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Comprehensive Review of MPox: Critical Evaluation of Outbreak Trends, Clinical Manifestations, and Therapeutic Approaches

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Abstract

The monkeypox virus (MPV) is the cause of monkeypox, a zoonotic viral illness that has become a major worldwide health issue because of its changing epidemiology, increased human-to-human transmission, and potential for large-scale outbreaks. The disease has mostly been endemic in Central and West Africa since it was first discovered in humans in 1970. The recent epidemics in 2022 and 2024, however, highlight how urgently a thorough grasp of its clinical presentations, diagnostic techniques, and treatment measures is needed. The severity of this illness varies according to the host's immune status, although it usually manifests as fever, lymphadenopathy, and a progressive rash. Immunocompromised people are more susceptible to serious side effects, such as bacterial superinfections, pneumonia, and encephalitis, even though the majority of cases resolve on their own. Men who have sex with men (MSM) were the majority of those infected by the 2022 outbreak, indicating possible sexual transmission. The primary methods of diagnosis are histopathological analysis and polymerase chain reaction (PCR)--based testing that targets conserved MPV genes. Vaccination programs and antiviral medications are essential for controlling outbreaks. The reappearance of monkeypox calls for better public health preparedness, faster diagnostic capabilities, and more surveillance. Future studies should concentrate on tailored antiviral treatments, next-generation vaccinations, and novel diagnostic techniques based on nanotechnology. To minimize

future outbreaks and keep monkeypox from becoming a persistent worldwide danger, a coordinated, interdisciplinary strategy is essential.

Abbreviations

DRC- Democratic Republic of Congo, EMA-, EOC- Emergency Operations Center, FDA- food and Drug Administration, FFP2- filtering facepiece, Monkeypox- monkeypox, MPV- monkeypox virus, MSM- men who have sex with men, MVA- modified vaccinia Ankara, PPE- personal protection equipment, PHEIC- public health emergency of international concern, PCR- polymerase chain reaction, RRT-rapid response team

Keywords: Monkeypox, virus, vaccines, antiviral therapy, orthopoxvirus

Introduction

Monkeypox is a zoonotic viral disease, affecting humans and animals. It was first isolated from primates in the year 1958. Later, the first human case of monkeypox was detected in the year 1970, from the Republic of Congo [1]. Monkeypox virus, a double-stranded DNA virus is similarly related to other viruses of the family *Poxviridae*, *Orthopoxvirus* genus, including variola virus (which causes smallpox), vaccinia virus (the primary component of the smallpox vaccine), and cowpox virus [2]. At the nucleotide level, research has demonstrated that any two orthopoxviruses share 96% of their core genomes [3]. The similarities between these viruses, however, are easiest to comprehend through common clinical aspects of illness. Both smallpox and monkeypox present as fevers and skin lesions that grow from vesicles to pustules, although monkeypox is usually more confined, less severe, and self-limiting. Due to the disease's unexpected worldwide spread outside of historically endemic African countries and the necessity for international cooperation to combat this previously ignored illness, the World Health Organization (WHO) proclaimed monkeypox a Public Health Emergency of International Concern in July 2022 [4]. A study suggests that males are more prone to contract infection than females; this is due to sex steroid hormones that affect infection-resistance genes in addition, to the androgenic inhibiting effect on immunity [5]. The 2022 epidemic often manifests as a systemic sickness with fever, myalgia, and a distinctive rash that includes papules that develop into vesicles, pustules, and crusts in the vaginal, anal, or oral areas. The incubation period for this outbreak is seven to ten days [6]. Additionally, there has been a surge in the occurrence and severity of monkeypox among immunocompromised people, such as those with AIDS. Atypical observations of more than 100 cutaneous lesions, necrotic or treatment-resistant lesions, hemodynamic instability, or subsequent sepsis are among the reports of severe monkeypox in this population [7]. There are now two recognized viral clades: the West African and Central African (Congo Basin) clades. Compared to West African viruses, those from Central Africa are more virulent [8].

