

The Resurgence of Mpox: A New Global Health Crisis

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The re-emergence of Mpox, formerly known as monkeypox, has signalled a concerning shift in the epidemiology of zoonotic diseases [1, 2]. Once considered a relatively contained pathogen, primarily affecting Central and West Africa, Mpox has crossed borders and oceans, leading to a global outbreak in 2022 [3, 4]. This editorial aims to discuss the history, biology, human transmission, and global spread of Mpox, as well as the clinical features, treatment, prevention strategies, and delayed epidemiological measures that have intensified the crisis.

Monkeypox virus (MPXV) was first identified in 1958 in laboratory monkeys, hence the name, though the virus's natural reservoir is believed to be small rodents [5]. The first human case was recorded in 1970 in the Democratic Republic of Congo (DRC) [6]. For decades, Mpox remained an endemic disease in rural parts of Central and West Africa, causing sporadic outbreaks with limited human-to-human transmission. However, the global health community largely over-

looked the potential for broader dissemination, focusing instead on more immediate global health threats [6].

Mpox is an *Orthopoxvirus* closely related to the variola virus, which causes smallpox [7]. The virus is double-stranded DNA with two distinct genetic clades: the Central African (Congo Basin) clade, known for its higher virulence and transmissibility, and the West African clade, which has a lower case fatality rate. The virus is transmitted to humans through direct contact with infected animals, particularly rodents, or close contact with infected individuals or contaminated materials. Human-to-human transmission occurs via respiratory droplets, bodily fluids, or skin lesions [6]. The two clades of Mpox have shown different patterns of transmission and severity [8]. The Central African clade (clade I, Ia and Ib) has a higher potential for human-to-human transmission and more severe outcomes. In contrast, the West African clade (clade II, IIa and IIb), which became prominent in the 2022 outbreak, is less virulent but has demonstrated an ability to spread more efficiently in non-endemic regions (Figure 1) [6]. The jump from animal reservoirs to humans has been facilitated by deforestation, urbanisation, and increased human-animal interaction, exacerbated by

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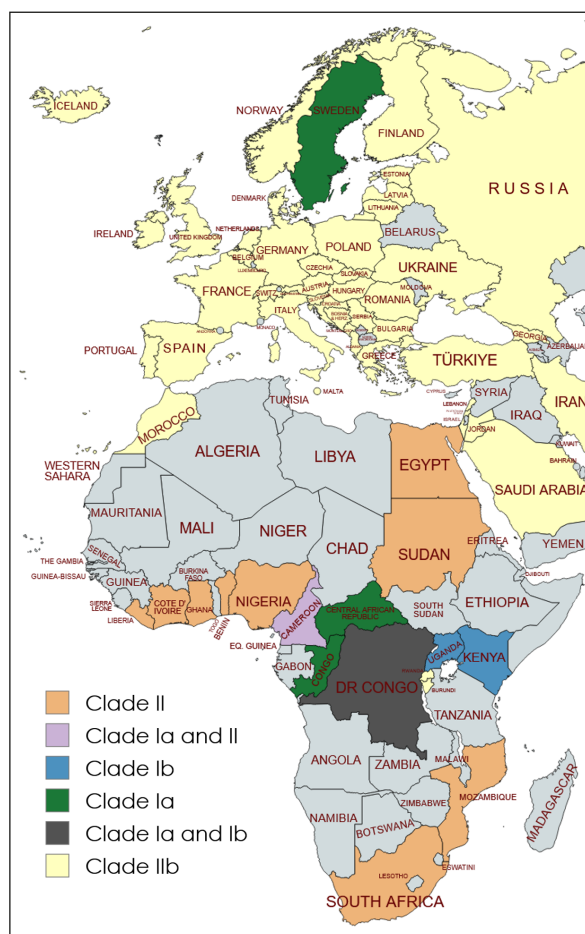


Figure 1 - African countries where monkeypox virus clade I and/or clade II have been detected, and European countries that have previously reported clade IIb; including Sweden recently reported clade Ib (2024).

a lack of vaccination coverage since the cessation of smallpox immunisation [9].

