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Monkeypox Virus (MPXV): Epidemiology, Pathogenesis, and Control Strategies: Exploring the Recent Resurgence of Monkeypox, Its Transmission Dynamics, Clinical Manifestations, and Public Health Responses

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Abstract

Monkeypox virus (MPXV) has re-emerged as a significant public health concern, with increasing cases reported worldwide. This zoonotic virus, primarily endemic to Central and West Africa, has demonstrated the potential for human-to-human transmission, leading to outbreaks in non-endemic regions. Unlike smallpox, which was eradicated through mass vaccination, monkeypox continues to persist due to the lack of widespread immunity and effective antiviral treatments. The resurgence of MPXV in recent years, particularly in non-endemic regions, underscores the urgent need for improved surveillance, vaccination strategies, and public health interventions. This review provides a comprehensive analysis of the epidemiology, pathogenesis, transmission dynamics, clinical manifestations, and public health responses associated with monkeypox. The epidemiology of MPXV highlights the virus's expanding geographical distribution, with increased outbreaks reported across continents due to global travel and environmental changes. The pathogenesis of MPXV is explored, focusing on its mechanisms of infection, immune evasion strategies, and the host immune response. Clinical manifestations vary from mild to severe, with complications such as secondary infections, pneumonia, encephalitis, and ocular involvement in some cases. Furthermore, this review examines transmission dynamics, including zoonotic spillover, human-to-human transmission, and environmental persistence. Public health responses, including vaccination campaigns, treatment protocols, and community awareness programs, play a crucial role in controlling outbreaks. Although vaccines such as JYNNEOS and ACAM2000 offer protection, challenges remain regarding vaccine accessibility and public acceptance. The role of antiviral treatments such as Tecovirimat (TPOXX) is also discussed, emphasizing the need for further clinical research. Finally, the review highlights future challenges, including the potential for viral mutations, disparities in healthcare infrastructure, and the need for global cooperation in combating MPXV. By understanding the epidemiology, pathogenesis, and transmission dynamics of monkeypox, this review aims to provide insights into effective control measures and preparedness strategies for future outbreaks. Strengthening surveillance, investing in research, and enhancing global collaboration will be key to mitigating the impact of MPXV in the years to come.

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INTRODUCTION

Monkeypox is a viral zoonosis caused by the monkeypox virus (MPXV), a member of the Orthopoxvirus genus. The virus was first identified in 1958 in research monkeys, with the first human case reported in 1970 in the Democratic Republic of the Congo (DRC). Historically, monkeypox has

been confined to Central and West African countries, but recent outbreaks have demonstrated its ability to spread globally [1].

The resurgence of monkeypox cases outside traditionally endemic regions has raised concerns among public health authorities worldwide. Factors such as increased global travel, deforestation, climate change, and reduced smallpox immunity have contributed to the expanding reach of MPXV [2]. Unlike smallpox, which was eradicated through mass vaccination, monkeypox remains a public health threat due to the absence of widespread vaccination programs and effective antiviral treatments. Understanding its transmission dynamics, clinical manifestations, and public health responses is critical in mitigating future outbreaks and preventing a potential global health crisis [3].

In addition to environmental and epidemiological factors, socio-economic conditions also play a significant role in the spread of monkeypox. Many affected regions lack the healthcare infrastructure needed for rapid diagnosis and effective containment, leading to prolonged outbreaks and increased morbidity [4]. Furthermore, stigma and misinformation surrounding the disease can hinder public health efforts, discouraging individuals from seeking medical attention or complying with preventive measures. Addressing these challenges requires an integrated approach that combines medical research, community engagement, and international cooperation [5].

The increasing frequency of outbreaks necessitates a comprehensive review of MPXV's epidemiology, pathogenesis, and control strategies. By examining the current knowledge of the virus, identifying gaps in research, and evaluating the effectiveness of existing public health interventions, this review aims to provide insights into developing targeted and sustainable prevention and control measures. A deeper understanding of monkeypox and its global implications will help inform future policies, improve healthcare preparedness, and mitigate the threat posed by emerging infectious diseases [6].

