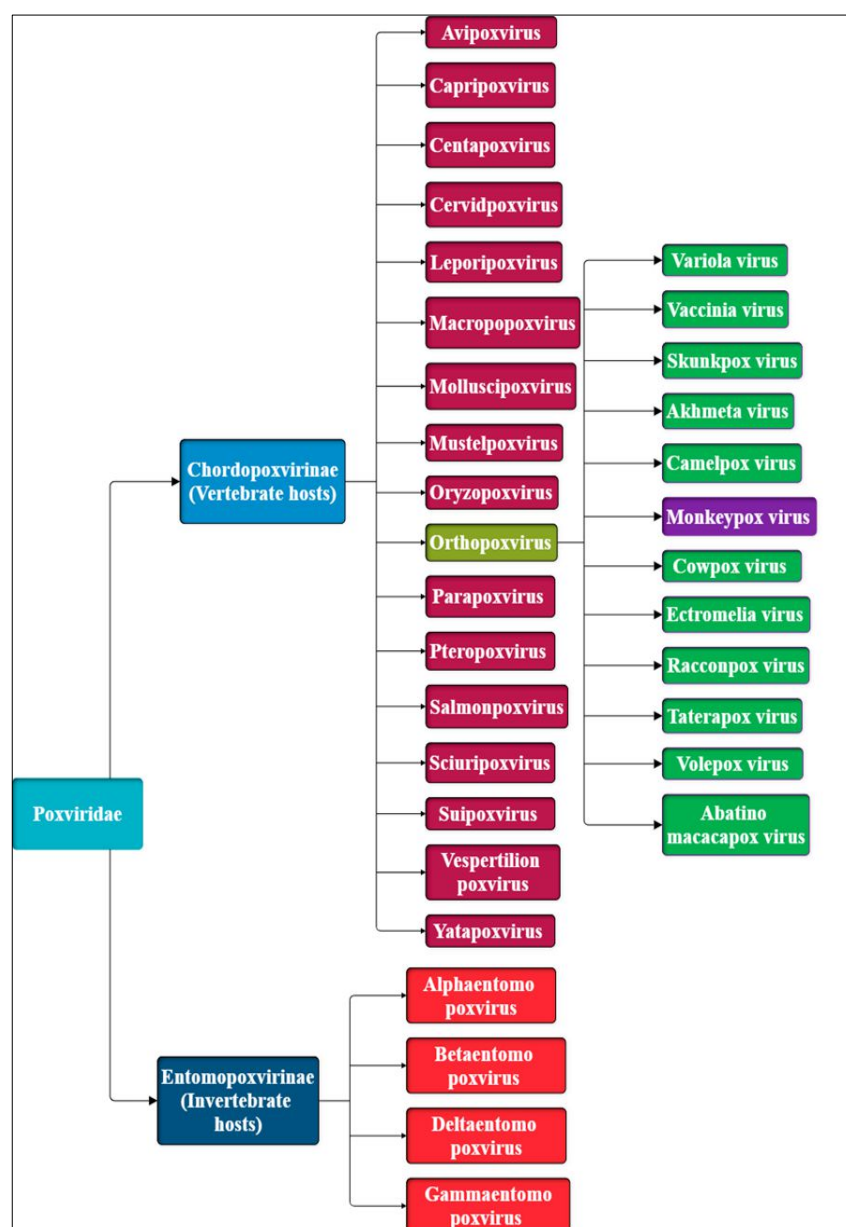


Fig 1: Taxonomic classification of the *Poxviridae* Family

4. Epidemiology and Pathogenesis

Mpox was first identified in 1958, when an outbreak of a pox-like illness occurred among captive Asian monkeys (*Macaca fascicularis*) transported from Singapore to a research facility in Copenhagen, Denmark [54]. Although the name suggests a primate origin, the actual reservoir hosts are believed to be African rodents. Today, mpox is considered a zoonotic disease endemic to forested regions of Central and West Africa, with intermittent outbreaks among humans [19]. Phylogenetic and epidemiologic studies have identified two genetically distinct clades of MPXV: the West African clade and the Congo Basin (Central African) clade. These clades differ in both severity and transmissibility. The Congo Basin clade (now known as Clade I) has a higher case fatality rate (CFR) of approximately 10.6%, while the West African lineage (Clade II) generally causes milder disease with a CFR around 3.6% [11].

