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The Mpox 2024 Outbreak: The Main Challenges

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The rising incidence of Mpox cases in Africa led the World Health Organization to declare a public health emergency of international concern on 14 August 2024.[1] Despite efforts to decrease the spread of Mpox, its control presents significant challenges due to complex epidemiology, evolving virological features, and variable clinical presentation. This paper examines the challenges of Mpox, primarily focusing on the transmission, epidemiology, clinical presentation, diagnostics, management, and infection control.

Epidemiological Trends and Transmission Dynamics

The Democratic Republic of the Congo (DRC) is the primary source for Mpox, especially due to its constant endemic presence. The DRC has consistently reported the maximum number of cases and fatalities, with thousands of cases in 2024.[2] Epidemics have affected the border countries and have recently been detected in Sweden and Thailand.[1] This resurgence represents a substantial challenge because of the potential increased virulence and mortality of clade 1, which could have led to the WHO declaration.

The virus is predominantly transmitted through close contact with infected individuals or animals, as well as through contact with contaminated surfaces and materials. Furthermore, transmission may occur via bodily fluids, and direct contact with skin lesions. The 2022 global outbreak revealed a novel transmission pattern that primarily affected men who have sex with men (MSM) in previously non-endemic regions. Although the incidence of Mpox infection among healthcare workers is limited, healthcare facilities may be at risk if infection control measures fail.[3] The transmission dynamics of the Mpox virus are influenced by its environmental presence, as the virus has the ability to persist on surfaces and materials for extended periods. The main transmission route of Mpox in 2024 appears to vary from that in 2022, as it encompasses animal-to-human transmission. Ongoing research examining the characteristics of the virus, affected populations, including children, and environmental impacts will be crucial in managing this public health problem.

Risk Factors for Infection

Several risk factors for Mpox infection have been identified in recent investigations. In Nigeria, close contact with infected individuals as well as high-risk sexual behaviors were identified as significant risk factors for adults.[4] A high incidence was observed among MSM during the 2022 outbreak, with additional risk factors including recent exposure to multiple sexual partners and attendance at large social events.[5] In contrast to the 2022 outbreak, children have been primarily susceptible to the infection in the 2024 outbreak.

Virological Features of Mpox

Mpox virus is an enveloped double-stranded DNA virus thatbelongs to the genus orthopoxvirus. Two primary clades of the virus are identified (clade I and clade II) (Congo and West Africa). Clade II can be divided into two subclades, IIa and IIb. Subclade IIb was the cause of the global Mpox outbreak in 2022, which was identified primarily among MSM. Furthermore, clade I has been demonstrated to be transmitted through sexual contact.[6] The Congo clade, which originated in Central Africa, is more pathogenic than the West African clade. However, while there were a few hospitalizations with severe disease during the 2003 U.S. outbreak in the West African clade, no deaths occurred. Congo MPV induces T-cell activation. Conversely, the production of inflammatory cytokines is diminished when human cells are obtained from individuals who have previously been infected with the monkeypox virus. It is possible that this virus may generate a modulator that suppresses host T-cell responses. A gene that inhibits complement enzymes is present in the Central African clade, but it is absent in the West African clade. The Central African and West African strains exhibit a nucleotide difference of 0.55-0.56%. Both strains share 53 genes. Mpox does not typically exhibits fewer mutations than the RNA viruses, however, the virus isolated from the 2022 Mpox outbreak appears to have a greater number of mutations. The virus isolated at that time exhibited 40 mutations. The evolution of the Mpox virus appears to have initiated in 2017. It has been circulating in humans since then and has been discovered

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to present a mutation rate approximately 10 times higher.[7] Clade I is linked to a case fatality rate (CFR) of 10.6%, while clade II to only 3.6%. Therefore, genetic differences between clades may account for the varying pathogenicity, virulence, and transmission patterns. The enes that may be accountable for the enhanced virulence of clade I include those for host range protein (D10L), complement inhibitor (D14L), apoptotic regulator (B10R), IL-1β binding protein (B14R), and serine protease inhibitor-like protein (B19R). The absence of D14L in clade II may be the primary factor contributing to the increased virulence of clade I.[8]

Challenges in Clinical Presentation

Recent epidemics have exhibited a more diverse array of symptoms than those previously described, indicating a significant evolution in the clinical presentation of Mpox. Mpox is distinguished by fever, headache, myalgias, chills, lymphadenopathy and a centrifugal rash with well-circumscribed, deep-seated pustules. However, the 2022 outbreak has exhibited a broader spectrum of severity, frequently encompassing lesions at the inoculation site.[9]

