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Epidemiology, Virology, Transmission, Symptoms and Treatment of Mpox: A Review

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Abstract

Mpox (previously named monkey pox) is caused by infection with monkey pox virus, a member of the genus *Orthopoxvirus* in the family *Poxviridae*. On August 14, 2024, the World Health Organization (WHO) declared a Public Health Emergency of International Concern about the upsurge of Mpox cases in the Democratic Republic of the Congo (DRC) and a growing number of countries in Africa. The virus can be transmitted from animal-to-human, human-to-human and from a contaminated environment-to-human. Index cases are infected by direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals, including through their bite or scratch. Symptoms include; fever, intense headache, lymphadenopathy (swelling of the lymph node), back pain, myalgia (muscle ache) and an intense asthenia (lack of energy). The infection is also characterized by Skin eruption period where rashes appear in various stages often beginning on the face and then spreading elsewhere on the body including leg, trunk and palm. Vaccination remains the most effective method of preventing mpox. The paper review the epidemiology, virology, transmission, symptoms and treatment of mpox.

Keywords: Epidemiology; Mpox; Transmission; Treatment; Virus.

1. Introduction

On August 14, 2024, the World Health Organization (WHO) declared a Public Health Emergency of International Concern about the upsurge of Mpox cases in the Democratic Republic of the Congo (DRC) and a growing number of countries in Africa. This announcement followed the Africa Centres for Disease Control and Prevention's (Africa CDC) declaration of a Public Health Emergency of Continental Security on August 13. The significant increase of clade I Mpox cases, in both endemic countries (those that have previously had Mpox outbreaks) and non-endemic countries (those that have historically not reported Mpox outbreaks), threatens the health security of the region, as well as countries outside Africa. In addition, clade I Mpox has a newer sub-clade referred to as clade Ib. Both clade Ia and clade Ib are circulating in DRC and have been detected in neighboring countries and in Sweden and Thailand (one case each associated with travel to Africa with known clade I cases).

In 2022, the world experienced a global outbreak of clade IIb Mpox, which led to more than 95,000 cases across 115 non-endemic countries and continues to occur in the United States. The Biden-Harris Administration responded by ensuring the JYNNEOS Mpox vaccine was available to at-risk populations in the U.S. In February, as the clade I Mpox outbreak grew in DRC, the Biden-Harris Administration established an incident response structure across federal departments and agencies to ensure a coordinated response and to take a proactive approach to U.S. domestic preparedness for potential clade I Mpox cases. Clade I Mpox causes a higher number of severe infections and has a higher mortality rate than clade IIb Mpox [1].

2. Mpox Infection

Mpox (previously named monkey pox) is caused by infection with monkey pox virus, a member of the genus *Orthopoxvirus* in the family *Poxviridae*. There are currently more than 80 poxviruses known to science and these poxviruses have been isolated from different species of birds, insects, reptiles, marsupials and mammals. Poxviruses that may cause human disease include the smallpox (or variola) virus and molluscum contagiosum virus. The former was eradicated by 1980 by mass-vaccination programs. In addition, human disease can be caused by infection with other poxviruses such as orf, cowpox and Tanapox viruses. These viruses are harbored by different animal species

and may spillover to the human population (i.e. they are zoonotic viruses) when there is sufficient exposure. Orf, cowpox and Tanapox viruses are not highly transmissible from person-to-person [2].

Mpox was first discovered in 1958 in Denmark when two outbreaks of a pox-like disease occurred in colonies of monkeys kept for research, hence the name 'monkey pox.' The World Health Organization (WHO) has renamed monkey pox to mpox in 2022, following extensive public comment and in order to reduce stigma associated with the unfortunate naming. The first human case of mpox was recorded in 1970 in the Democratic Republic of Congo. Mpox has been historically reported from several countries from West and Central Africa (WCA). This distribution of mpox virus is attributed to the fact that it is naturally harbored by animals that are found in this part of Africa. It is believed that rodents, most likely certain species of squirrels found in the deep forested areas of this region of Africa, may be the natural host of the virus. Mpox infections in humans have historically been noted in these countries albeit at a relatively low level. Prior to the 1970s, it is suspected that infections were masked by smallpox (it appears clinically similar and may be misdiagnosed) and/or cases were low due to smallpox vaccine induced cross-immunity [3].

