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MONKEYPOX: AN EMERGING ZOONOTIC DISEASE

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Monkeypox is a viral infectious disease, having zoonotic significance. The disease is caused by monkey pox virus, a double standard DNA virus, belonging to genus *Orthopox virus*, family *poxviridae*, and is closely related to the Variola (VARV), Cowpox (CPX), and Vaccinia (VACV) viruses. It is 200–250 nm brick-shaped or oval enveloped virus with characteristic surface tubules with dumbbell-shaped core component and the viral genome is of 190 kb (Figure 1). The prevalence of the disease is mostly observed in the tropical rainforests of West and Central Africa. The first outbreak was recorded in a monkey during 1958 as a small pox-like disease having fever, chills and rashes like symptoms. The first human case was reported in a 9-month-old child in the Democratic Republic of the Congo on September 1 1970 (Okyay *et al*., 2022). Recently In May 2022, the monkeypox disease outbreak was noticed in non-endemic countries and by June 15, 2022, the disease was reported in around 36 non-endemic countries. A total of 16,016 laboratory confirmed cases of MPXV infection and five deaths reported in 75 countries across all six WHO Regions as of July 22 2022. On 23rdJuly 2022, WHO declared it as public health emergency of international concern (PHEIC). In India outbreak was first reported on 14thJuly 2022 in Kerala.

Epidemiology

The virus is found naturally in West and Central Africa near tropical jungles. In Africa, the case fatality rate ranges from 1 to 10%, with young children dying at a higher rate. However, the case-fatality rate in non-immunized children who are against smallpox ranges from 1% to 14%. Till date, the disease has been endemic in nearly 11 countries of the Central

and Western African regions with thousands of case reports annually. In 2003, there was first-ever MPXV outbreak in nonendemic countries, like USA. World Health Organization classified the MPXV genome, into Congo Basin (Central African) clade designated as Clade one (I) and West African clade as Clade two (II) with two sub-clades IIa and IIb. Currently, the biggest outbreak came across 75 countries, for which the West African clade was mainly responsible. A total of 7892 no of cases were confirmed between January 1 to July 7 2022, which included three deaths, from 63 Member States in five World Health Organization (WHO) Regions (Lahariya *et al*., 2022).Most of the cases have been reported from WHO European region, however, some cases have also been reported from Eastern Mediterranean, Western Pacific Region and Americas region of WHO. In endemic counties like Nigeria the outbreak is underway since 2017. In India, two Monkeypox cases were confirmed through clinical-epidemiological history and laboratory investigation.

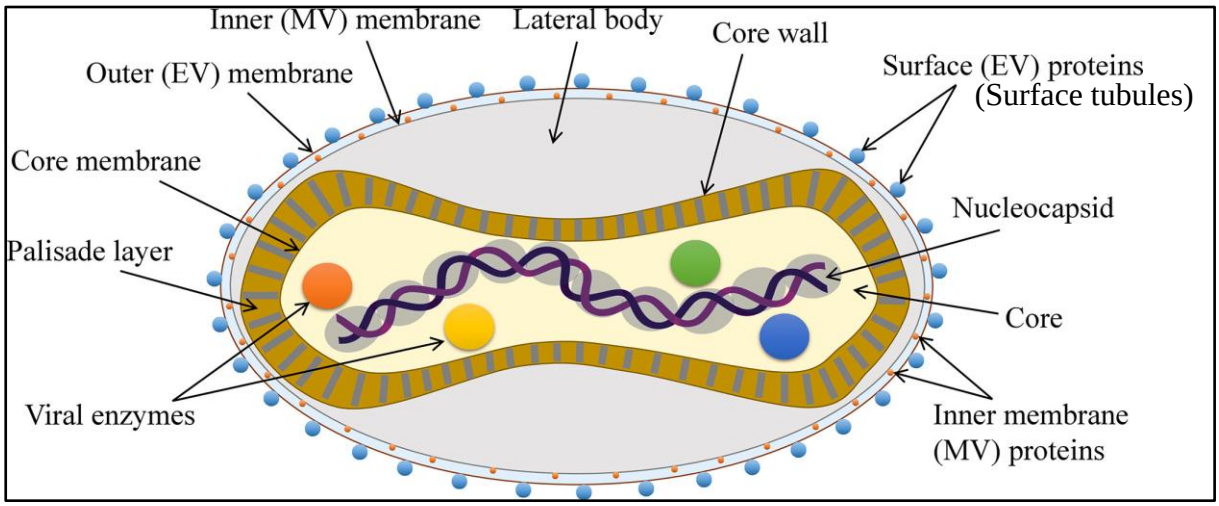

Figure 1. Structure of Monkey Pox Virus (MPXV)

Transmission

Monkeypox virus spread through direct contact with monkeypox lesions i.e., rash and scabs of clinically affected persons, often skin-to-skin contact, as well as contact with their saliva, upper respiratory secretions, and mucous membrane of the anus, rectum, or vagina. Congenital transmission can also occur through the placenta from mother to foetus. While close physical contact is a well-known risk factor for transmission (Ranjan *et al*., 2022) in endemic areas. Animal-to-human transmission occurs by bite or direct contact with the infected animal's blood, body fluids, or lesions. However, in non-endemic areas, transmission can occur by transferring infected animals from endemic to non-endemic areas (Figure 2).

