


# From Primate Myth to Global Concern: Understanding the Human Mpox Virus Pandemic

Isabella Khan <sup>a\*</sup>

<sup>a</sup> Faculty of Arts & Science, University of Toronto

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**ABSTRACT:** This analysis delves into the enigmatic nature of the Human Mpox Virus (formerly Monkeypox), a pathogenic virus that affects humans and has recently garnered attention due to its wide range of hosts and a global pandemic in 2022. Despite its misleading name, which implies primate transmission, the true origins and hosts of Mpox remain unknown, sparking debates about its classification and concerns about stigmatization. Through a thorough examination of the virus's historical emergence, clinical manifestations, evolving epidemiology, and transmission patterns, this analysis aims to provide valuable insights into this infectious disease. By understanding its complexities, effective control and prevention strategies can be developed. Mpox, belonging to the Orthopoxvirus species, shares genetic similarities with other poxviruses such as smallpox and cowpox. Early recognition of symptoms is vital for prompt diagnosis and isolation, as there is no permanent cure for Mpox. Preventive measures involve surveillance, early detection, isolation, and vaccination. By further exploring Mpox's complexities, advancements can be made in controlling and preventing this infectious disease.

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**KEYWORDS:** Mpox, pandemic, Orthopoxvirus, zoonotic reservoir, healthcare disparities.

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\* Corresponding Author - Email Address: [bella.khan@mail.utoronto.ca](mailto:bella.khan@mail.utoronto.ca)

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## **Importance of Understanding Mpox in the Context of a Global Pandemic**

Human Monkeypox Virus (Mpox), belonging to the Orthopoxvirus species, is a pathogenic virus that affects humans. Alongside other well-known illnesses, such as smallpox and cowpox, Mpox has captured attention due to its ability to infect a wide range of mammalian species as well as the recent pandemic, which spread to several endemic and non-endemic countries. Mpox is closely related to its Orthopoxvirus counterparts, including the vaccinia virus (VACV), the cowpox virus (CPXV), and the variola virus (VARV). Although the originated host remains a mystery, Mpox may infect a wide taxonomically diverse range of mammalian species. Despite its misleading name, which wrongly implies primate transmission, the zoonotic reservoir of Mpox remains unknown, with many scientists, medical professionals, and patients criticizing the classification of the virus. This analysis delves into the pathogenesis, epidemiology, and preventive strategies associated with Mpox, while also addressing the controversial naming of the virus and its implications. Through an examination of the virus's historical emergence, clinical manifestations, evolving epidemiology, and transmission patterns, valuable medicinal insights can be gained which will lead to a deeper understanding of this enigmatic infectious disease and open the doors to explore effective measures for its control and prevention.

### **Early Identification and Outbreaks**

Mpox was first identified at a Danish research laboratory in 1958 when monkeys experienced outbreaks of what appeared to be a pox-like disease. The attribution of the emergence of "monkeypox" is ascribed by the World Health Organization (WHO) to this occurrence.<sup>1</sup> The virus was not detected in humans until 1970 when the first confirmed case was found in a nine-month-old boy from the Democratic Republic of the Congo.<sup>2</sup>

#### *Human Cases and Outbreaks in the Democratic Republic of Congo*

From 1981 to 1986, the Democratic Republic of Congo, formerly known as Zaire, reported 37 documented cases of Mpox.

Between February 1996 and February 1997, an extensive Mpox outbreak took place in the same region. The outbreak sparked concerns regarding retaining smallpox virus samples for research purposes to compare them with related viruses such as Mpox. In 13 villages situated in Zaire, 71 clinical cases of Mpox were reported, among six resulting in fatalities, from February to August 1996. The highest number of secondary cases was recorded in August, at the outbreak's peak. All 11 specimens collected tested positive for Mpox, and minor genetic variations were observed in comparison to other strains collected between 1970 and 1979. Despite David Heymann, former executive director of WHO's Communicable Diseases Cluster, expressing concern regarding the issue, the outbreak continued, with the organization reporting 170 new cases<sup>1</sup> between March and May of 1997.<sup>3</sup> Nevertheless, Heymann cautioned that a portion of the cases might be chickenpox.