Initial attempts to understand mpox pathogenesis date back to 1969. A major challenge in studying disease progression has been the lack of suitable animal models that accurately mimic human infection. Common laboratory animals like guinea pigs and hamsters are often non-susceptible or fail to reproduce the full clinical spectrum [2, 31, 37].

MPXV is believed to be stable on surfaces (fomites), and only a low infectious dose may be needed to cause disease. A retrospective analysis of 338 mpox cases in the DRC during the 1980s found that 72.5% of infections were traced to animal sources, while the remaining 27.5% likely resulted from human-to-human transmission [38].

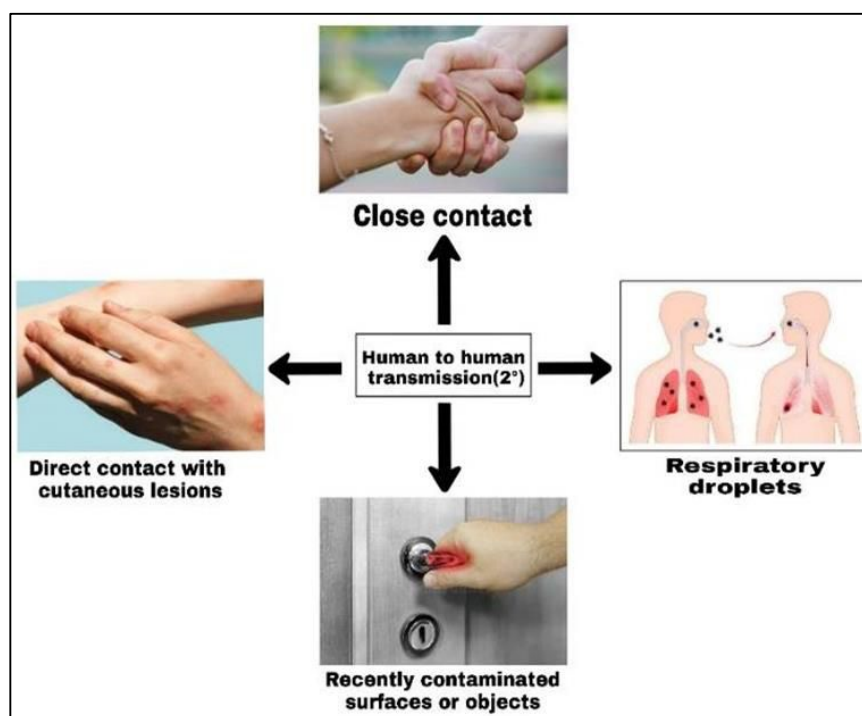
However, sustained person-to-person transmission has historically been limited. *Seroprevalence* surveys suggest that up to 28% of infected individuals may be asymptomatic, potentially contributing to occasional silent spread [28, 55]. Risk factors for transmission include close physical contact, such as sleeping in the same bed or sharing utensils. Respiratory droplets may also play a role in transmission during prolonged face-to-face contact [6, 38, 52]. Vertical transmission from mother to foetus has been reported, leading to congenital infections. Although close

physical contact is a clear route of transmission, the possibility of sexual transmission remains under investigation [73]. Environmental risk factors, such as sleeping on the ground, bushmeat hunting, and living near forests, also increase the risk of animal-to-human transmission [22, 25, 40].

Animal-to-human transmission usually occurs via direct contact with infected animals or their bodily fluids, including saliva, respiratory secretions, and skin or mucosal lesion exudates. Viral shedding in faeces may also contribute to environmental contamination [36]. In regions with limited food access, hunting and consumption of small mammals have been implicated as a major risk factor [36].

MPXV enters the human body through oropharyngeal, nasopharyngeal, or intradermal routes, where it initially replicates at the inoculation site and then spreads to local lymph nodes [37]. After an incubation period of 1 to 3 weeks, early symptoms appear, including fever, chills, sore throat, backache, headache, malaise, and lymphadenopathy [15, 70]. These are followed by the appearance of a rash, typically on the face and extremities. The lesions progress from macules to papules, vesicles, pustules, and finally scabs, which resolve in 2-4 weeks [6].

Histologically, lesions are characterized by acanthosis (epidermal thickening), necrosis, spongiosis, and inflammatory cell infiltration. Blister formation and degeneration of infected cells are common features [69]. Complications can include secondary bacterial infections, bronchopneumonia, sepsis, encephalitis, and ocular involvement, which may lead to blindness and corneal scarring. The most frequent long-term outcome is pitted scarring at the site of healed lesions [47]. Severe disease is more frequently observed in young children, immunocompromised individuals, and pregnant women, who are more susceptible to pneumonia, pharyngeal abscesses, and encephalitis [68]. Patients remain infectious until all lesions have crusted and scabs have fallen off, revealing a new layer of skin. The case fatality rate for mpox is estimated to range from 0% to 11%, depending on clade, access to healthcare, and host factors [5, 73].