3. Virology of Mpox

Mpox is caused by Mpox virus, a member of the genus Orthopoxvirus in the family Poxviridae, is characterized by its brick-shaped or oval morphology with a diameter of~200–250 nm [4]. Its genome consists of a linear, double stranded DNA with a length of ~197 kb and encoding about 180 proteins [5]. Additionally, Mpox virus possesses dumb bell shaped nucleocapsid enveloped by ovoid lipid-containing particles (figure 1). The genomic structure of Mpox virus closely resembles that of other Orthopoxviruses, characterized by a highly conserved central core region, variable regions at the left and right ends and a tandemly repeated inverted terminal repeat [4].

The central core region of Mpox virus shares more than 90% sequence homology with other orthopoxviruses, particularly within the open reading frame (ORF) located between C10L and A25R [5]. Species and strain-specific characteristics of orthopoxviruses are often found in the variable regions at the ends of the genome. A better understanding about these ORFs may provide insights into its host tropism, pathogenesis, and differences in immune regulation [6]. Based on genomic and phylogenetic analysis conducted in 2022, the prevalent strain of Mpox virus was identified as belonging to the B.1 lineage of the West African clade. The B.1 lineage exhibits multiple mutations in genes associated with virulence, host recognition, and immune evasion [7]. In comparison to previously obtained complete genome sequences of Mpox virus isolated in Nigeria from 2017 to 2018, the Mpox virus strains that emerged in 2022 exhibited a higher number of single nucleotide polymorphisms (SNPs). The Mpox virus strain isolated in 2022 exhibit ~50 SNPs, indicating an approximately 6–12-fold increase in the predicted substitution rate of Mpox virus compared to the strains isolated from 2018-2019 (1–2 nucleotide substitutions per genome every year) [8]. The functional significance of these mutations is yet to be fully understood, but this high mutation rate may help explain the sudden appearance and heightened transmissibility of Mpox virus in non-endemic regions.

Figure-1. Structure of the intracellular mature orthopox virion [9]

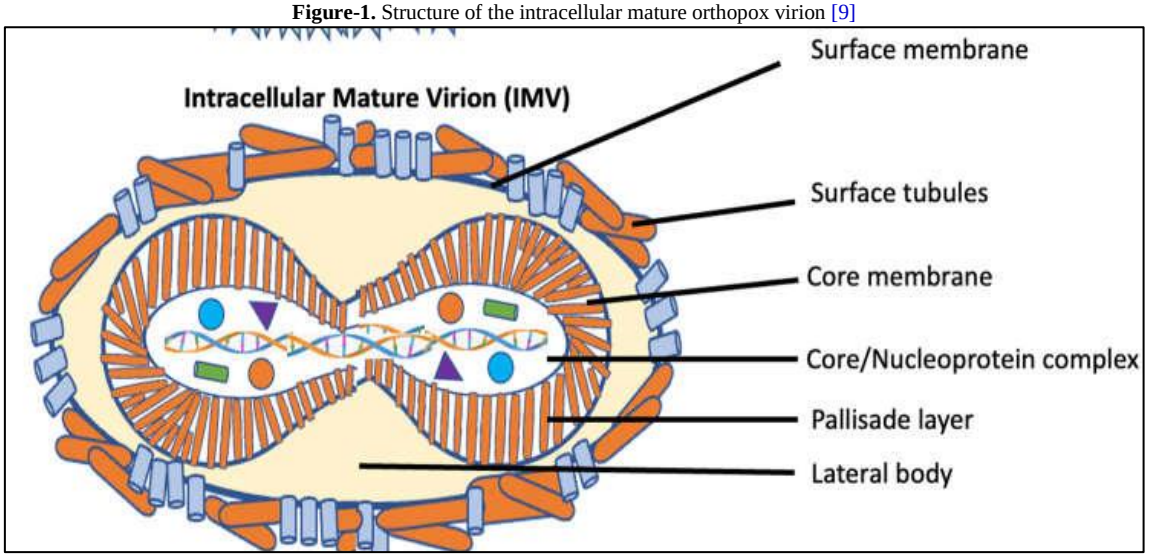
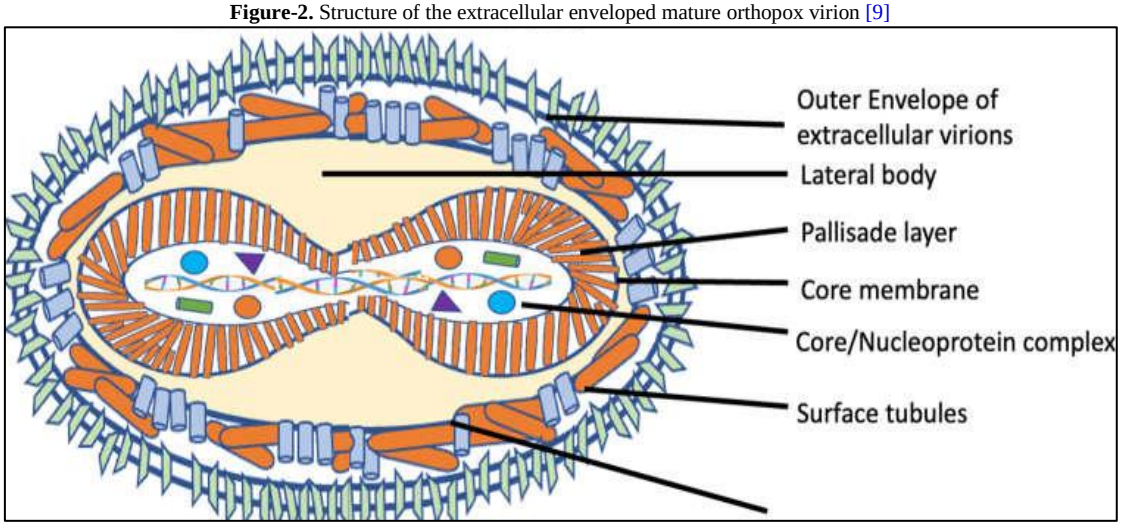