In the Katako-Kombe region, numerous instances of a virus were previously researched by a team assembled by the World Health Organization. Ali Khan, from the Centers for Disease Control and Prevention (CDC), led the Zairian Ministry of Health and the WHO. Regardless of experiencing unrest and violent attacks on the local community, Khan and his team visited 12 villages at the outbreak's epicentre in February 1997 and produced a detailed report on April 11th. According to the report, the infection rate increased dramatically from 30% to 73% among the 89 people studied, with 73% of individuals contracting the virus from others. The report also highlighted that one patient appeared to have spread the virus to eight other individuals, twice the previous highest transmission chain. Researchers tested a sample from a person infected in 1996. They found that the virus was not evolving to become more virulent or contagious, eradicating increased virulence or contagion concerns.<sup>4</sup>

## **Taxonomical Evolution**

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<sup>1</sup> The World Health Organization reported 58, 52, and 60 cases in May, June, and July, respectively.

The name "monkeypox" immediately spiked controversy because of the disease's association with African countries, leading many scientists to believe this name is discriminatory and stigmatizing; demanding a name change.<sup>5</sup> As of November 28<sup>th</sup>, 2022, the World Health Organization (WHO), began referring to the disease as "Mpox".<sup>6</sup> To eliminate the pre-existing name of "monkeypox", numerous clinical studies and existing licensed vaccines changed the title to further proceed to documentation. The WHO stated that "monkeypox" will discontinue in a year.<sup>7</sup> Mpox virus has been divided into two genetic subclades: The Congo Basin Clade, also known as the Central African clade, and the West African clade. Utilizing Roman numerals for each clade, The Congo Basin Clade was renamed Clade I, while the West African clade was renamed Clade II, with two phylogenetically separate subclades, IIa and Iib.<sup>8</sup>

### **Genetic Subclades and Epidemiological Traits**

Although geographically separated, these groups exhibit distinct epidemiological and clinical traits. West African populations have experienced a case fatality rate (CFR) below 1%, In contrast, the Congo Basin clade (also known as the Central African clade) exhibited a CFR reaching up to 11%, with instances of human-to-human transmission occurring as many as six consecutive occasions. The origins of Mpox are yet to be fully understood, but it is believed to be a zoonotic disease transmitted to humans through contact with infected animals or animal products.<sup>9</sup> The clinical manifestations of Mpox include fever, headaches, muscle aches, and a characteristic rash that starts from the face and gradually spreads to the torso and extremities. The rash quickly evolves to form fluid-filled blisters that eventually become pustular and then crust over. The lesions typically last between two and four weeks and may leave scars.<sup>10</sup>

A systematic review explored how Mpox has spread since its discovery in 1970 in the Democratic Republic of the Congo. The research synthesis established that human Mpox has now been detected in 10 African countries and four other nations.<sup>11</sup> These countries include Nigeria, where it returned after 40 years of absence, and the United States, which saw an outbreak in 2003 associated with

rodents imported from Africa.<sup>12</sup> Between 2010 and 2019, cases have increased, possibly due to the withdrawal of smallpox vaccines that provided some protection against Mpox.<sup>13</sup> Monitoring and detection programs are vital tools in understanding the ever-evolving epidemiology of Mpox.<sup>15</sup> Historical trends in occurrence rates, distribution, and control of the spread of the infection in endemic compared to non-endemic regions have not been extensively studied.

### **Mechanisms of Mpox Transmission and Disease Progression**

The transmission of the monkeypox virus is the starting point of its disease-causing ability and its impact on the body. It can occur due to close contact between animals and humans, or between humans themselves. The pathogenesis of Mpox is thought to enter the body through the respiratory tract or contusions in the skin. Various African animals have been infected with Mpox, including tree squirrels, rope squirrels, and Gambian pouched rats.<sup>14</sup> The virus replicates in the regional lymph nodes and then spreads to other organs, including the liver, spleen, and bone marrow. In humans, the disease is generally self-limiting, but severe cases can occur, especially in immunocompromised individuals. In terms of diagnosis, treatment, and spread prevention, early recognition of symptoms is vital for prompt diagnosis and isolation of infected individuals. There is no known cure. Treatment is primarily palliative and includes pain management, hydration, and wound care. Albeit the lack of supported evidence on the effectiveness of Mpox, the use of vaccines and immune therapies used to treat smallpox and acquired immunodeficiency syndrome (AIDS) may help alleviate the symptoms and progression of Mpox. In high-risk populations, such as immunocompromised individuals, the disease can be severe and lead to complications such as pneumonia and encephalitis.<sup>15</sup>

