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"Monkey Pox: A Review Of The Current State Of Knowledge"

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Abstract: Monkeypox is a zoonotic disease caused by the Monkeypox virus, which belongs to the Orthopoxvirus genus. This review aims to provide an overview of the current state of knowledge on Monkeypox, including its epidemiology, clinical features, transmission, diagnosis, treatment, and prevention. We will also discuss the recent outbreaks and the global response to the disease. Additionally, we will highlight the gaps in our understanding of Monkeypox and suggest areas for future research.

Keywords: Monkeypox, Orthopoxvirus, zoonotic disease, epidemiology, clinical features, transmission, diagnosis, treatment, prevention.

INTRODUCTION

Monkey pox virus (MPXV) is a zoonotic orthopox virus closely related to the variola virus (which causes smallpox) and vaccinia virus (used in the smallpox vaccine). The virus was first discovered in 1958 in captive monkeys, but it didn't get much attention until occasional human cases started to appear in the Democratic Republic of the Congo (DRC) in 1970. After that, outbreaks of monkey pox have occurred in non-endemic areas, posing a threat to public health. However, the disease has remained endemic in some parts of West and Central Africa.

VIROLOGY AND STRUCTURE

Monkey pox is a double-stranded DNA virus belonging to the Orthopox virus genus in the Poxviridae family. There are two clades of MPXV: the West African clade, which tends to produce less severe disease, and the Central African (Congo Basin) clade, which has a greater fatality rate. About 200 proteins are encoded in the about 197 kb viral genome, some of which are involved in immune evasion.

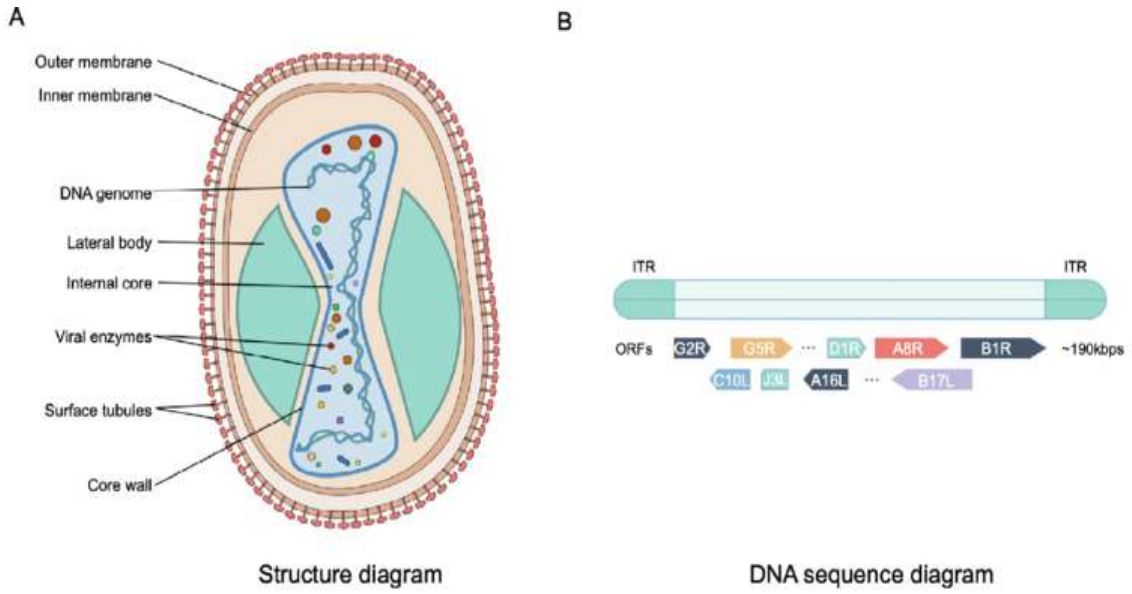

Fig1:- Structure of Monkeypox virus

https://www.researchgate.net/publication/363637385/figure/fig1/as:11431281090853894@1666201211292/virological-characteristics-of-monkeypox-virus-mpxv-a-structure-of-two-mpxv.png

TRANSMISSION

Primarily a zoonotic illness, monkey pox is spread from animal to human via direct contact with diseased animals' bodily fluids or rodents and primates. Although it happens less frequently, contact with lesions, respiratory droplets, and contaminated bedding can all lead to human-to-human transmission. The most important risk factor for transmission during the rash phase is thought to be close contact with an infected person. Additionally, the virus can spread vertically from the mother to the developing foetus, which could lead to congenital infection.

