

# Monkeypox as a Re-emerging Zoonosis: Transmission Dynamics, and One Health Mitigation Strategies

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## ABSTRACT

Monkeypox (Mpox) is a re-emerging zoonotic disease that is caused by a double-stranded DNA virus, part of Orthopoxvirus genus. It has become an international public health emergency, and has been sent to World Health Organization as a Public Health Emergency of International Concern in 2022 and in 2024. This article reviews the viral pathogenicity, natural reservoirs and transmission of Mpox and discusses mitigation strategies based on One Health paradigm and in line with United Nations Sustainable Development Goals (SDGs). Other primates are incidental hosts, with wild African rodents as main reservoir species. Zoonotic spillover happens via direct contact with mucous membranes, exposure via percutaneous inoculation at hunt or butchering, respiratory droplets, and fomite contact. A comprehensive One Health framework (human health surveillance, veterinary biosecurity and environmental monitoring) with more specific SDG integration not only facilitates equitable distribution of resources, but also reduces stigma and boosts the world's resistance to future zoonotic events.

**Keywords:** Monkeypox, zoonotic disease, One Health, SDGs.

## INTRODUCTION

Zoonotic infections (zoonoses) are diseases caused by harmful pathogens like fungi, viruses, bacteria and parasites transmitted naturally from vertebrates to humans [1,2]. Zoonoses comprise more than 60% of all known human infectious diseases and about 75% of emergent human pathogens and constitute a major problem in human, animal and environmental health [3,4]. More than anything else, it is important to note that zoonotic diseases contribute to billions of illness cases each year, which results in significant morbidity and mortality, and exacerbates the healthcare systems of the regions during outbreaks [5,6]. Outbreaks often result in limiting agricultural trade, culling livestock, travel restrictions and substantial production losses – especially in vulnerable economies [7]. Pathogens are constantly spilling over into humans due to increased contact with animal reservoirs from human encroachment on wild areas, rapid urbanization, industrial farming, and climate change [8,9]. Monkeypox (Mpox) has become a known, ongoing global public health threat, illustrating the power of small, localized threats to quickly cross national boundaries. It has been known to occur in Central and West Africa, and many outbreaks of the virus have occurred across the world and have now become a public health priority [10]. This infection was discovered in animals in 1958 and in humans in 1970. The first animal isolation took place at Statens Serum Institute in Copenhagen, Denmark. The virus was found following two smallpox-like disease outbreaks among crab-eating Macaques (*Macaca fascicularis*) imported from Singapore for scientific studies [11].

Although the name suggests otherwise, monkeys are an accidental host: the main natural host is thought to be the small African mammal, particularly the rodent, the cord squirrel and Gambian marsupial rat

[12]. Human infection occurred in Basankoso Province, Democratic Republic of Congo (Zaire) for the first time. The virus was diagnosed in a 9-month-old infant admitted to a local hospital with smallpox like symptoms [13]. The virus was discovered during WHO's intensive smallpox eradication campaign, which had uncovered the possibility that the virus could pass from animal to human [14].

Mpox was declared a Public Health Emergency of International Concern (PHEIC) twice by the World Health Organization (WHO): first in July 2022 with the emergence of a new outbreak of Clade IIb in rapid global spread, and second in August 2024 when there was an increase in the mutated Clade Ib strain in Africa [15]. Its ability for sustained international transmission chains, however, demonstrates its multi-country outbreak potential and the importance of not neglecting the endemic infectious diseases [16]. This review aims to clarify the basics of monkeypox infection as a zoonotic infection and its control through One Health approach and in response to Sustainable Development Goals.

## Causative virus

Monkeypox virus (MPXV) is a large, enveloped, double-stranded DNA (dsDNA) virus and member of the genus Orthopoxvirus and family Poxviridae (Figure 1).

The MPXV genome is about 197 kilobase pairs (kb) long, with nearly 190 non-overlapping genes. The central genomic region consists of important genes that are strictly conserved among orthopoxviruses essential for the replication of the virus and the formation of its structure. Host range-determining and immune evading proteins are encoded in the terminal regions [17]. Virions are brick shaped or oval shaped and measure about 200 x 250 nm across. Contains a linear dsDNA genome packaged into a nucleoprotein core (dumbbell-shaped) that also contains viral transcription factors and enzymes (including viral DNA-dependent RNA polymerase) so that ssRNA transcription can occur in the cytoplasm, separate from the host cell nucleus [18].

Symmetrically positioned on both sides of the central core are the so-called lateral bodies, which contain proteins that include enzymes that participate in the early stages of host immune system modulation.