Secondary bacterial infections and systemic involvement, such as myocarditis or encephalitis, can complicate severe Mpox. Young children, patients with chronic illness, and immunocompromised individuals, particularly those with advanced HIV, are at higher risk for severe disease.[10] Complications necessitating medical treatment may occur in up to 40% of patients and include rectal pain, anorectal abscesses, odynophagia, and penile edema. Most patients experience a self-limited illness, with 1% to 13% requiring hospital admission depending on the virological characteristics, underlying illness, and capacity of the healthcare system. During the 2022 Mpox outbreak, the CFR was less than 0.1%. Although the 2024 Mpox outbreak-associated mortality was reported as 2.9% in DKC,[11] it may differ in non-African countries based on the capacity of the healthcare system.

Diagnostic Challenges

Diagnosing Mpox accurately remains a challenge, especially with the emergence of different viral clades. Depending on the stage of the lesions, which range from maculopapular to pustules, the skin lesions of Mpox may resemble other viral infections and sexually transmitted bacterial infections. Mpox should be considered in the differential diagnosis for papulovesicular or vesiculopustular lesions and genital lesions or ulcers.[5]

Differential Diagnoses

- Molluscum Contagiosum: Presents with comparable deep-seated umbilicated pseudopustules but lacks prodromal symptoms and exhibits a chronic course.

- Herpes Simplex Virus: Can present with similar vesicular lesions; however, typically involves painful ulcers and inguinal lymphadenopathy.

- Varicella (chickenpox): Frequently confused with Mpox, especially clade I type, due to similar vesicular rash presentation. Lesions are typically itchy and begin developing on the trunk and face.

- Syphilis: Primary syphilis can manifest with a painless solitary genital ulcer that may resemble monkeypox lesions.

- Lymphogranuloma venereum: Can cause proctitis, which may be mistaken for anorectal monkeypox lesions.

- Impetigo: Caused by group A *Streptococcus*; can present with vesicles and pustules, although the characteristic golden crust indicates impetigo.

- Orf: Although it can induce localized skin lesions that resemble Mpox. However, a history of contact with sheep, goats, or dairy cows aids in differentiating these conditions.

Visual assessment is crucial for diagnosing and staging lesions; however, a more robust diagnostic tool, such as the detection of viral DNA by polymerase chain reaction, remains the gold standard for diagnosis.[9]

Mpox Vaccination

In 2022-2023, the global Mpox epidemic underscored the urgent need for effective vaccines against Mpox. Currently, there are two primary types of vaccines used for mpox prevention:

1. First and second-generation smallpox vaccines: These vaccines contain live vaccinia virus and offer cross-protection against MPXV as a result of the genetic similarity between orthopoxviruses (ACAM2000 and Aventis Pasteur Smallpox Vaccine).

2. Third-generation smallpox/Mpox vaccines: These are live, attenuated, non-replicating vaccines based on the Modified Vaccinia Ankara (MVA) strain. The most frequently used is MVA-BN (marketed as Jynneos in the US, Imvanex in the EU, and Imvamune in Canada). The WHO has recently included this vaccine in the prequalification list. It is recommended that individuals over the age of 18 receive two doses with a four-week interval.[12]

Recent advances in Mpox vaccines

1. Dose-sparing strategies: Due to limited vaccine supply during the 2022 pandemic, intradermal administration of MVA-BN has been continued in fractional doses (0.1 ml) in some countries. Studies have demonstrated that intradermal administration exhibits an immunogenicity analogous to the standard subcutaneous route and allows for dose savings.[9-13]

2. Single-dose regimens: While the standard MVA-BN regimen involves the administration of two doses 28 days apart, some countries adopted single-dose strategies to maximize vaccine coverage. The efficacy of single-dose regimens is currently being assessed through ongoing research.[14]

3. Novel vaccine platforms: Researchers are exploring novel vaccine platforms for Mpox, including subunit vaccines, DNA vaccines, viral vector-based vaccines and mRNA-based vaccines.[15]

Vaccination recommendations encompass the following: Identifying target groups for vaccination, maintaining focused vaccination efforts for high-risk populations, evaluating the efficacy of new third-generation smallpox/Mpox vaccines (such as Imvanex/Jynneos) in infection prevention and symptom reduction, investigating

optimal vaccination strategies including dosing schedules and administration methods (e.g., intradermal vs subcutaneous), monitoring long-term vaccine effectiveness and safety in real-world settings, ensuring equitable global distribution of Mpox vaccines, especially in African endemic regions, and resolving vaccine hesitancy through evidence-based communication.