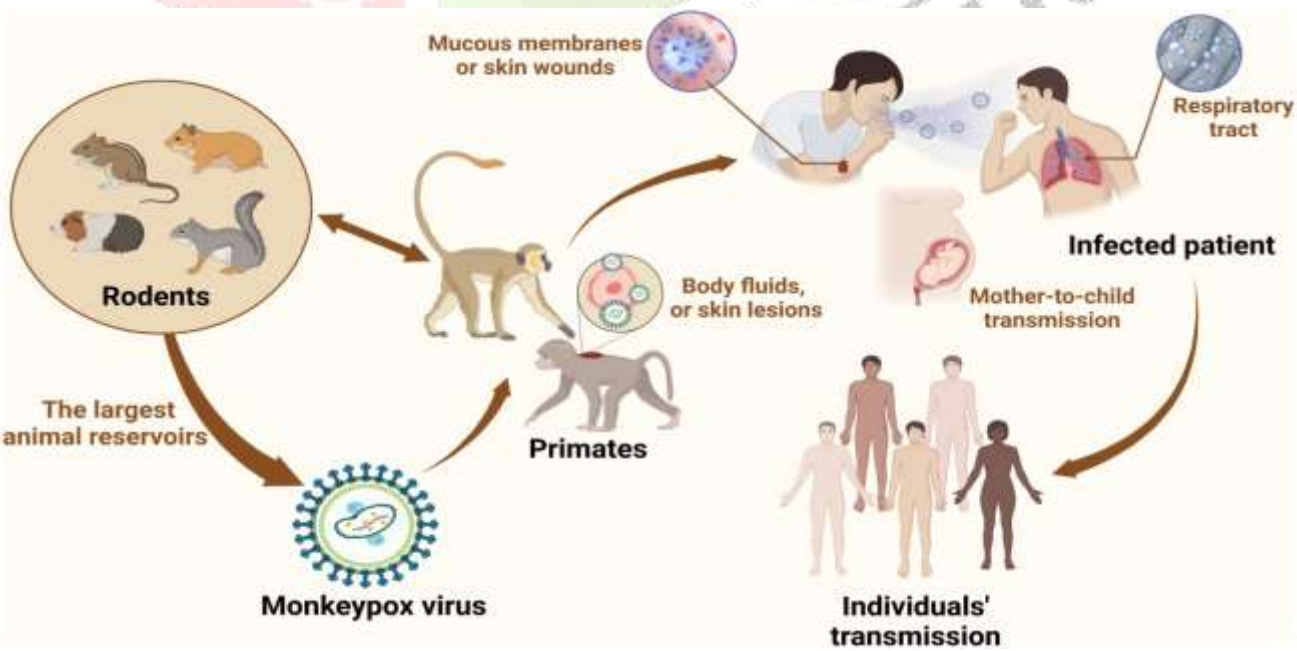

Fig 2:- Transmission cycle of monkey pox
https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2023.1132250/full

MPV is an enveloped DNA virus belonging to the Poxviridae family, and smallpox is also one of the most prevalent viruses in this family. Wildlife trafficking, habitat degradation, and climate change contribute to the transmission of MPV from new species to other species and increase the bond between people and animals. In the case of wildlife trafficking and illegal hunting, animals are caught, trapped, transported, and sold as food, medicine, and pets. Wildlife trade markets promote disease dissemination, making it possible for viruses from many neighboring species to jump the species barrier. Animal-to-human transmission is mediated by bites, scratches, and slaughtering. Human-to-human transmission occurs through close contact with infected people, such as through respiratory droplets and skin contact, especially MSM. The virus can remain on fomites, such as bedding, linen, and clothes.

CLINICAL PRESENTATION

The incubation period for monkey pox is five to twenty-one days. Although usually milder, symptoms are similar to smallpox. Usually, the illness begins with vague symptoms like fever, headache, aches in the muscles, and lymphadenopathy. A recognizable rash that develops from macules to papules, vesicles, and pustules, finally crusting and healing. Before spreading to other areas of the body, the rash frequently begins on the face and extremities.

Fig 3:- Clinical features of monkey pox
https://www.medicoverhospitals.in/diseases/monkeypox-disease/

The disease ranges in severity; the West African clade has an approximate 1% case fatality rate, whereas the Congo Basin clade is linked to more severe consequences and a 10% case fatality rate. Children and those with compromised immune systems are more vulnerable to serious illness.

A Times of India study states that historically, the case fatality rate from monkeypox in India has been as high as 11% in the general population and higher in youngsters. The case fatality rate has been between 3 and 6 percent recently.

Fig:4 A news report from Times of India
https://timesofindia.indiatimes.com/city/mumbai/monkeypox-ward-ready-city-hosps-told-to-be-vigilant/articleshow/91752455.cms

Diagnosis

Since the clinical presentation of monkeypox might overlap with other diseases including chickenpox, measles, or smallpox, laboratory confirmation is necessary for the diagnosis. Polymerase chain reaction (PCR) testing, which finds viral DNA from lesion swabs or crusts, is the gold standard for diagnosis. Though they are less frequently employed, further diagnostic techniques include serological testing, electron microscopy, and virus isolation.