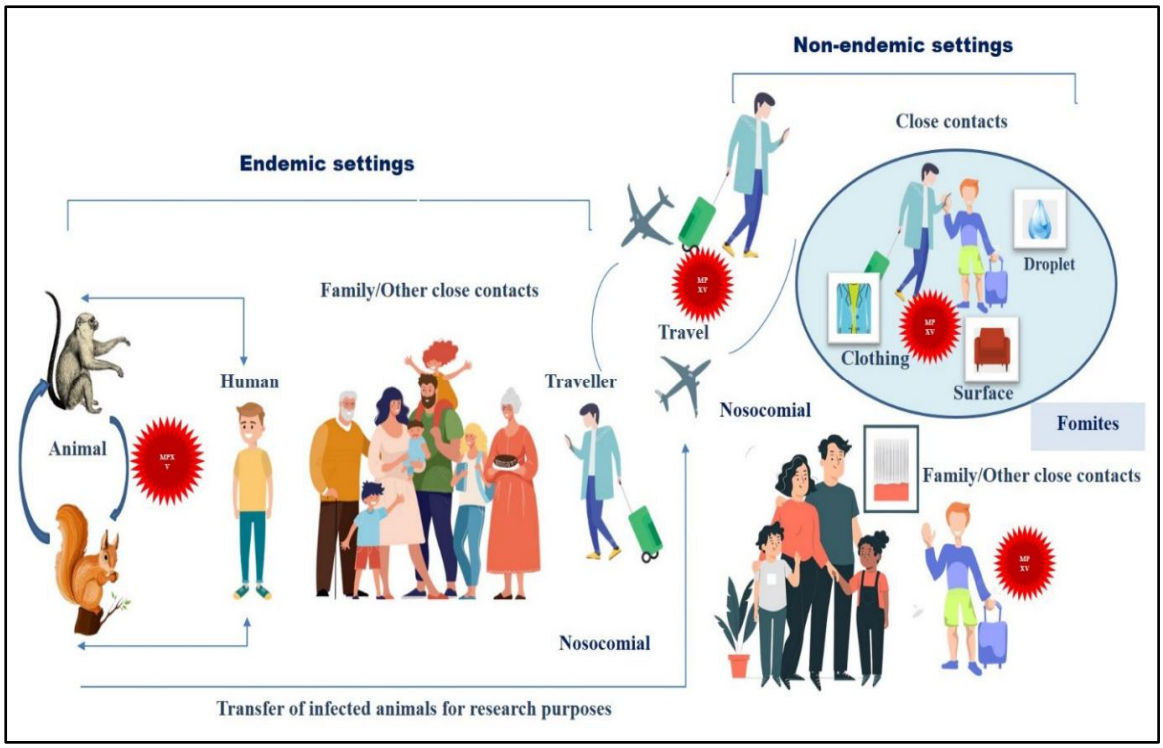

Figure 2. Transmission of MPXV
(adopted from Ranjan *et al.*, 2022)

Pathogenesis

MPXV transmission is similar as that of smallpox virus, that infiltrates the host system. Virus replicates atthe inoculation site, mostly respiratory or pharyngeal mucosa. After replication virus enters into blood stream resulting in primary viraemia (Figure 3). The virus spreads to the local lymph node via monocytic cells and replicates further. Following replication, the virus enters the bloodstream, causing secondary viraemia, and the virus spreads to other organs, such as the skin, lungs, and gastrointestinal tract, where clinical signs and symptoms of the disease manifest (Ranjan *et al.*, 2022).

Clinical Manifestation

The incubation period of the virus is usually from 6 to 13 days. The disease has two phases, first is invasion phase that is characterized by fever, headache, myalgia, weakness and lymphadenopathy, a characteristic feature of monkeypox infection that distinguishes it from chickenpox or smallpox infection. Second one is skin eruption phase, which usually starts within 1-3days of the appearance of fever. The skin lesions are mostly appeared on the face (95%) and extremities like palm and feet. Other than these areas, oral mucous membranes, genitalia and conjunctivae as well as corneais also affected. In the early stages,

the lesion shows central epidermis necrosis and may extend to the superficial layer of dermis in humans. Later on, a necrotic area surrounded by edema and clefts develops in the interstitial space of cells, and cellular debris and fluid are deposited in this space. The rash first appear as macules, sequentially progress towards papules, vesicles and pustules, and then forms crusts which dry up and fall off. It is usually a self-limited disease with the symptoms lasting from 2 to 4 weeks. However, in some cases bronchopneumonia has been reported in humans (Okyay *et al.*, 2022).