Figure-2. Structure of the extracellular enveloped mature orthopox virion [9]



4. Epidemiology of Mpox

The World Health Organization (WHO) declared the virus a "public health emergency of international concern" while emphasizing that Mpox is "not the new COVID". This is the second emergency alert relating to Mpox from the global health agency in two years. The current outbreak is triggered by Clade 1, believed to be a more serious variant that can spread through skin-to-skin contact. Mpox has been identified in Africa since 2022, originally traced to the Democratic Republic of the Congo (DRC). In 2023, a new strain of Clade 1 was discovered in DRC – Clade 1b.

A different outbreak of the virus's earlier Clade 2 variant is also spreading, although at lower levels, with more than 100 countries reporting infections by last month. Clade 2 is believed to cause milder infections and has a fatality rate of 0.2 percent compared with 3.9 percent for Clade 1. A new, potentially more deadly strain of the virus is rapidly spreading within Africa and has been discovered in Asia and Europe. Burundi, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Ghana, Ivory Coast, Kenya, Liberia, Mozambique, Nigeria, Pakistan, the Philippines, the Republic of the Congo, Rwanda, South Africa, Sweden, Thailand and Uganda have reported cases – a total of 18. Here's where Mpox disease has spread from January to August this year:

Africa: According to data from the Africa Centres for Disease Control and Prevention (Africa CDC, 2024) and the governments of Kenya, Mozambique, Uganda and the Ivory Coast, the Clade 1 variant of Mpox has been detected in the following countries this year:

Table-1. Clade 1 variant number of cases and death in Africa in 2024

S/N	Country	No. of cases	No. of death
1	Burundi	8	0
2	Cameroun	35	2
3	Central Africa Republic	213	0
4	Cote d'Ivoire	28	1
5	Republic of Congo	146	1
6	Democratic Republic of Congo (DRC)	13,791	450
7	Ghana	4	0
8	Liberia	5	0
9	Nigeria	24	0
10	Rwanda	2	0
11	South Africa	22	3
12	Uganda	4	0
13	Kenya	1	0
14	Mozambique	1	0

The DRC is experiencing the biggest outbreak of the disease ever recorded with thousands of people infected as of August 21. The government declared an epidemic in December 2022. Nearly all reported cases – 96 percent – across Africa are in the DRC, where children younger than 15 accounted for 60 percent of the cases, Africa CDC said. The new Clade 1b strain has been detected in countries neighbouring the DRC: Kenya, Rwanda and Uganda, which had not previously reported any cases since the outbreak began in 2022. So far, 541 deaths have been recorded from Mpox, with 535 in the DRC (97 percent). The Africa CDC does not classify deaths according to strain. In Ivory Coast, authorities said, the outbreak is linked to the 2022 Clade 2 variant.