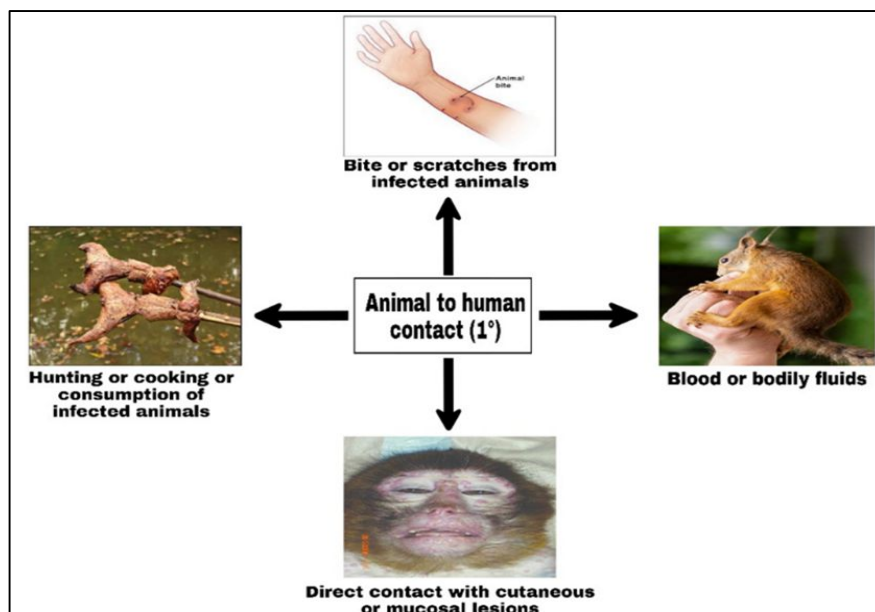


Fig 2: Transmission pathways of the *monkeypox virus*

• Clinical Features

The clinical presentation of mpox closely resembles a milder form of variola virus infection (smallpox), although with some distinguishing features [41]. It can affect both adults and children, and typically progresses through three distinct phases: the incubation, prodromal, and eruptive (skin lesion) stages [15, 35, 39, 47, 55].

• Incubation Phase

The incubation period ranges from 5 to 21 days, during which the virus replicates without causing symptoms [24, 30, 73].

• Promodoral Phase

The incubation period ranges from 5 to 21 days, during which the virus replicates without causing symptoms. This is followed by the prodromal phase, usually lasting 1 to 5 days, characterized by nonspecific systemic symptoms such as fever, headache, chills, sore throat, myalgia, and

pronounced fatigue. A defining clinical hallmark is lymphadenopathy, which occurs early and may be unilateral or bilateral, affecting cervical, axillary, or inguinal lymph nodes [1, 32, 50, 56]. This feature is particularly important in differentiating mpox from diseases with similar rash patterns, such as varicella or measles.

• Eruptive Phase

A rash typically appears within one to three days after fever onset. It follows a centrifugal distribution, beginning on the face or oral mucosa and spreading to the extremities, trunk, palms, and soles. Lesions evolve in a synchronous progression from macules to papules, vesicles, pustules, and finally crusts that slough off over a two to four-week period, often leaving behind pitted or depigmented scars [2, 30, 50]. In some cases, lesions may appear at different stages simultaneously within the same area, deviating from the classic uniform rash pattern [55].