The Central African variant of human monkeypox illness was linked to increased viremia, mortality, morbidity, and human-to-human transmission during the 2003 U.S. outbreak [9]. According to reports, the West African haplogroup (4%) has a lower death rate than the central African clade (10%), which is said to be more severe [10].

The objective of this review is to comprehensively study and summarize the available data on monkeypox including epidemiological trends, modes of transmission, characterize the clinical features, diagnostic techniques, treatment strategies, and public health interventions that will aid in the management of this disease during this crucial timeframe.

Epidemiology of Monkeypox

Monkeypox, caused by the monkeypox virus (MPV), is a zoonotic illness that caused widespread concern due to its shifting incidence and transmission patterns. As mentioned earlier, first isolated from laboratory monkeys in Denmark in the late 1950s, it was identified as a human pathogen in the 1970s in the Democratic Republic of the Congo. Ever since, It has generally affected mainly African countries such as Benin, Cameroon, Nigeria, and the Central African Republic. The virus is divided into two clades: Central African (Clade I) and West African (Clade II). It is further divided into subclades with clade I divided into subclades Ia and Ib and clade II divided into subclades IIa and IIb [11,12]. The scientific investigations indicate that the epidemic of 2022 was attributed to clade II, specifically subclade IIb. Since its discovery, the epidemiology of monkeypox has evolved considerably, with Clade I initially being the most common strain, causing recurrent outbreaks in the Democratic Republic of the Congo. Clade II, on the other hand, was very uncommon until its resurgence in Nigeria in 2017, indicating a significant change in the disease's transmission trends. The resurgence of Clade II in Nigeria in 2017 was notable for a significant shift from zoonotic to human-to-human transmission, including potential sexual spread. The 2022 global outbreak, the first significant transmission outside of Africa, resulted in approximately 85,000 confirmed cases in at least over 100 nations. The rise in instances coincided with a decrease in smallpox vaccination rates and the end of vaccination programs that had previously given cross-protection against orthopoxviruses, including monkeypox [11,13–15].

In the year 2003, the United States witnessed its first outbreak. This was seen to have involved over 70 cases in six states and was traced back to pet prairie dogs who had gotten the virus from African rats. It was observed that prairie dogs living with these rodents were the source of transmission. Subsequent occasional instances linked to travel from endemic areas have been documented. For example, in 2021, a monkeypox patient in the United States had recently traveled from Nigeria, highlighting the persistent potential of imported cases. Transmission of monkeypox occurs through various modes. Animal-to-human transmission happens via direct contact with infected animals or bushmeat. Human-to-human transmission can occur through direct contact with infectious sores or body fluids, and indirectly via contaminated materials like clothing or linens. Respiratory secretions may also play a role, though less is known about this route. Other transmission routes include vertical transmission from mother to fetus, and percutaneous inoculation through needlestick injuries or during tattooing [12,16–20].

The 2022 outbreak primarily impacted males who have intercourse with other men (MSM), which contributed to more than 90% of the cases reported [21–23]. The highest prevalence was seen amongst men about 30-40 years old, with a considerable proportion of infected people having pre-existing HIV. The outbreak revealed a disturbing pattern of increased human-to-human transmission, especially through close contact, as well as a probable increase in virus transmission by sexual means [22]. This

epidemiological transition has resulted in variable mortality rates, ranging from 1 to 10%, underlining the greater risk in high-density areas and among those with impaired immune systems. Some of the common clinical presentations observed during outbreaks were fever with chills, sore throat, cough, malaise, rash, lymphadenopathy, and myalgia as reported during the outbreaks. The rash usually appears in a centrifugal pattern, beginning on the face and spreading to other body areas [24,25]. Usually, monkeypox is self-resolving and is seen to resolve within a month, severe complications can occur among immunocompromised individuals, pregnant women, and children [26].