Asia: The Philippines, Thailand and Pakistan reported new Mpox cases this month. In Thailand, authorities confirmed a new case of Clade 1b on Thursday, Asia's first case of the new strain. The individual, identified as a 66-year-old European male, reportedly returned from an unnamed African country currently experiencing a "large" outbreak of the Clade 1 variant. He reportedly does not have serious symptoms and was believed to have transited

through a Middle Eastern country en route to Thailand. In the Philippines, authorities said the milder Clade 2 variant has been confirmed in the most recent case there – a 33-year-old Filipino male with no travel history. The patient is the country's 10th confirmed case since 2022 and authorities say Mpox has likely been spreading quietly for a while. Pakistani authorities said its first patient reported this year is a male infected with Clade 2. However, authorities said last week they are trying to trace the patient, who is believed to have travelled to another province before the test results were released.

Europe: In Europe, Sweden recorded one case, zero deaths. The Sweden reported an Mpox case on August 15 which was confirmed to be the more serious Clade 1 variant. It is "highly likely" that Europe will record more cases of Clade 1 because of frequent air travel between Europe and Africa, according to the European Centre for Disease Prevention and Control. However, sustained transmission might be low in Europe if cases are quickly diagnosed and if testing, surveillance and contact tracing are used, the agency said. The European Union has ruled out closing its borders to hard-hit countries.

Americas: No countries in North or South America have reported new Clade 1 cases so far. However, they should be "alert" to possible Clade 1 and Clade 2 cases, the Pan American Health Organization said on August 9. The region reported more than 62,000 cases of the Clade 2 virus from 2022 to July 2024, including 141 deaths. There are no confirmed cases of Clade 1 in Oceania or the Middle East.

5. Transmission of Mpox

The virus can be transmitted from animal-to-human, human-to-human and from a contaminated environment-to-human. Index cases are infected by direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals, including through their bite or scratch. Human infections through the handling of infected monkeys, Gambian giant rats and squirrels have been documented in Africa, while eating inadequately cooked meat of infected animals has also been identified as a possible risk factor for transmission [10]. Human contact with materials contaminated with the virus can also lead to infection. The virus enters the body through broken skin (even if not visible), the respiratory tract, or the mucous membranes (of the eyes, nose, or mouth) [11].

Human-to-human (HHT) or secondary transmissions occur primarily through droplet respiratory particles requiring prolonged face-to-face contact, or by direct or indirect contact with skin lesions or body fluids of an infected person, and by contact with objects recently contaminated by patient fluids or lesion material (such as clothing or linens). There is limited evidence on the persistence of variola-related viruses on materials (that may act as fomites), under controlled environmental conditions, but there is evidence to suggest that vaccinia virus may persist from weeks to months underscoring the importance of environmental de contamination. During human monkey pox outbreaks, household members of active cases are at greater risk of infection due to their proximity, while hospital associated acquired infections have been noted in Democratic Republic of Congo as well as in the UK [12]. There is some suspicion that sexual transmission may be one route of person-to-person transmission, but there is yet to be evidence to support this [10]. Furthermore, transmission may also occur by inoculation or vertically via the placenta (congenital monkey pox) [10]. It is advised that affected individuals should avoid close contact with immune compromised persons (including those with HIV infection) until all crusts are gone [11].

6. Signs and Symptoms of Mpox

Clinical manifestations of mpox usually develop within 5–21 days of infection (incubation period), with infection usually mild-to-moderate in nature and can be divided into two periods.

• Invasion/prodromal period (0-5 days) with clinical manifestations of fever, intense headache, lymphadenopathy (swelling of the lymph node), back pain, myalgia (muscle ache) and an intense asthenia (lack of energy)

• Skin eruption period (within 1-3 days after appearance of fever) where rashes appear in various stages often beginning on the face and then spreading elsewhere on the body. The face (in 95% of cases), and palms of the hands and soles of the feet (in 75% of cases) are most affected. The evolution of the rash which occurs over a period of 10 days, progresses through the following stages: Maculopapular (lesions with a flat base), Vesicles (small fluid filled blisters), Pustules (pus-containing rash), Crust (dried blisters) and conjunctivitis (figure 3) [11]

The Nigeria outbreak showed that all parts of the body can be affected by monkey pox. However, the parts of the body most affected by rashes were in the following order from most affected to the least affected; face, legs (figure 4), trunk (figure 5), arms, palms (figure 6), genitalia and soles [12].