During the life cycle of MPXV, there are two different forms of the virus that are infectious:

**Intracellular Mature Virus (IMV):** Inner membrane-enclosed; released from cell upon cell lysis; mainly responsible for host-to-host transmission.

**Double-layered Envelope:** an inner lipid envelope and an outer lipid envelope with a distinct outer surface protein (A33R, B5R). This envelope is called an extra-cellular Enveloped Virus (EEV) and is important because it is responsible for systemic hematogenous spread within the host organism [19].

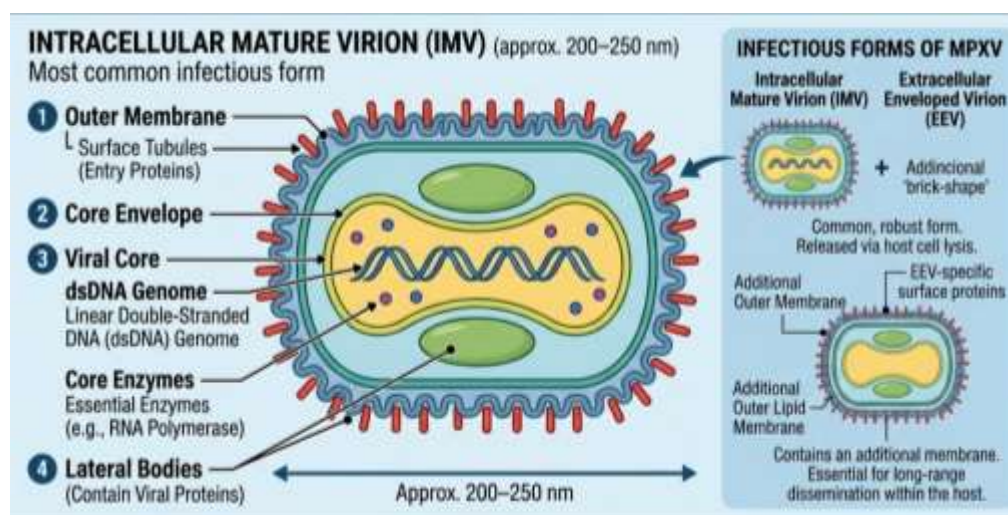


Figure 1: Monkeypox virus structure

## Natural Reservoirs

Although it's named after its most common association, non-human primates are not the primary natural reservoir; they are merely accidental hosts. Wildlife is the reservoir for the environmental persistence of MPXV and occurs in tropical rainforest biomes [20]. It is primarily maintained in wild in Africa by rodents and amplified by these rodents (Table 1).

- **Primary reservoirs:** Endemic viruses that are part of the African rodents' life cycles in rainforest environments. Rope squirrels (*Funisciurus*), tree squirrels (*Heliosciurus*), Gambian pouched rats (*Cricetomys*) and dormice (*Graphiurus*) are critical reservoir species.
- **Accidental Hosts:** Non-human primates and humans.
- **Human-rodent interaction by ecological spillover drivers:** deforestation, land conversion for agriculture, climate disruption and growth of human population in wildlife habitats [21].

Table 1: Natural reservoirs of rodent species

| Reservoir Species                                              | Geographic Habitat               | Tissue Localization & Shedding                                                                     |
|----------------------------------------------------------------|----------------------------------|----------------------------------------------------------------------------------------------------|
| <b>Rope Squirrels</b><br>( <i>Funisciurus</i> spp.)            | Central/West African rainforests | High levels in respiratory tissue, skin lesions and salivary glands, shed in saliva.               |
| <b>Sun Squirrels</b><br>( <i>Heliosciurus</i> spp.)            | Arboreal canopy zones            | Latent in lymphatic and epithelial tissues; low-level viral shedding [22].                         |
| <b>Gambian Pouched Rats</b><br>( <i>Cricetomys gambianus</i> ) | Burrowing forest/savanna beds    | Subclinical infection; viral persistence in mucosal membranes, urine and blood.                    |
| <b>Dormice</b> ( <i>Graphiurus</i> spp.)                       | Forested areas                   | High tropism for nasopharyngeal and cutaneous tissues; transmitted by skin abrasion or bites [23]. |

## Pathogenicity

MPXV enters the host and initiates a cascading pathophysiological process following entry. Surface glycoproteins interact with glycosaminoglycans in membrane and cellular entry and replication. The virus is taken up by macropinocytosis and/or membrane fusion, and its core is released into the cytoplasm of the host cell where it uses its own enzymatic system for early transcription and replication [24].