Epidemiology

Up until recent international outbreaks in 2022, monkeypox was mostly limited to West and Central Africa. The Democratic Republic of the Congo, Nigeria, and other nations in the region are home to endemic cases of the virus, which occasionally break out as a result of human contact with wildlife. There are worries regarding the possibility of long-term transmission outside of Africa when cases from the 2022 worldwide outbreak were recorded in non-endemic nations in Europe, North America, and Asia. These epidemics have been attributed to various factors, including increased travel worldwide, lowered immunity as a result of the smallpox vaccination's discontinuation, and altered human-animal relations.

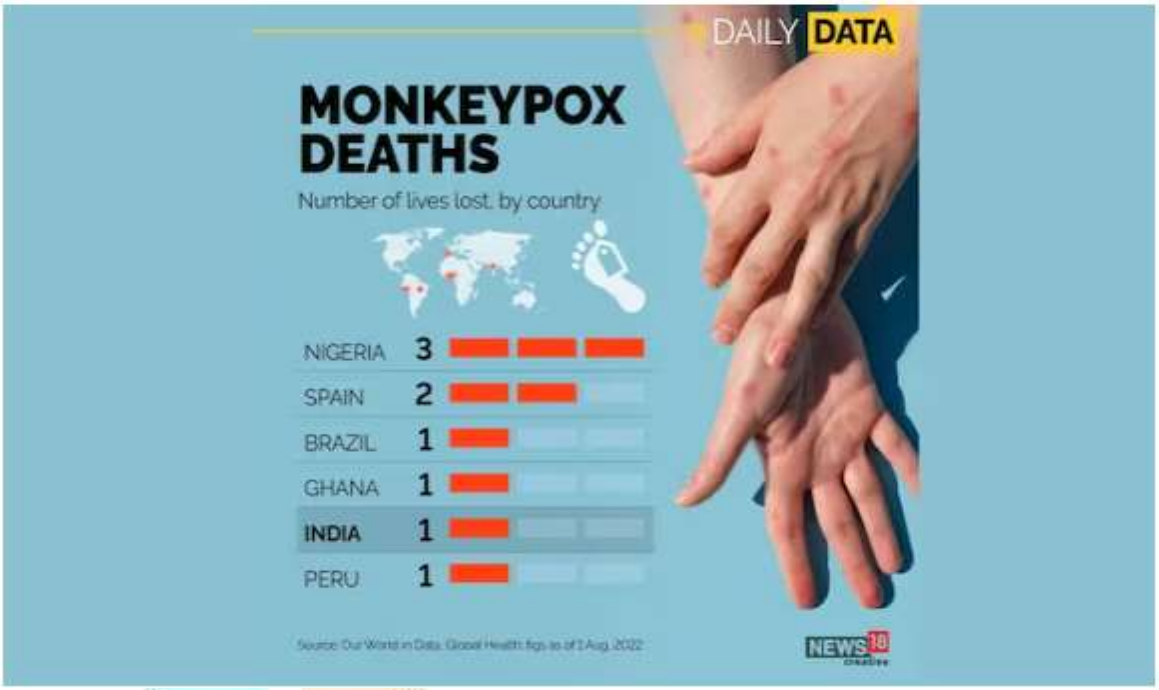

Fig:5 Global data depicting death rates from monkey pox

https://www.cnbctv18.com/healthcare/monkeypox-cases-in-india-list-of-states-that-reported-infection-14237672.htm