Given the resurgence of monkeypox and its propagation beyond Africa, it is critical to strengthen surveillance, research, and prevention efforts. The reduction in smallpox immunization has increased susceptibility to monkeypox, particularly among the unvaccinated. Preventive strategies include preventing contact with wild animals, imposing stringent quarantine measures on animals, and informing the public about the disease. The development of viable vaccinations and diagnostic techniques is critical in addressing the growing global danger of monkeypox. As the disease progresses, coordinated measures are required to monitor and contain its spread, ensuring that healthcare systems and public health responses are adequately prepared for future problems [9,17,27–30]. Kindly refer to Figure 1 for an illustrative overview of the epidemiological aspects of monkeypox.

Clinical features

In over 90% of patients, monkeypox is characterized by firm or rubbery, well-circumscribed, deep-seated lesions that develop as a rash that progresses through various stages before desquamation. These stages are macular, papular, vesicular, and pustular which finally form crusts. The rash can be localized to a single spot on the body or diffuse over different parts of the body at different times, primarily involving the face and extremities [31,32]. However, there is also a high prevalence of genital, perianal, and oral lesions which can easily be misdiagnosed as a sexually transmitted disease [33]. Lesions in the anogenital area may lead to dysuria [31,34].

Generalized symptoms include fever, myalgias, or malaise with lymphadenopathy of the groin, neck, and upper jaw at any point of the disease [31]. Other symptoms involved are intense headache, shortness of breath, difficulty swallowing, vomiting, and back pain. In a typical scenario, symptoms last for 1-2 weeks [32]. Hospitalization and pain management may be required for severe anogenital pain caused by proctitis rectal perforation and soft-tissue superinfections [31]. The severity of the disease is higher in children than in adults; children are prone to infections with orthopoxviruses. Affected individuals remain infectious from the initiation of fever until the vesicles have scabbed [32]. Both monkeypox and smallpox caused by the orthopoxviruses show noticeable similarities; i.e. incubation period of 14 days, prodromal fever, and a centrifugal maculopapular rash as indicated in Table 1. At the molecular level, the central 240 genomic region of MPV is 96.3% identical to the variola virus; the causative agent of smallpox, and the amino acid sequences of the virion proteins encoded in this region are up to 99.2% similar. Nevertheless, these viruses differ in the region encoding the virulence factors resulting in varying severity between the two [32].

There is also a slight possibility of monkeypox co-infection with varicella-zoster virus. In contrast to varicella zoster infection which causes lesions with regional pleomorphism, monkeypox lesions are

typically at the same stage of evolution in one region [32]. Despite monkeypox being a mild disease, there are concerns for adverse outcomes in immunocompromised, pregnant, and pediatric populations [34]. Severe complications may involve sepsis, encephalitis, balanitis, myocarditis, urethritis, and bronchopneumonia when the skin gets infected with bacteria which later spread [31,32]. There can also be ocular complications ranging from simple conjunctivitis to complete vision loss. Vertical transmission of the virus in pregnant women has been shown to lead to fetal demise and spontaneous abortions [32].

Diagnosis

As this illness progresses, it may be hard to diagnose monkeypox just only on clinical findings and symptoms and patients with proctitis or lymphadenopathy, those with influenza-like symptoms following high-risk exposure, and those who present with an unexplained acute rash, including mucosal lesions in the conjunctiva, mouth, penis, vagina, or anorectal area, should all undergo diagnostic procedures [5,6]. As a result, several diagnostic methods have been adopted to identify monkeypox over time. Common methods for diagnosing monkeypox include viral culture (preferred), electron microscopy visualization, immunohistochemistry, anti-orthopoxvirus IgG and IgM, and real-time PCR tests [5]. The ideal samples for these tests are skin lesions, which comprise swabs of the lesion surface and/or exudate, roofs from many lesions, or lesion crusts. Typically, these tests include taking various types of samples from the patients. Some rarely used methods include skin biopsy if necessary [6]. Although monkeypox's histological characteristics are similar to those of cowpox, smallpox, and vaccinia, they can be used to distinguish it from other illnesses including varicella and the herpes simplex virus.