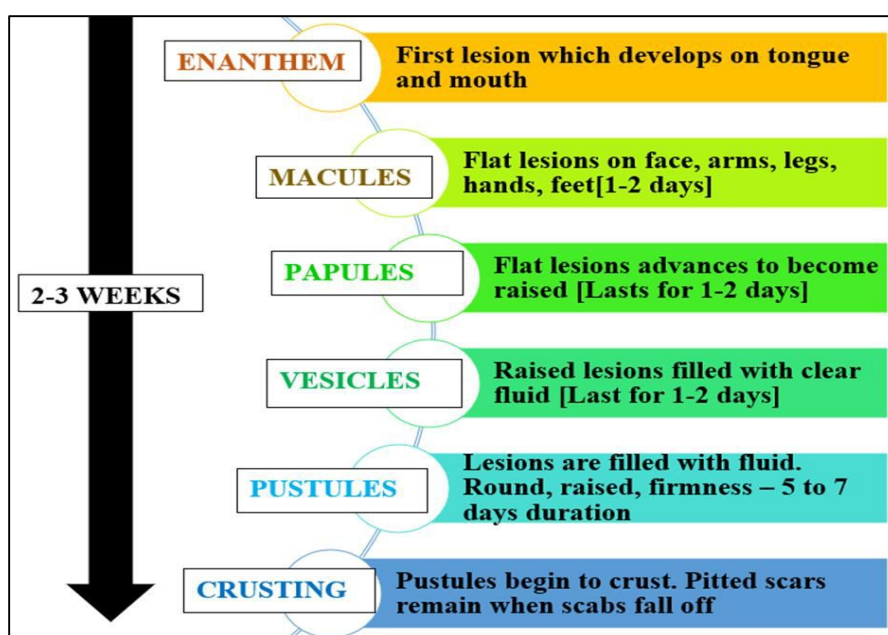


Fig 3: Sequential development of skin lesions in *monkeypox* (MPOX)

• Systemic Findings and Complications

Although generally self-limiting, mpox can lead to complications requiring hospitalization. These may include mucosal ulcers, dysphagia, nausea, vomiting, and adenopathy. Laboratory abnormalities frequently observed include elevated transaminases, hypoalbuminemia, low blood urea nitrogen, leucocytosis, and thrombocytopenia [35, 49, 56, 77].

More severe outcomes such as secondary bacterial infections, bronchopneumonia, sepsis, encephalitis, and ocular complications (e.g., keratitis, corneal ulceration) may occur, particularly in immunocompromised individuals and

children. Permanent pitted scarring is the most common long-term sequela [47, 68]. Patients remain infectious from symptom onset until all lesions have crusted, scabs have fallen off, and new skin has formed [73].

• Clinical Features in Animals

In the 2003 U.S. outbreak, infected prairie dogs presented with signs including respiratory distress, cough, fever, conjunctivitis, inappetence, and skin lesions. Similar symptoms were also observed in infected non-human primates, helping establish animal models for research and zoonotic surveillance [8].

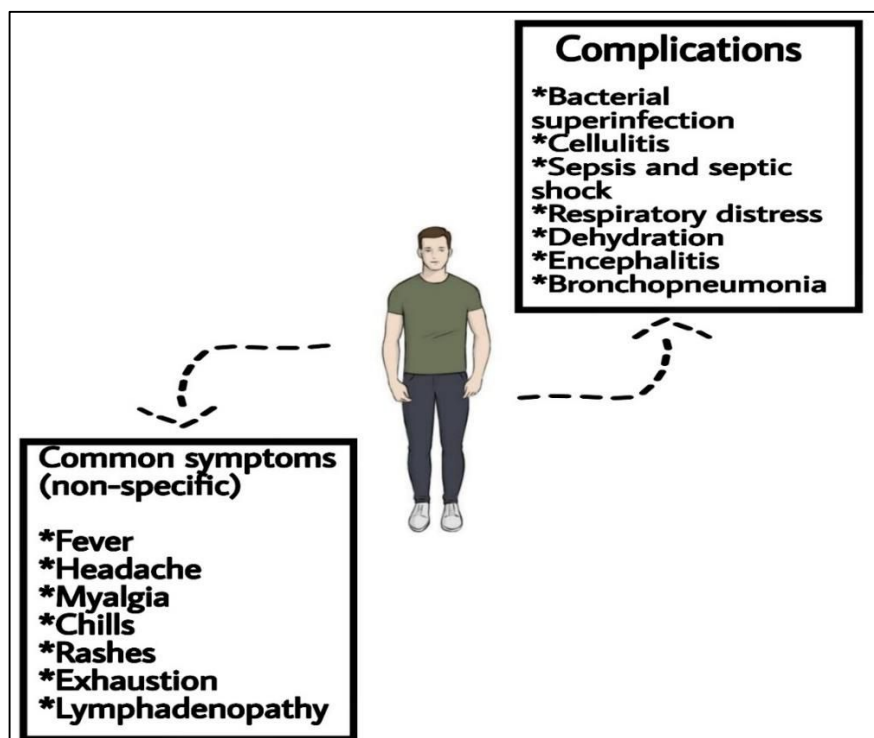


Fig 4: Common symptoms and potential complications associated with *monkeypox* (mpox) infection in humans