The 2022-2023 Mpox outbreak marked a turning point in the virus's epidemiology. Cases were first identified in the United Kingdom in May 2022, quickly followed by reports from other European countries and the United States of America (USA). Unlike previous outbreaks, primarily confined to Africa, this outbreak spread rapidly across multiple continents [10]. The speed and scale of the transmission highlighted gaps in global surveillance and the vulnerability of populations without immunity due to the discontinuation of smallpox vaccination [11].

Before the 2022 outbreak, isolated cases of Mpox

had been reported outside Africa, primarily in travellers returning from endemic regions. In 2003, the USA experienced a small outbreak linked to imported animals, but it was swiftly contained. However, these isolated incidents did not significantly change global health policies or preparedness [11]. The 2022 outbreak differed in its sustained person-to-person transmission, raising alarms about the virus's potential to become endemic in non-African regions [9, 11].

The recent Mpox health emergency, particularly in the DRC, highlights concerns beyond sexual transmission, with a significant risk of wider transmissibility, especially among children. In the African context, clade I has predominantly affected the paediatric population. Notably, 29% of confirmed cases in the new region of the DRC involve sex workers, with 75% of cases in adults aged 18 or older. Interestingly, as seen with HIV in Africa, 50% of these cases are in women, indicating a broader demographic impact [12-15]. According to the Ministry of Public Health of the DRC, during the first 28 epidemiological weeks of 2024, 15 provinces (out of 26 of the country) have reported more than 11,806 cases, with more than 2,298 confirmed, also including 459 deaths, with provinces reported incidence rates over 33.14 cases/100,000 pop., such as Sud-Kivu, high mortality rates, such as Equateur province (17.41 deaths/100,000 pop.) and a case fatality rate (%CFR) of 20% for the provinces that have confirmed cases (Table 1).

On 15 August 2024, Sweden reported one imported case from Africa due to MPXV clade Ib (Figure 1). The case was an adult who returned from an area where clade Ib transmission was reported. The mode of transmission is under investigation. Contacts of the case have been informed and are being monitored [16]. Previously, and as of 8 August 2024, 22,662 confirmed Mpox cases have been reported by 29 European Union/ European Economic Area countries via The European Surveillance System (TESSy) as part of the outbreak driven by clade IIb (Figure 1). Most cases (93%) were reported during an intense circulation period in 2022. Globally, up to August 6, 2024, more than 122 countries have reported Mpox, for a total of 99,518 cases and 207 deaths [17].

The WHO categorises cases into suspected, probable, confirmed, and discarded, while the ECDC simplifies this to confirmed and probable. Definitions and contact tracing guidelines vary across

the four countries analysed, reflecting differing approaches to Mpox case management [18]. Mpox presents with symptoms similar to those of smallpox, though it is generally less severe. The incubation period ranges from 6 to 13 days, followed by a prodromal phase characterised by fever, headache, myalgia, and lymphadenopathy. A distinctive rash appears 1-3 days after the onset of fever, beginning on the face and extremities before spreading to other body parts. The rash progresses through macular, papular, vesicular, and pustular stages before crusting over and resolving within 2-4 weeks. However, during 2022-2023, many cases presented directly genital lesions without any prodromal period [19].

While most cases are self-limiting, complications such as secondary bacterial infections, respiratory distress, and encephalitis can occur, particularly in immunocompromised individuals [20]. Additionally, there have been reports of potential cardiac involvement in patients infected with Mpox [21].

A systematic review and meta-analysis revealed a hospitalisation rate of 7% for Mpox cases, with 15 reported deaths [22].

Histopathological examination of samples of patients infected with Mpox revealed consistent findings across all sites. A broad dermo-epidermal ulceration with a purulent base was observed, accompanied by necrotic keratinocytes and marked neutrophilic exocytosis. Additionally, the dermis exhibited an inflammatory infiltrate, primarily composed of CD3+ T-cells, with balanced CD4+ and CD8+ populations [23]. Transmission electron microscopy confirmed the presence of monkeypox virus-like particles at various stages of morphogenesis within the dermis and epidermis. These findings highlight the uniformity of histological damage caused by Mpox across different lesion sites [23].