There are several molecular targets used for diagnosis in monkeypox. The D6R gene is a conserved region exceeding 100 nucleotides in length that is shared across the entire *Poxviridae* family, making it a common target for pan-poxvirus detection using real-time PCR [55,56]. Within the *Orthopoxvirus* genus, the E7R gene, encoding the DNA-dependent RNA polymerase subunit 18 (rpo18), and the E9L gene, responsible for encoding the viral DNA polymerase, have conserved primer targets [57]. The B6R gene, which encodes an extracellular envelope protein, serves as a specific marker for monkeypox. Additionally, the B7R, F3L, and N3R genes are of diagnostic significance in PCR-based methods due to their high conservation in monkeypox [55].

Management and Treatment

While supportive care is necessary for more severe forms of monkeypox to prevent more serious adverse consequences, symptomatic therapy is typically sufficient for mild cases [35]. Many drugs, such as Tecovirimat, Brincidofovir, Cidofovir, Ribavirin, and Tiazofurin, have been developed in recent years to treat monkeypox and its various forms. Mechanisms and details of each drug have been indicated in Table 2. However, at the time of writing this article, no drug has received FDA approval for its use against monkeypox, and all these drugs are in the various stages of clinical trials.

Tecovirimat

TPOXX, also known as ST-246, is an antiviral drug currently under consideration for the treatment of monkeypox [36]. Its primary mechanism of action is to inhibit the virus by specifically targeting the P37 protein, which prevents the virus from maturing and exiting the infected cell [35–37]. On January 6, 2022, the European Union approved this drug for smallpox treatment. Numerous animal studies have demonstrated its effectiveness in treating monkeypox when administered after the disease becomes clinically apparent [35]. According to various reports, tecovirimat has been used in at least eighteen patients in the U.S. children under 5 years old, and an infant as young as 10 days old in the United Kingdom. In the UK [31]. Studies also indicate that tecovirimat reduces the fatality rate, with a 90% chance of survival [36]. A retrospective observational study involving seven pox-infected patients showed that administering 600 mg of tecovirimat orally twice daily for two weeks reduced the duration of illness (with hospitalization lasting 10 days) and was well tolerated by patients. Tecovirimat, however, may not be as effective in immunocompromised individuals and there might be a necessity to increase the number of days and dosage for the drug. Multiple animal trials also reported that this drug may not have any serious side effects and is well-tolerated, except for mild headache, nausea, and pain in the injection site [35].

Brincidofovir

Brincidofovir has antiviral activity against certain virus families which include adenovirus, cytomegalovirus, herpesviruses, polyomaviruses, and lastly, poxviruses. This drug has also recently received FDA approval in 2021 for the treatment of smallpox [35]. Its primary mechanism of action is inhibiting viral DNA replication by targeting viral DNA polymerase [35,36]. Although limited data, studies on animals demonstrated antiviral activity against orthopoxvirus infections [35]. The drug significantly reduced viral replication and increased survival rates in animals infected with orthopoxviruses, making it a promising candidate for human use [35,36]. In addition, some studies have also suggested that this drug may reduce the severity and duration of monkeypox infections. Except for nausea, vomiting, and diarrhea, this drug does not have any adverse effects [35].

Cidofovir

DNA polymerase is inhibited by cidofovir. It is also useful against poxviruses and has been authorized for the treatment of cytomegalovirus retinitis in HIV patients. It has exhibited anti-monkeypox viral action. This drug can prevent death only when it is administered before the beginning of the rash. Due to its nephrotoxic effects, the administration has only been studied in the very early stages of symptoms in high-risk contacts of confirmed cases in human instances. Headache, asthenia, fever, skin rash, nausea, vomiting, and problems in the eyes are the most frequent side effects. Nephrotoxicity is the primary dose-limiting toxicity linked to cidofovir treatment; this effect is dose-dependent. For patients who are hypersensitive to cidofovir or other medications that include sulfonamides, the medication should not be administered [35].