### **Controlling Transmission Among At-Risk Populations**

Outbreaks in non-endemic regions may have evolved to become more transmissible among humans. Mpox has been reported in several non-endemic areas, such as the United States and Great Britain. Controlling Mpox outbreaks among at-risk populations, such

as gay, bisexual, and other men who have sex with men (GBM), requires early recognition of symptoms and prompt diagnosis and treatment. Peter, a 28-year-old gay man, openly admitted contracting Mpox at a beach party he attended not too far from New York City. While isolated in Seattle, he pondered about the individuals he had been with at the party and recalled a “little hard spot” located on another man’s body. Peter advised gay men to be vigilant for signs of Mpox on themselves and their partners during sexual activities and said, “Don’t be afraid to say something.”<sup>16</sup> By preventing transmission to others and reducing disease severity for those already affected, communities can help reduce stigma and fear while promoting safe and effective prevention methods. Educating and supporting these groups is also essential to reduce stigma and fear among them. Overall, a combination of strategies is necessary to prevent and control Mpox. These preventative methods include surveillance, early detection, isolation of affected individuals, and vaccination. Further research into the virus’ pathogenesis, transmission, and the development of effective vaccines and treatments will be fundamental in this fight against Mpox.<sup>17</sup>

### **Mpox in Non-Endemic Countries**

Non-endemic countries such as the United States of America and Canada have also been affected by Mpox<sup>18</sup>. Mpox was mostly reported in African countries, and as Mpox is not native to North America, the outbreak of Mpox cases was overwhelming in the United States of America. Those at risk, in this case, the GBM community, understood that a behaviour change was needed to see a change in the positive direction. According to a joint survey from the CDC, Emory University, and Johns Hopkins University, data showed that those who limited the number of casual sexual encounters reduced the majority of Mpox transmission.<sup>19</sup> Over 25,000 cases of Mpox have been reported in the United States of America since May 2022, with 38% of those infected also being HIV-positive. An outbreak of Mpox also revealed itself in Canada in May 2022, shortly after the United States announced their public safety concerns. The Public Health Agency of Canada (PHAC) reported 168 cases as of

June 17<sup>th</sup>, 2022.<sup>20</sup> The individuals who have experienced the most severe manifestations are those who are HIV-positive and have not sought or received proper treatment for their condition.<sup>21</sup> Some patients in the United States required lengthy hospitalizations, with deaths also being reported.<sup>22</sup>

## **Disparities Between Western and Impoverished Populations**

Those from impoverished endemic locations, versus those belonging to a wealthier setting, are more likely to encounter health complications. Sharmistha Mishra, an infectious disease physician from the Emerging and Pandemic Infections Consortium in Toronto, states that access to healthcare is very important. The likelihood that mild cases will be recognized and recorded, with access to sufficient care and diagnosis, reduces assessed case fatality rates.<sup>23</sup>

### *Healthcare Disparities*

Furthermore, the health disparities between African and impoverished countries compared to Western countries have contributed to significant challenges in addressing Mpox outbreaks. The African health system has insufficient testing and monitoring capabilities, which has led to 50% of Mpox cases being misdiagnosed as other infections with comparable symptoms, such as chickenpox. From 1970 to 2018, cases of Mpox have increased with a 10% mortality rate. Mpox has a relatively low contagion rate yet still poses a threat because of the “already drained” healthcare system within African countries.<sup>24</sup> The Mpox epidemic has increased cases among Blacks and Hispanic/Latino communities, with HIV being more prevalent in the Black population than in Hispanics/Latinos.<sup>25</sup>

### *Attention Disparities*

In addition to health disparities, attention disparities have also been evident when it comes to addressing Mpox outbreaks. Historically, diseases that primarily affect marginalized or low-income populations in African and impoverished countries have often received less attention and resources compared to outbreaks in Western countries. This discrepancy in attention can lead to delayed

response and limited efforts to control and prevent the spread of the disease in vulnerable regions. These disparities highlight the urgent need to address health inequalities and strengthen healthcare systems in vulnerable regions to effectively combat the spread of Mpox and other infectious diseases.