EPIDEMIOLOGY OF MONKEYPOX

Historical Overview of Monkeypox Outbreaks

A historical perspective on monkeypox outbreaks provides insight into its epidemiological trends and geographic spread. The table below summarizes key outbreaks of MPXV over the years:

Year	Location	Key Observations
1958	Denmark	First identification of monkeypox virus in captive monkeys used for research.
1970	Democratic Republic of the Congo (DRC)	First human case reported in a 9-month-old child.
1980s	Central & West Africa	Increased cases, likely due to waning smallpox immunity.
2003	United States	First outbreak outside Africa, linked to imported rodents from Ghana.
2017	Nigeria	Largest outbreak in West Africa, highlighting resurgence.
2022	Global	Widespread outbreaks across over 100 countries, with sustained human-to-human transmission.

Geographical Distribution and Recent Outbreaks

MPXV is endemic in Central and West Africa, with the highest burden observed in the DRC, Nigeria, and Cameroon. In recent years, outbreaks have been reported in non-endemic countries, including the United States, the United Kingdom, and several European nations. The 2022 outbreak was notable for its unprecedented global spread, affecting over 100 countries [7].

Reservoirs and Modes of Transmission

The natural reservoirs of MPXV are believed to be small mammals, including rodents and non-human primates. Human infections occur through direct contact with infected animals, consumption of bushmeat, or exposure to contaminated materials. Human-to-human transmission primarily occurs via respiratory droplets, direct skin contact with lesions, or contact with contaminated objects [8].

Risk Factors for Infection

Individuals at higher risk include healthcare workers, close contacts of infected individuals, and those engaged in activities involving animal handling. The waning immunity from smallpox vaccination, which previously provided cross-protection, has contributed to increased susceptibility among younger populations [9].

PATHOGENESIS OF MONKEYPOX VIRUS

Viral Structure and Mechanism of Infection

MPXV is a double-stranded DNA virus belonging to the Poxviridae family, specifically the Orthopoxvirus genus. It shares significant structural similarities with the variola virus, the causative agent of smallpox. The virus is brick-shaped, measuring approximately 200-250 nm in diameter, and possesses a complex structure that includes a lipid membrane, surface tubules, and a core containing the viral genome. MPXV has two infectious forms: the intracellular mature virus (IMV), responsible for cell-to-cell transmission, and the extracellular enveloped virus (EEV), which facilitates dissemination within the host (Figure 1).

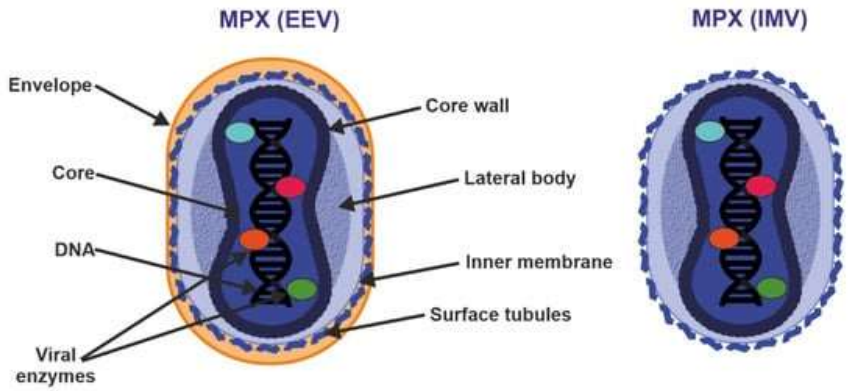

Figure 1. Viral Structure of Monkeypox Virus.

The infection process begins when MPXV enters host cells via macropinocytosis or endocytosis. Once inside the host cell, the virus uncoats and releases its genetic material into the cytoplasm, where replication occurs entirely independent of the host's nucleus. MPXV utilizes its own DNA-dependent RNA polymerase to transcribe early viral genes, which play a role in immune evasion and cellular manipulation. Subsequent intermediate and late gene expressions lead to the formation of new viral particles, which are then released either through cell lysis or budding [10].

Immune Response and Host Interactions

Following infection, MPXV triggers an immune response involving both the innate and adaptive immune systems. The virus can evade immune defenses by producing immunomodulatory proteins, including complement regulatory proteins and interferon inhibitors, which allow it to establish infection and spread systemically. The host immune response includes the activation of antigen-presenting cells, such as dendritic cells and macrophages, which present viral antigens to T cells. This leads to the production of pro-inflammatory cytokines, including interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α), which contribute to the clinical manifestations of fever and inflammation.

Humoral immunity plays a crucial role in controlling MPXV infection, with B cells producing neutralizing antibodies that target viral antigens. However, individuals with weakened immune systems, such as those with HIV/AIDS or other immunocompromised conditions, are at higher risk of severe disease progression due to an inadequate immune response. Studies have also indicated that prior smallpox vaccination confers partial immunity against MPXV, reducing disease severity and transmission potential [11].