Prevention and Vaccination Strategies

The CDC advises that hospitalized cases of monkeypox should be isolated in a room with negative air pressure. In addition, the Spanish Ministry of Health advised medical professionals treating monkeypox patients to wear personal protective equipment (PPE) to prevent contact and airborne transmission which includes a gown, gloves, eye protection, and FFP2 masks. Additional recommendations state that patients with active skin lesions from infection should be kept isolated at home and should make every effort to avoid contact with their surroundings and pets. When possible, the affected person should cover the lesions and wear a surgical mask until the crust falls off and a new layer of skin forms [35]. Recent outbreaks in the years 2022 and 2024 have led to the development of several vaccines which have been an important part of controlling the spread of monkeypox. These include JYNNEOS, ACAM2000, and LC16m8 [38].

JYNNEOS (Imvamune/Imvanex)

JYNNEOS, now a primary alternative to ACAM2000, has recently received approval from both the FDA and the European Medicines Agency (EMA) for preventing orthopoxvirus infections, including smallpox and monkeypox, in individuals aged 18 and older [35]. It utilizes a modified strain of the vaccinia Ankara (MVA) virus, classified as a third-generation, non-replicating vaccine [35,38]. The recommended dosing schedule involves administering two subcutaneous injections 28 days apart, with full protection taking effect two weeks after the second dose [35,38]. Studies have proved that this vaccine is extremely safe including in high-risk, immunocompromised patients with its side effects only including mild headaches, myalgia, and nausea [35].

ACAM2000

ACAM2000, a second-generation live vaccinia virus vaccine, is FDA-approved for smallpox prevention. Unlike non-replicating vaccines, ACAM2000 replicates within the body to generate immunity against orthopoxviruses, such as monkeypox. It is administered using the scarification technique, which typically results in a skin lesion, signaling successful vaccination. Full immunity develops around 28 days after the dose is given. However, compared to JYNNEOS, ACAM2000 is associated with a higher rate of side effects, such as eczema vaccinatum and myopericarditis. It is also contraindicated in individuals with severe allergies, atopic dermatitis, hypertension, diabetes, high cholesterol, pregnancy, or those who are immunocompromised [35].

LC16m8

This third-generation vaccine is developed from the Lister strain of the smallpox vaccine, cultivated in rabbit kidney cells [36,38]. While clinical data in humans is limited, animal studies have shown highly promising outcomes, demonstrating the vaccine's ability to prevent both the onset and transmission of the disease with minimal to no adverse effects. Additionally, several other studies have confirmed that the vaccine can offer long-term immunity against various strains of monkeypox, further highlighting its potential as an effective tool in controlling orthopoxvirus outbreaks [35].

Recent Research and Developments

The endemic nature of monkeypox has slowly taken the form of an epidemic due to reported cases in different far-off countries [39–41]. Establishing a preventive strategy is the first thing to do whenever a global infectious disease outbreak occurs. This is the situation with the resurging monkeypox outbreak [39]. The FDA-approved smallpox vaccine, which has been tested against monkeypox and has smallpox approval status, is now only available to a limited number of workers [39,42,43]. According to the most recent regulations, people infected with the monkeypox virus should be kept isolated until all symptoms have completely subsided and the rash has healed, which may take up to four weeks [44]. By combining biomarker-based theory with in silico and bioinformatic statistical and molecular models, improved treatments with fewer side effects, better delivery, lower potential for resistance, and superior pharmacokinetic qualities could be developed for viral diseases. Bio-based approaches enable effective screening, diagnosis, prognosis, and mitigation of vaccination and adaptive treatment measures [39,45,46]. Better cellular targets, creative drug-targeting techniques, and enhanced drug delivery systems are the next steps in creating more effective antivirals to combat infectious diseases like monkeypox [47,48]. The genetic similarities between smallpox and monkeypox were taken into consideration when most of these markers were released, which offers a path forward for possible future treatments [49–52].

Nanotechnology-based treatments are another significant advancement that portends improved monkeypox therapy choices in the future [53]. This treatment provides new, affordable, and all-encompassing choices for treating a variety of illnesses. The fundamental idea is to modify current and novel antivirals' physicochemical characteristics and associated pharmacological qualities at the nanoscale [54].