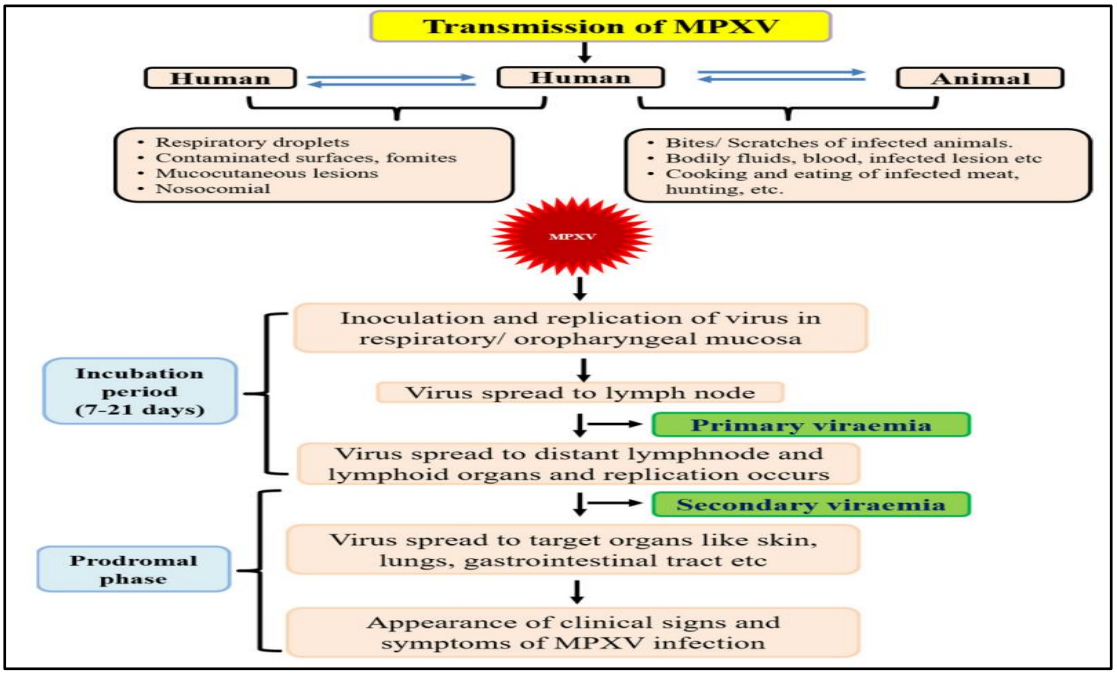

Figure 3.Pathogenesis of MPXV infection
(adopted from Ranjan *et al.*, 2022)

Diagnosis

Diagnosis is done through clinical signs and molecular assays like PCR is the gold standard for laboratory diagnosis. A generic PCR test for *Orthopox* virus is carried, especially from the blister fluid of the vesicular lesions in 97% cases. In addition to that, haemagglutination inhibition assays, electron microscopy, ELISA, Western blotting, or immunohistochemistry are also used for confirmation.

Therapeutics and Prophylactics

Drugs like tecovirimat (TPOXX, ST-246), Cidofovir and Brincidofovir have been used (Choudhary *et al.*, 2022). Tecovirimat was FDA approved for treatment of small pox but can be administered under "Expanded Access Investigational New Drug" (EA-IND) protocol.

Though Cidofovir and Brincidofovir are not FDA approved for monkey pox, but are used for treatment. Vaccination against monkeypox with vaccinia virus (a live attenuated vaccine against the smallpox virus) is about 85 % effective. JYNNEOS™ (also known as Imvamune or Imvanex) is a live vaccine approved by FDA, produced from the strain Modified non-replicating Vaccinia Ankara-Bavarian Nordic (MVA-BN). ACAM2000 also is a live vaccinia virus available under EA-IND for monkey pox.

Conclusion

Every country requires proper preparedness and quick response to handle such outbreaks. The outbreak readiness measureslikevirus isolation facilities, equipment's and reagents for laboratory diagnosis and, dedicated beds, training of group of health care workers as members of rapid response team (RRT) in standard elements of care should be emphasized. Implementation of strict surveillance system, especially for travellers coming from different countries as well as the building of containment zones for the identified suspected cases should also be prioritized. The scientist needs to understand the epidemiology, mutations, or changes that is occurring in virus as well as to focus on the development of vaccines and drugs against the re-emerging virus.

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