6. Diagnosis

The diagnosis of *monkeypox* relies on careful clinical evaluation and a detailed history. Clinicians should inquire about risk factors such as recent travel to endemic areas, contact with wild animals or exotic pets, and close contact with known *monkeypox* cases. Characteristic clinical features (like fever, rash, and lymphadenopathy) should raise suspicion, but definitive diagnosis is made via laboratory testing, typically by detecting viral DNA using a polymerase chain reaction (PCR) assay on lesion samples [64]. A high index of suspicion is especially important given the atypical presentations observed in the 2022 outbreak, for example, some patients presented with genital or anal lesions and minimal prodromal symptoms, which differ from the classic *monkeypox* presentation seen in prior endemic outbreaks. When evaluating an acute rash illness with nonspecific symptoms (fever, headache, muscle aches, fatigue, etc.), *monkeypox* should be included in the differential diagnosis alongside diseases like chickenpox, measles, and other vesicular rashes. One distinguishing feature of *monkeypox* is the presence of lymphadenopathy (swollen lymph nodes) during the early prodromal stage, which is not typically seen in varicella (chickenpox) or variola (smallpox) infections [47]. Noting this finding can aid

in clinical differentiation of *monkeypox* from other rash-causing illnesses.

7. Prevention and Control

• Isolation and Infection Control Guidelines

Preventing *monkeypox* infection involves both public health measures and individual precautions. It is advisable to avoid contact with potentially infected animals, especially rodents or primates that appear sick or are found dead in regions where *monkeypox* is known to circulate. Likewise, avoid handling materials such as bedding or clothing that have been in contact with infected animals [7]. If a person is suspected or confirmed to have *monkeypox*, they should be isolated from others to prevent spread of the disease. The patient should ideally be placed in a single-person room; they should wear a mask, and their lesions should remain covered [26].

Close contact behaviours that facilitate transmission (such as sharing a bed, room, or eating utensils with an infected person) must be avoided. Strict hand hygiene is essential—washing hands thoroughly with soap and water or using an alcohol-based sanitizer after contact with infected people or animals can reduce the risk of transmission. Isolation precautions should be maintained until the infectious period has fully passed, meaning all lesions have crusted over, the

scabs have naturally separated, and a fresh layer of healthy skin has formed ^[64].

• Personal Protective Practices

For healthcare workers, consistent use of personal protective equipment (PPE) including gloves, masks (preferably N95), eye protection, and gowns is recommended when interacting with suspected or confirmed cases ^[74]. Updated interim guidance in 2024 reaffirmed the importance of contact and droplet precautions, with airborne precautions advised during aerosol-generating procedures ^[10].

• Public Health Interventions and Surveillance

In addition to individual-level precautions, public health interventions are essential to contain outbreaks. Contact tracing, ring vaccination, and targeted awareness campaigns have helped limit community spread in recent outbreaks ^[20]. Enhanced genomic surveillance has also improved understanding of clade-specific transmission patterns, including sustained circulation of Clade IIb in non-endemic regions and emergence of Clade I in DRC and Central Africa ^[9, 71].

Long-term *monkeypox* control requires robust surveillance, especially in endemic regions with weak health infrastructure. Investment in diagnostic capacity, risk communication, community education, and laboratory networks are crucial. Over the long run, comprehensive strategies to reinforce health system resilience will enhance the capacity for early detection and containment, thereby helping to avoid large-scale outbreaks in the future ^[75].

8. Vaccination and Therapeutics

• Smallpox-Derived Vaccines

Evidence from past research suggests that prior smallpox vaccination confers significant cross-protection against *monkeypox*. Historical data indicate that the smallpox vaccine is about 85% effective in preventing *monkeypox* infection ^[73]. Individuals who have been vaccinated for smallpox may experience milder illness if they do contract *monkeypox* ^[27, 31]. This protective effect is attributable to the close genetic relationship between the smallpox (*Variola*) virus and the *monkeypox virus*; in fact, smallpox immunization has been shown to protect laboratory animals from lethal *monkeypox* challenges ^[13]. However, because routine smallpox immunization was discontinued worldwide in the early 1980s, a growing portion of the population has no immunity to either smallpox or *monkeypox*. This loss of population-level immunity is thought to contribute to the increased susceptibility to *monkeypox* outbreaks in recent decades ^[62]. Ongoing research is needed to determine how well previous smallpox vaccines or newer vaccines might control the current *monkeypox* outbreaks ^[9].

• ACAM2000 and JYNNEOS (MVA-BN)

There are two vaccines currently approved for *monkeypox* prevention in high-risk individuals.