The 2024 Mpox outbreak emphasizes the need for a coordinated global response. The significance of improved surveillance is underscored by the global spread of clade I, which has spread from the Democratic Republic of the Congo to Sweden and Thailand. The Mpox pandemic persists in Africa, despite the absence of any new countries reporting novel cases. Therefore, the disease's complex epidemiology, evolving clinical presentation, and diagnostic challenges necessitate constant research and attention. Key research areas include:

1. Potential complications and a wide spectrum of symptoms, particularly in immunocompromised individuals and vulnerable populations such as children.

2. Enhanced rapid diagnostic instruments to differentiate Mpox from similar diseases.

3. Advanced vaccination strategies, including novel techniques.

Clinicians must maintain high awareness for Mpox, particularly in patients with atypical rashes or from high-risk groups. Continued research is indispensable for developing rapid diagnostics, effective treatments, and vaccines. Mitigating the effects of this evolving public health threat and preventing future outbreaks will necessitate a comprehensive approach to these challenges.

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REFERENCES

1. WHO. WHO Director-General declares mpox outbreak a public health emergency of international concern 2024 [updated 14 August 20244 September 2024]. [CrossRef]
2. Nachega JB, Mohr EL, Dashraath P, et al.; Mpox Research Consortium (MpoxReC). Mpox in Pregnancy - Risks, Vertical Transmission, Prevention, and Treatment. *N Engl J Med*. 2024;391:1267-1270. [CrossRef]
3. Safir A, Safir M, Henig O, et al. Nosocomial transmission of MPOX virus to health care workers -an emerging occupational hazard: A case report and review of the literature. *Am J Infect Control*. 2023;51:1072-1076. [CrossRef]
4. Ogoina D, Dalhat MM, Denue BA, et al.; Nigerian Infectious Diseases Society (NIDS) mpox study group. Mpox Epidemiology and Risk Factors, Nigeria, 2022. *Emerg Infect Dis*. 2024;30:1799-1808. [CrossRef]
5. Gupta AK, Talukder M, Rosen T, Piguet V. Differential Diagnosis, Prevention, and Treatment of mpox (Monkeypox): A Review for Dermatologists. *Am J Clin Dermatol*. 2023;24:541-556. [CrossRef]
6. Masirika LM, Kumar A, Dutt M, et al. Complete Genome Sequencing, Annotation, and Mutational Profiling of the Novel Clade I Human Mpox Virus, Kamituga Strain. *J Infect Dev Ctries*. 2024;18:600-608. [CrossRef]
7. Kumar N, Acharya A, Gendelman HE, Byrareddy SN. The 2022 outbreak and the pathobiology of the monkeypox virus. *J Autoimmun*. 2022;131:102855. [CrossRef]
8. Zinnah MA, Uddin MB, Hasan T, et al. The Re-Emergence of Mpox: Old Illness, Modern Challenges. *Biomedicines*. 2024;12:1457. [CrossRef]
9. Mitjà O, Ogoina D, Titanji BK, et al. Monkeypox. *Lancet*. 2023;401:60-74. [CrossRef]
10. Liu BM, Rakhmanina NY, Yang Z, Bukrinsky MI. Mpox (Monkeypox) Virus and Its Co-Infection with HIV, Sexually Transmitted Infections, or Bacterial Superinfections: Double Whammy or a New Prime Culprit? *Viruses*. 2024;16:784. [CrossRef]
11. ECDC. Epidemiological update, week 37/2024: Mpox due to monkeypox virus clade I 2024 [updated 17 September 202419 September 2024]. [CrossRef]
12. WHO. WHO prequalifies the first vaccine against mpox 2024 [updated 13 September 202416 September 2024]. [CrossRef]
13. Harris E. Lower Dose of Mpox Vaccine Was Safe, Effective. *JAMA*. 2024;331:1983. [CrossRef]
14. van Ewijk CE, Miura F, van Rijckevorsel G, et al.; Dutch Mpox Response Team; Members of the Dutch Mpox Response Team. Mpox outbreak in the Netherlands, 2022: public health response, characteristics of the first 1,000 cases and protection of the first-generation smallpox vaccine. *Euro Surveill*. 2023;28:2200772. [CrossRef]
15. Fang D, Liu Y, Dou D, Su B. The unique immune evasion mechanisms of the mpox virus and their implication for developing new vaccines and immunotherapies. *Virol Sin*. 2024;S1995-820X(24)00135-4. [CrossRef]