Immune Response and Host Interactions

Following infection, MPXV triggers an immune response involving innate and adaptive immunity. The virus can evade immune defenses by producing immunomodulatory proteins, allowing it to establish infection and spread [12].

Clinical Manifestations

Monkeypox presents with an incubation period of 5-21 days, followed by a prodromal phase characterized by fever, lymphadenopathy, and malaise. The hallmark of MPXV infection is a centrifugal rash that progresses from macules to pustules and eventually scabs. Severe cases can lead to complications such as secondary bacterial infections, pneumonia, encephalitis, and ocular involvement [13].

TRANSMISSION DYNAMICS

Zoonotic Transmission

Animal-to-human transmission occurs through bites, scratches, or direct handling of infected wildlife. The increasing encroachment of humans into wildlife habitats has facilitated spillover events.

Human-to-Human Transmission

MPXV spreads through close physical contact, respiratory droplets, and fomites. Recent outbreaks have highlighted the role of sexual contact in transmission, particularly in high-risk populations.

Environmental and Nosocomial Transmission

Fomites, including bedding, clothing, and surfaces, can harbor MPXV, contributing to its spread in healthcare settings and households. Nosocomial infections among healthcare workers highlight the importance of stringent infection control measures [14].

PUBLIC HEALTH RESPONSES AND CONTROL STRATEGIES

Surveillance and Early Detection

Enhanced surveillance systems, rapid case identification, and contact tracing are essential for curbing outbreaks. Genomic sequencing of viral strains aids in understanding transmission patterns and detecting potential mutations.

Vaccination Strategies

Vaccination remains a key tool in MPXV control. The JYNNEOS (Imvamune or Imvanex) vaccine, a non-replicating modified vaccinia Ankara (MVA) vaccine, is approved for monkeypox prevention. The older ACAM2000 vaccine is also effective but carries a higher risk of adverse effects.

Treatment and Supportive Care

Currently, there is no specific antiviral treatment for MPXV, but supportive care and symptom management play a crucial role. Tecovirimat (TPOXX), an antiviral initially developed for smallpox, has shown promise in treating severe MPXV cases.

Public Health Interventions

Community awareness campaigns, risk communication, and behavioral modifications can reduce transmission. Travel restrictions, quarantine measures, and isolation protocols have been employed during outbreaks to contain the spread [15].

CONCLUSION

The resurgence of monkeypox highlights the need for robust public health strategies, enhanced surveillance, and global cooperation. Understanding the epidemiology, pathogenesis, and transmission dynamics of MPXV is critical for devising effective control measures. The expansion of monkeypox beyond traditionally endemic regions underscores the necessity of coordinated international efforts to

curb its spread. Early detection through enhanced surveillance, rapid diagnostic tools, and effective contact tracing remains vital in preventing large-scale outbreaks. Vaccination strategies, particularly the use of JYNNEOS and ACAM2000, play a key role in mitigating disease severity and limiting transmission. However, challenges such as vaccine accessibility, distribution logistics, and vaccine hesitancy must be addressed to ensure widespread immunization coverage. The development of novel antiviral treatments, including Tecovirimat (TPOXX), Brincidofovir, and Cidofovir, provides hope for effective therapeutic options, but further clinical studies are needed to confirm their efficacy and safety in diverse populations. Public health interventions must emphasize education and awareness programs to reduce stigma, misinformation, and fear associated with monkeypox. Strengthening healthcare infrastructure, particularly in resource-limited settings, will improve outbreak preparedness and response capabilities. Additionally, interdisciplinary collaboration among virologists, epidemiologists, policymakers, and healthcare professionals is crucial in advancing research efforts and shaping evidence-based policies.

Moving forward, continued investment in research, global cooperation, and proactive public health strategies will be necessary to control and eventually eliminate monkeypox as a global health threat. The lessons learned from past and recent outbreaks should guide future preparedness efforts, ensuring that societies are equipped to manage and mitigate the risks associated with MPXV and other emerging infectious diseases. The resurgence of monkeypox highlights the need for robust public health strategies, enhanced surveillance, and global cooperation. Understanding the epidemiology, pathogenesis, and transmission dynamics of MPXV is critical for devising effective control measures. Ongoing research into vaccines and antiviral treatments, coupled with public health interventions, will be pivotal in mitigating the impact of future outbreaks.

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