- ACAM2000 is a second-generation live vaccinia virus vaccine derived from the original smallpox vaccine, given via percutaneous inoculation. The vaccine produces a local lesion indicating viral replication, which can potentially spread to others. It is contraindicated in immunocompromised individuals, pregnant women, and those with eczema due to the risk of serious adverse events such as myocarditis ^[64].

- JYNNEOS (also known as Imvamune or Imvanex) is a third-generation, non-replicating modified vaccinia Ankara (MVA) vaccine, approved by the FDA and EMA. It is safe for immunocompromised individuals and is administered as a two-dose series, 28 days apart ^[23]. JYNNEOS is currently the preferred vaccine for outbreak control in most non-endemic settings.

• Antivirals

Tecovirimat (TPOXX), originally developed for smallpox, has shown promise in treating mpxv by inhibiting the VP37 envelope protein needed for viral egress. It has been granted emergency use authorization in multiple countries during outbreaks ^[52]. Brincidofovir, another antiviral, has been explored for use in *Orthopoxvirus* infections but with limited data on efficacy and notable gastrointestinal side effects ^[1, 58].

• Vaccine Policies and Prophylaxis

For pre-exposure prophylaxis (PrEP), vaccination is recommended for individuals at occupational risk, such as laboratory personnel working with *Orthopoxviruses* and designated healthcare workers. The U.S. Advisory Committee on Immunization Practices (ACIP) supports vaccination for these groups based on shared clinical decision-making ^[9].

For post-exposure prophylaxis (PEP), vaccination with MVA-BN within 4 days of exposure may prevent onset of disease; administration within 5-14 days may reduce symptom severity ^[57]. Ring vaccination strategies around confirmed cases have been central to outbreak control efforts.

9. Global health perspective and future directions

Endemic regions, particularly in Central and West Africa, face structural challenges, limited diagnostic capacity, under-resourced healthcare systems, and insufficient vaccine access. In contrast, non-endemic countries face diagnostic unfamiliarity, clinical misrecognition, and misinformation. Global equity in surveillance, diagnosis, and prevention tools remains a significant hurdle.

Monkeypox, as a zoonotic pathogen, highlights the need for a One Health approach that bridges human, animal, and environmental health. Integrated surveillance of animal reservoirs, wildlife trade, and land use patterns is essential. This strategy becomes especially urgent given the increased frequency of zoonotic spill over events linked to deforestation, wildlife trafficking, and urban encroachment ^[24, 56].

Critical research needs include, Better understanding of asymptomatic or subclinical MPOX transmission; studies on vaccine durability and breakthrough infections; Development of broad-spectrum antivirals targeting *Orthopoxviruses*; Evaluation of simplified, scalable diagnostic tools for low-resource settings. Furthermore, International health bodies must also coordinate standardized case definitions, treatment protocols, and vaccine deployment strategies, especially in outbreak-prone countries.

10. Conclusion

Monkeypox reaffirms the threat posed by emerging and re-emerging zoonotic viruses. Although smallpox eradication was a public health triumph, it has also created a gap in

population immunity, leaving many vulnerable to related viruses like mpox. The 2022-2025 outbreak has highlighted both gaps and strengths in our global health framework. As of May 31, 2025, over 140,000 confirmed cases of mpox have been reported across 129 countries, with Clade I transmission persisting in multiple Central and Eastern African nations ^[72]. Although global case numbers have declined from their peak, the risk of resurgence remains high, especially in endemic regions and among unvaccinated populations. Preventing future outbreaks requires a sustained global vigilance, strong surveillance networks, and equitable access to vaccines, diagnostics, and therapeutics. The response to mpox should be integrated into broader pandemic preparedness frameworks, alongside efforts to counter antimicrobial resistance and climate-sensitive diseases. Monkeypox is not merely a rare tropical disease; it is a test case for global epidemic intelligence and response systems. Acting now, with coordinated investment and international cooperation, is essential to contain mpox and mitigate future *Orthopoxvirus* threats.

11. Ethical approval

Not applicable.

12. Conflict of interest

The authors declare that there is no conflict of interest.

13. Author contributions

Conceptualization: KD, AV, NQM; Methodology: NQM; Investigation: NQM; Writing original draft: KD, AV, KMDR; Writing, review and editing: NQM; Visualization: KMDR, Supervision: NQM. All authors have read and approved the manuscript.

14. Data availability

All data are available on reasonable request to the corresponding author.

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