No specific antiviral treatment for Mpox exists, and management is primarily supportive. Antiviral agents like tecovirimat or cidofovir, initially de-

Table 1 - Cumulated number of suspected and confirmed cases, % positivity, deaths, population, incidence and mortality rates and case fatality rates, at the provinces with confirmed Mpox cases in DRC during epidemiological weeks 1 to 28, 2024, reported by the Ministry of Public Health of DRC (<https://www.minisanterdc.cd/>).

Province	Cases		% Positivity	Deaths	Population*	Rates		
	Suspected	Confirmed				Incidence**	Mortality***	%CFR***
Equateur	5,356	485	9.06	298	1,712,000	28.33	17.41	61.4
Sud-Kivu	2,213	913	41.26	17	2,755,000	33.14	0.62	1.9
Sankuru	1,158	54	4.66	49	6,565,000	0.82	0.75	90.7
Sud-Ubangi	1,069	216	20.21	29	3,570,000	6.05	0.81	13.4
Tshopo	609	186	30.54	24	2,582,000	7.20	0.93	12.9
Tshuapa	410	238	58.05	24	1,789,000	13.30	1.34	10.1
Mongala	377	87	23.08	7	1,950,000	4.46	0.36	8.0
Maniema	195	60	30.77	1	2,654,000	2.26	0.04	1.7
Nord-Kivu	128	36	28.13	0	7,574,000	0.48	0.00	0.0
Nord-Ubangi	115	7	6.09	6	2,417,000	0.29	0.25	85.7
Bas-Uélé	87	4	4.60	3	1,250,000	0.32	0.24	75.0
Kasai	67	3	4.48	1	3,165,000	0.09	0.03	33.3
Kinshasa	43	4	9.30	0	13,916,000	0.03	0.00	0.0
Kwango	21	4	19.05	0	2,416,000	0.17	0.00	0.0
Lualaba	12	1	8.33	0	2,993,000	0.03	0.00	0.0
Total	11,860	2,298	19.38	459	57,308,000	4.01	0.80	20.0

*National Institute of Statistics of the Democratic Republic of the Congo. March 2021.

**Confirmed cases/Population x 100,000 pop.;

***Deaths/Population x 100,000 pop.;

****Deaths/Confirmed cases x 100.

veloped for smallpox, have shown some efficacy against Mpox in animal studies and are used in severe cases under compassionate use protocols [24, 25]. Vaccinia immune globulin (VIG) can be administered in cases of severe disease or complications. The smallpox vaccine, which provides cross-protection against Mpox, has been utilised in ring vaccination strategies during outbreaks [26]. Preventing Mpox transmission requires a multifaceted approach. In endemic regions, efforts should focus on reducing human-animal contact, particularly with potential reservoir species, and improving public health education about the risks of zoonotic diseases. In non-endemic regions, reintroducing smallpox vaccination, especially for high-risk populations, could provide significant protection. The 2022 outbreak underscored the need for robust surveillance systems, rapid diagnostic capabilities, and international collaboration to prevent the spread of Mpox [27].

The WHO's response to the 2022 Mpox outbreak was criticised for delaying declaring a Public Health Emergency of International Concern (PHEIC). Despite the rapid spread of the virus and the clear evidence of sustained human-to-human transmission, the PHEIC was not declared until July 2022, two months after the initial cases were reported outside Africa [28].

The 2022 Mpox outbreak is a stark reminder of the interconnectedness of global health and the need for proactive rather than reactive public health measures. The delayed response by international health authorities, particularly the WHO, highlights the critical importance of timely action in controlling emerging infectious diseases. Now, in 2024, it is critical to coordinate actions, invest in research, and enhance surveillance and clinical and molecular diagnostics, among other key aspects, including vaccination in risk groups.

The global health community must strengthen surveillance systems, invest in research on zoonotic diseases, including the One Health approach, and ensure that prevention and treatment strategies are accessible to all populations, especially those in endemic regions. Only through a coordinated, evidence-based approach can we hope to prevent future outbreaks of Mpox and other emerging infectious diseases.

Conflicts of interest

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