### **Severity in Immunocompromised Patients**

Typically, individuals exhibiting severe cases are characterized by HIV infection with CD4 cell counts of less than 200 cells/ml, a significant indicator of severe immunosuppression.<sup>26</sup> Healthcare providers must identify the underlying risk factors and optimize immune function to reduce or avoid severe illness. The best treatment for Mpox in immunocompromised patients should be to optimize immune function, limit immunosuppressive medication use unless indicated by a physician, and utilize antiretroviral therapy for HIV-positive patients. Early recognition of symptoms is essential for prompt diagnosis and isolation of infected individuals. There may also be medical countermeasures to help treat severe illnesses such as oral/intravenous tecovirimat (TPOXX), cidofovir/brincidofovir, and vaccinia immune globulin intravenous (VIGIV), although data regarding their effectiveness against Mpox remains uncertain.<sup>27</sup> These countermeasures should be chosen based on individual clinical factors and other relevant medical factors on a case-by-case basis.

### **Public Health Management**

Smallpox vaccines are effective in protecting against those at risk of contracting Mpox. As a result of smallpox and Mpox belonging to the same genus of virus, Orthopoxvirus, smallpox vaccines produce antibodies that recognize Mpox pathogens. The Food and Drug Administration (FDA) approved JYNNEOS vaccine, known to protect humans against smallpox, is currently used as the primary defence against Mpox in the United States of America.<sup>28</sup> A case-control study assessed the efficacy of JYNNEOS vaccination in preventing medically attended Mpox disease among adults. The vaccine effectiveness was calculated as  $(1 - \text{odds ratio for vaccination in case patients vs. controls}) \times 100$ . The researchers found the vaccine



to be effective. The study results showed 66.0% of patients who received two doses (full vaccination) had a more protective effect than the 35.8% of patients who received one dose (partial vaccination). Conclusively, the two-dose vaccination unveiled the highest level of protection against Mpox. The study showed those infected with Mpox had not received either the partial or full vaccination.<sup>29</sup> The Public Health Agency of Canada has authorized three types of smallpox vaccine including lyophilized (freeze-dried) vaccine, frozen liquid formulation vaccine, and Imvamune<sup>®</sup> which is currently provided provincially for pre- and post-exposure to Mpox.<sup>30</sup>

## **Conclusion**

The global outbreak of Mpox has emerged as a pressing public health concern, demanding immediate attention and collaborative efforts. The escalating number of cases in non-endemic countries underscores the need for comprehensive research investigations, wide-ranging epidemiological studies, and swift, confirmatory diagnoses to understand the virus better. Moreover, identifying natural animal reservoirs and comprehending associated zoonosis is crucial for devising effective prevention and control measures. Continuing research on the historical emergence, clinical manifestations, and evolving epidemiology of Mpox is essential for devising viable control and prevention strategies. Ensuring widespread access to vaccines and antiviral drugs, including JYNNEOS and Imvamune, should be prioritized to combat the rising incidences of monkeypox. To strengthen global preparedness against future outbreaks, increased investment in research and development for new treatments and vaccines becomes imperative. Additionally, heightened awareness regarding the risks of zoonotic diseases and the promotion of preventive measures are vital steps in averting future outbreaks. The Mpox epidemic has shed light on significant disparities in healthcare between impoverished countries and Western nations, impacting the effectiveness of Mpox outbreak management. Addressing these disparities and fostering equitable healthcare systems is paramount to effectively combat Mpox and safeguard vulnerable communities. Rigorous international efforts, evidence-

based strategies, and equitable resource allocation are necessary to combat Mpox effectively. By uniting our collective expertise and resources, we can work towards a safer and healthier global community, better equipped to address emerging infectious diseases.

## Notes

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- <sup>10</sup> World Health Organization, “Mpox (Monkeypox),” WHO Newsroom Factsheets, April 18, 2023.
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- <sup>14</sup> World Health Organization, “Multi-Country Monkeypox Outbreak: Situation Update” (WHO: Disease Outbreak News, June 27, 2022).
- <sup>15</sup> World Health Organization, “Mpox (Monkeypox),” WHO Newsroom Factsheets, April 18, 2023.
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- <sup>18</sup> World Health Organization, “Multi-Country Monkeypox Outbreak in Non-Endemic Countries,” *Disease Outbreak News* (WHO, May 29, 2022).

<sup>19</sup> Mary Kekatos, “How US Came Back from Mpox Outbreak,” *ABC News*, December 11, 2022.

<sup>20</sup> Matthew Croxen et al., “Two Draft Canadian Monkeypox Virus (MPXV) Genomes,” *Virological*, June 21, 2022.

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