The research community is working hard under these pressures to develop a treatment that can effectively combat monkeypox and other infectious diseases. The majority of recent developments are still considered theoretical because they relate to diseases that are predominantly caused by smallpox, although tremendous progress is being made in the areas of vaccine and drug development. Therefore, more effort must be made to create modern therapy alternatives that target monkeypox specifically. They must use an integrated approach to coordinate their efforts with the medical industry for clinical experimentation. Medical authorities' recommendations have been explained properly, and specific workforce demographics and susceptible persons have been taken into consideration while developing immunization and treatment regimens. Before the monkeypox epidemic turns into another pandemic of the century, a coordinated and inclusive approach will be required to educate the community and general public in awareness initiatives addressing mitigation, adaptation, and disease management [39,55–59].

Outbreak of 2024

On the 14th of August 2024, WHO determined and declared the outbreak of monkeypox in the Democratic Republic of Congo (DRC) and various other countries in the African region as well as in the surrounding areas [60,61].

Clade Ib MPV, a new strain of Monkeypox was found in September last year in DRC. WHO has declared the emergence as a public health emergency of international concern (PHEIC). This is the second PHEIC regarding monkeypox, the first was in July 2022 during the outbreak of the Monkeypox strain clade II. Phylogenetic analysis of the strains of MPV genome sequences from the south Kivu province shows that the MPV belongs to the clade I lineage. PCR analyses are being used to precisely detect clade Ib viruses. Neighboring countries also affected include; Burundi, Kenya, Rwanda, and Uganda. Based on the provided statistics and data, it is shown that the majority of the cases are among the adult population where the disease may have spread through sexual contact, identified among sex workers and their customers [60].

On July 24, 2024, Burundi declared a monkeypox outbreak after the confirmation of three cases. Upon investigating 545 alerts by August 17, the country confirmed 142 monkeypox cases out of 358 suspects; this marked the positivity rate at 39.7%. About 38% of the cases were from Bujumbura Nord, an urban district. According to statistics, men accounted for 55.6% of the cases, and children under five accounted for 28.9%. The National Emergency Operations Centre (EOC) with the support of WHO has responded with surveillance and public awareness. The country faces challenges due to limited resources and a lack of isolation facilities. However, no deaths were reported [62,63].

In Kenya, the first case was confirmed on 29 July 2024 involving a 42-year-old man who traveled from Uganda. By mid-August 14 suspected cases were identified, one of which tested positive for monkeypox clade Ib. Public Health Emergency Operations activated by the country's Ministry of Health has formed Incident Management teams, and begun intense surveillance along major travel routes. National media channels actively disseminated awareness and prevention messages. No deaths were reported in Kenya either [64].

On 24 July 2024, Rwanda confirmed its first two cases in a 33-year-old woman and a 34-year-old man both having recent travel history to DRC. Four cases were confirmed by early August. A National Rapid Response Team (RRT) was deployed by the government to mobilize resources to affected and high-risk areas including Rubavu and Rusizi, both of which border the DRC. Intense surveillance was launched in healthcare facilities and awareness was spread through radio, TV, and social media. WHO has been closely working across all three countries along with other partners to prevent the spread of monkeypox by strengthening laboratory diagnostics, improving awareness, and maintaining isolation and treatment [64,65].

Conclusion

The resurgence of monkeypox as a significant global health concern underscores the urgent need for enhanced surveillance, research, and coordinated public health responses. The 2022 and 2024 outbreaks have highlighted the evolving epidemiological patterns of monkeypox, including increased human-to-human transmission and possible sexual transmission routes, necessitating a re-evaluation of containment and prevention strategies. A comprehensive understanding of monkeypox's clinical manifestations, diagnostic techniques, and therapeutic approaches is critical in mitigating its impact. The disease presents with a characteristic rash, systemic symptoms, and complications that can be severe in immunocompromised individuals, pregnant women, and children. Advances in molecular diagnostics, particularly real-time PCR and histopathological studies, have greatly improved early and accurate detection, allowing for timely intervention.