Dissemination Path includes:

**Primary Replication:** Infection starts at entry point.

**Lymphatic Spread:** The virus spreads through local lymph channels to regional lymph nodes, resulting in prominent lymphadenopathy.

**Primary & Secondary Viremia:** After viral amplification in the lymphatic system, there is a primary viremia, seeding of internal organs (liver, spleen). Replication following the initial infection leads to secondary viremia and virus dissemination to the skin and mucous membranes [25].

## Transmission Dynamics

MPXV may cause subclinical infections in rodents that are either mild or asymptomatic. This evolutionary change enables the virus to exist in wild populations without reducing the number of hosts [26]. Table (2) summarizes the type and route of MPXV transmission with potential risk exposure.

Table 2: Transmission dynamics of MPXV

| Type of Transmission                    | Transmission Route                                                                                               | Primary Risk Exposure                                                                     |
|-----------------------------------------|------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| <b>Zoonotic (Animal-to-Human)</b>       | Direct contact with blood or exudates from lesions or body fluids of infected animals; animal bites or scratches | Consumption of bushmeat, handling of infected rodents, butchering and skinning [27].      |
| <b>Direct Human-to-Human</b>            | Direct contact with infectious skin lesions, bodily fluids or respiratory secretions                             | Close physical contact, at home care or close clinical contact without PPE.               |
| <b>Trans-placental transmission</b>     | Mother-to-Fetus                                                                                                  | Congenital mpox, severe fetal complications, perinatal outcomes.                          |
| <b>Indirect Exposure Human-to-Human</b> | Contamination of materials (fomites) or length of direct contact with other people through respiratory droplets  | Using the same bedding, towels, clothes, or medical equipment of an infected person [28]. |

## Zoonotic Transmission Dynamics

The virus is transmitted to humans when they are hunted, handled or consume the blood, bodily fluids, respiratory droplets and/or the cutaneous lesions of infected rodents ( Figure 2).

**Direct Muco-cutaneous Contact:** Direct contact with the mucous membranes (eyes, mouth) or skin of an infected animal with the body, including contact with scabs, bodily fluids, or lesions of the skin [29].

**Per-cutaneous Inoculation:** When handling live or dead animals, there is an immediate route of viral entry through animal bites, scratches or abrasions of the skin.

**Dietary and Occupational Exposure:** Humans are exposed to high levels of viruses in animal tissues and blood through trapping, skinning, butchering of wild game (bushmeat) and consuming inadequately cooked meat [30].

**Respiratory droplets:** Exposed to live infected animals for a prolonged period of time can transmit through aerosols and mucosal secretions.

**Fomite Exposure:** Indirect contamination may occur via animal cages, bedding or soil contaminated with infectious urine, feces or saliva [31].

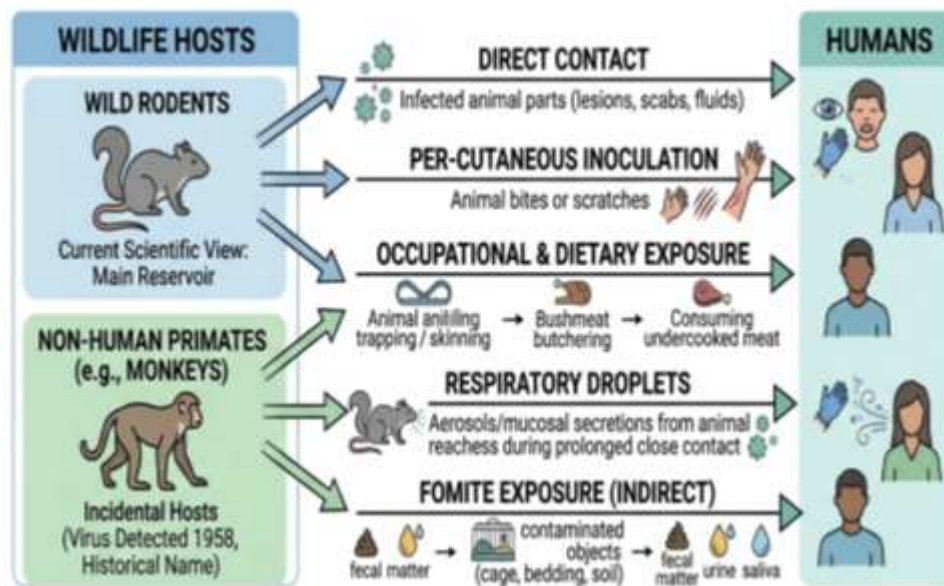


Figure 2: Zoonotic transmission of Monkypox infection.