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Figure-3. Conjunctivitis (NCDC, 2020) [13]

Figure-4. Legs Rashes (NCDC, 2020) [13]

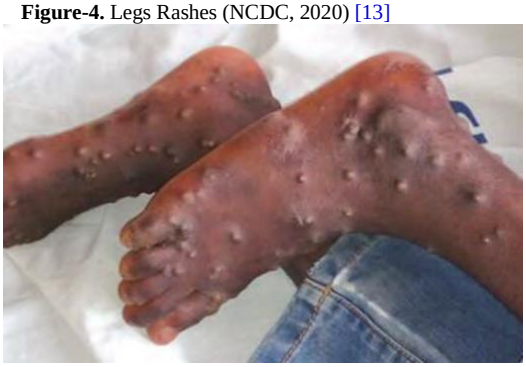

Figure-5. Skin Rashes (NCDC, 2020) [13]

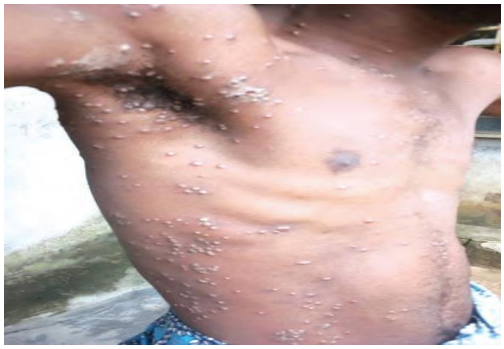

Figure-6. Palm Rashes (NCDC, 2020) [13]

7. Treatment of Mpox

Mpox outbreaks can be controlled by diagnosis and laboratory confirmation of cases. This allows for contact tracing and monitoring to enables the pro-active recognition of any other linked cases of mpox. It is recommended that confirmed cases of mpox isolate to ensure that risk of transmission is minimized. Isolation may be through self-isolation at home if circumstances allow, but cases may be isolated in hospital if so required. The World Health Organization did not recommend mass- vaccination as a measure to contain the outbreak. Nonetheless, the United States and certain European nations are providing smallpox vaccination to high-risk households and identified close contacts up to 14 days after exposure and gay and bisexual men with multiple sex partners (Imvanex, Bavarian Nordic, Kvistgrd, Denmark). Although endemic in West and Central Africa, Africa has only recently been donated mpox vaccine doses which will be for health care workers and highly affected areas. Although being endemic in West and Central Africa, Africa has just lately received donations of mpox vaccine doses to be administered to medical personnel and severely impacted regions [13].

The smallpox virus (virus that caused the now eradicated smallpox disease in humans) and mpox virus is closely related. Smallpox vaccination which was provided through mass-vaccination programs during the smallpox eradication program provides some level of cross-immunity to mpox. Residual immunity from smallpox vaccination in the population aged 40 (in South Africa smallpox vaccination was abandoned during 1980) and above may also contribute to preventing cases or lead to more mild infections. There is about 85 % protection offered by the smallpox vaccine (which was used to eradicate the human pox virus disease known as smallpox) and mpox. Currently the WHO did not recommend mass-vaccination as a measure to contain the 2022 outbreak. There are currently two mpox vaccines on the market: the ACAM2000 vaccine and the Jynneos vaccine. Vaccines can be administered either before or after a person is exposed to the virus, but for the maximum protection, vaccination prior to exposure is advised. A virus that has been altered in YNNEOS®, a modified vaccinia Ankara strain vaccination (MVA-BN), cannot replicate in the human body. Bavarian Nordic is the manufacturer of JYNNEOS®. For those 18 years of age and older, it is administered as 2 doses, at least 28 days apart. The live-attenuated smallpox vaccination ACAM2000TM also protects against mpox. Emergent BioSolutions produces ACAM2000TM. ACAM2000TM administration demands specialized training and resources. ACAM2000TM is not recommended for those who have a severe immunodeficiency, are pregnant or nursing, have a heart condition or have risk factors for a heart condition, have active eczema, or are younger than 12 months old. Based on its safety profile and ease of administration, JYNNEOS® is the chosen vaccine for usage [14].

8. Conclusion

The Mpox virus can be transmitted from animal-to-human, human-to-human and from a contaminated environment-to-human. Index cases are infected by direct contact with the blood, bodily fluids, or cutaneous or mucosal lesions of infected animals, including through their bite or scratch. Symptoms include; fever, intense headache, lymphadenopathy (swelling of the lymph node), back pain, myalgia (muscle ache) and an intense asthenia (lack of energy). The infection is also characterized by Skin eruption period where rashes appear in various stages

often beginning on the face and then spreading elsewhere on the body including leg, trunk and palm. Vaccination remains the most effective method of preventing mpox.

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