While no specific antiviral treatment for monkeypox has received full FDA approval, promising candidates such as Tecovirimat, Brincidofovir, and Cidofovir have shown potential in mitigating disease severity. The role of vaccinations, particularly JYNNEOS and ACAM2000, has been pivotal in outbreak control. However, challenges persist in vaccine distribution, accessibility, and public acceptance, particularly in resource-limited settings. Looking forward, future research should focus on novel antiviral drug development, improved vaccine formulations, and innovative diagnostic tools, including nanotechnology-based approaches. Additionally, global health policies must prioritize education, surveillance, and rapid response mechanisms to prevent future outbreaks from escalating into pandemics.

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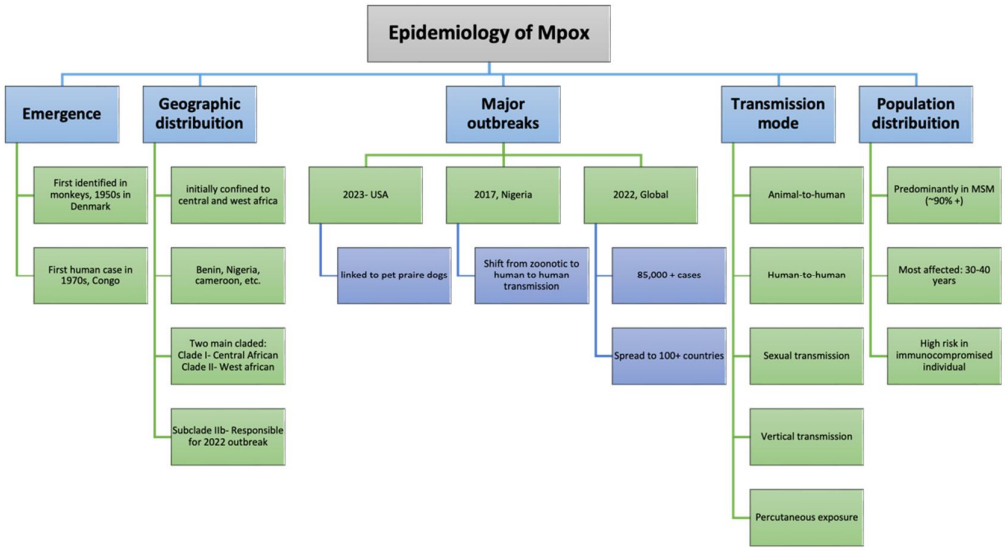
Figure Legend and figure

Figure 1. Illustrated epidemiology of Monkeypox



Tables

Table 1. Differences between Monkeypox and Smallpox

Feature	*Monkeypox*	*Smallpox*
Causative agent	Monkeypox Virus	Variola Virus
Incubation period	7-14 days	10-14 days
Prodromal symptoms	Fever, lymphadenopathy, myalgia	High fever, severe fatigue
Rash progression	Macules → Papules → Vesicles → Pustules → Crusts	Similar progression but more severe
Lesion distribution	Centrifugal (face & extremities)	More generalized
Severity	Usually self-limiting, severe in immunocompromised	High mortality (30%)
Transmission	Direct contact, respiratory droplets	Primarily respiratory droplets

Table 2. Different types of drugs currently used for the treatment of Monkeypox

Drug Name	*Mechanism of Action*	*Approval Status*	*Adverse Effects*
Tecovirimat (TPOXX)	Inhibits P37 protein, preventing DNA maturation	Approved in the EU, investigational in the US	Headache, nausea, injection site pain
Brincidofovir	Inhibits viral DNA polymerase	FDA-approved for smallpox	Nausea, vomiting, diarrhea
Cidofovir	Inhibits viral DNA polymerase	Approved for cytomegalovirus, investigational for monkeypox	Nephrotoxicity, nausea, vomiting
Ribavirin	Inhibits viral RNA synthesis	Not FDA-approved for monkeypox	Anemia, liver toxicity