### Primary Drivers of Rodent-to-Human Spillover

**Subsistence hunting:** Exposure to a high risk of physical contact when hunting and dressing small forest rodents for consumption.

**Peri-domestic contamination:** Excretions of wild rodents contaminate grain, water and surfaces in the home [32].

**Intermediate animal vectors:** Human owners of domestic animals can be secondarily exposed to the virus from domestic animals through intermediate animal vectors as captive rodents kept with domestic animals, such as prairie dogs [33].

### Concepts of One Health approach to MPXV

As zoonotic pathogen control is dependent on an integrated approach to control human, animal and environmental interfaces [34] as shown in Figure (3) :

**Human health:** Real-time diagnostic surveillance by PCR, ring vaccination with 3rd generation non-replicating vaccines (MVA-BN), distribution of antiviral therapeutics (Tecovirimat), and evidence-based risk communication campaigns [35].

**Veterinary health:** Developing systematic bio-surveillance in wild rodent populations (such as *Funisciurus* and *Heliosciurus* squirrels), curbing legal and illegal wildlife trade, setting up of biosafety measures in live-animal trade markets, and managing pet isolation measures during domestic outbreaks [36].

**Environmental health:** Use of environmental surveillance (wastewater testing by municipalities), monitoring land-use changes that brings deforestation and climate change that promotes the migration of rodents as reservoirs to the peri-urban habitat of humans [37,38].

**Integrated data governance:** Building collaborative multi-sectoral platforms to bring together clinical epidemiological monitoring, wildlife viral testing and environmental mapping into a single, early-warning system [39].

There is still a need for cross-sectoral collaboration and cooperation between global health actors, wildlife authorities, and local communities to stop the transmission cycle at the human-animal-environment nexus [40].



Figure 3: Principles of One Health approach to controlling monkeypox infection.

## Achieving Sustainable Development Goals with monkeypox

### Healthcare Systems and Equity (SDG 3 & 10)

The global response should address the challenge of health inequity by ensuring low- and middle-income countries, especially in hard-hit parts of Africa, have sufficient supplies of mpox vaccines, diagnostic test cartridges, and treatment. Infrastructure for achieving Good Health and Well-being (SDG 3) must be resilient, meaning the health system must be able to respond to acute mpox outbreaks without the disruption of routine, essential services for other conditions [41,42].

### 'One Health' Framework (SDG 17)

**Interconnected Health:** Since it is a zoonotic disease, a “One Health” approach is needed to mitigate its impact. Therefore an integrated human, animal and environmental health monitoring model required to gain an understanding of animal reservoirs and the potential for future spillover events.

**Global Collaboration:** Fulfilling Partnerships for the Goals (SDG 17) requires concerted action between international organizations (Africa CDC, WHO, UNICEF and others) to share surveillance data, set up joint incident management processes and guide financing for humanitarian support [43].

### Basic Living Conditions (Goal 1, 6 & 11)

**Sanitation and Hygiene:** Expanding access to clean water and sanitation (SDG 6) is a necessary, but not medical, need that enables communities to practice basic infection prevention and control measures that are essential to stop the transmission of mpox, as frequent hand washing [44].

**Reducing Overcrowding:** This infection is spreads quickly in areas where there is a high population density and a lack of infrastructure. The SDG targets of making human settlements safe and inclusive (SDG 11) and addressing extreme poverty and malnutrition (SDG 1) automatically decrease the vulnerability of population to viral outbreaks [45].

## Human rights (SDG 16)

**Rights-based strategies:** Public health interventions should be non-discriminatory and respect human rights; they should not stigmatize affected populations as this can foster the underground spread of the disease and hamper contact tracing.

**Community Engagement:** Local communities must be empowered to overcome the issues of misinformation, culture and vaccine hesitancy. Using local knowledge, gained over many years in dealing with other diseases, helps ensure that care and education is culturally appropriate [46] as illustrate in Figure (4).



Figure 4: Monkeypox infection and achieving Sustainable Development Goals.

## CONCLUSION

Monkeypox is a long-term biosecurity threat that is based on complicated ecological spillovers and general health care weaknesses globally. To successfully deal with this resurgent zoonotic disease, a paradigm shift from emergency responses to ecosystem management is needed. Implementation of the One Health approach allows for integrated clinical surveillance, comprehensive animal monitoring of animals and wildlife markets by public health officials and enhanced surveillance of land use changes to break the transmission cycle at the human-animal-environment interface. In addition, linking Mpox response measures to SDGs is a key to sustainable global resilience. Finally, it is vital that there is collaboration between sectors and equitable distribution of resources to stop future zoonotic outbreaks and protect global public health.

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