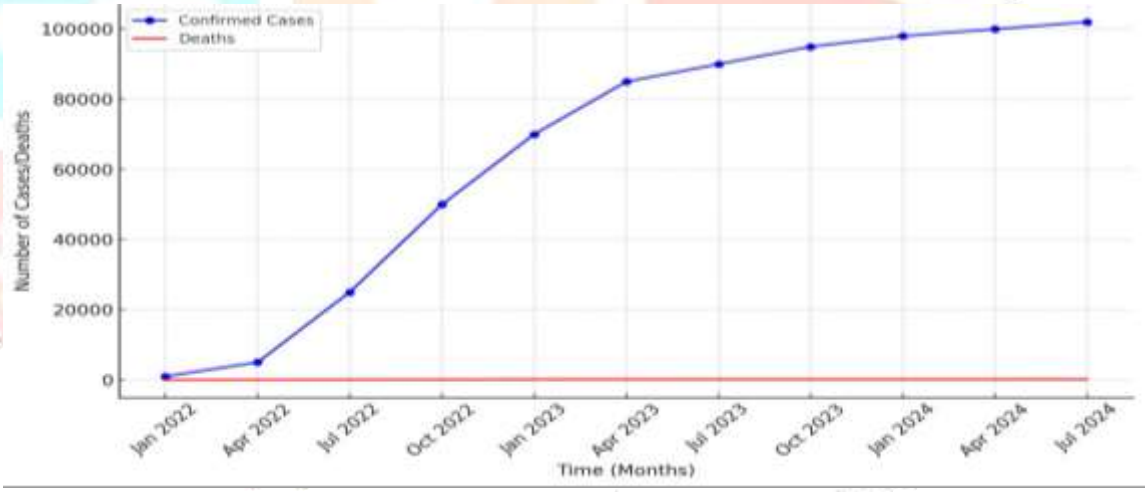

Fig 6: Global epidemiology of Mpox Virus (2022-2024)

According to the National Centre for Disease control, Directorate General of health Services, Government of India On 27th March 2024, the last case was also reported from Kerala. Total 30 laboratory confirmed cases were reported from Kerala (15 cases) and Delhi (15 cases). Self- reporting to the health care provider has been the modality for case detection in India. There are no reported cases of Mpox in India as of now.

Prevention and Control

Vaccination against smallpox provides cross-protection against monkeypox due to the antigenic similarities between the two viruses. The cessation of routine smallpox vaccination following the eradication of smallpox has left a large portion of the global population susceptible to monkeypox infection. Vaccinia-based vaccines, such as ACAM2000 and JYNNEOS (also known as Imvamune or Imvanex), have been used in outbreak settings to control the spread of monkeypox.

Preventive strategies also include minimizing contact with wild animals, especially in endemic regions, and using personal protective equipment (PPE) for healthcare workers treating infected patients. In outbreak settings, ring vaccination (vaccinating close contacts of confirmed cases) has been employed as an effective containment strategy.

Treatment

Currently, there is no specific antiviral treatment approved for monkeypox. However, antivirals used for smallpox, such as tecovirimat (TPOXX) and cidofovir, have shown promise in treating severe monkeypox cases. Supportive care, including hydration, pain management, and treatment of secondary bacterial infections, is essential in managing monkeypox patients.

Table 1 **list of treatments for monkeypox management**

S.NO	TREATMENT	ROUTE	DOSE	CLINICAL EFFICACY	ADVERSE EVENTS	CONTREAINDICATIONS	USE IN SPECIFIC POPULATION
1	**Vaccinia Immune Globulin Intravenous**	**IV**	Adults:6000 U/kg (9000 U/kg might be taken into consideration if the patient doesn't respond to the first dose); Pediatrics: Children should not use this medication because it has not been proven safe and effective in people under the age of 18	Passive immunity is provided by antibodies derived from the combined human plasma of people who have received the smallpox vaccination	Dizziness, rigors, nausea, headache	An IgA deficit with antibodies against IgA, a history of IgA hypersensitivity, a history of severe systemic or anaphylactic reactions to human globulins, and isolated vaccinia keratitis	Use caution in pregnant women and patients with renal insufficiency
2	**Tecovirimat**	**PO,IV**	For adults, take 600 mg twice daily for 14 days. For children (13 kg to less than 25 kg), take 200 mg BID for 14 days. For those between 25 and 40 kg, take 400 mg BID for 14 days. For those over 40 kg, take 800 mg BID for 14 days. 14 days at 600 mg twice a day	Restrain orthopoxvirus VP37 envelope wrapping protein	Headache, nausea, abdominal pain, vomiting	Have not reported	PO: Hepatic/ renal adjustment not needed. IV: should not be administered to patients with severe renal impairment
3	**Cidofovir**	**IV**	5 mg/kg once weekly for two	Selectively inhibits	Diarrhea, nausea,	Serum creatinine > 1.5	It is required to change the

			weeks, followed by 5 mg/kg IV once every other wee	orthopoxvirus DNA polymerase-mediated viral DNA synthesis by cellular phosphorylation	vomiting, and abdominal pain	mg/dL; urine protein ≥ 100 mg/dL (≥ 2+ proteinuria); history of clinically severe hypersensitivity to probenecid or other sulfa-containing drugs; CrCl ≤ 55 mL/minute	dosage based on renal function
4	**Brincidofovir**	**PO**	Adults over 48 kg should take 200 mg once per week in two doses. Adults and pediatric patients between 10 kg and 48 kg should take 4 mg/kg of oral suspension once per week in two doses. Pediatric patients under 10 kg should take 6 mg/kg of oral suspension once per week in two doses	Cidofovir diphosphate selectively inhibits orthopoxvirus DNA polymerase-mediated viral DNA synthesis	Fever, infection, proteinuria, iritis, hypotony of the eye, decreased serum bicarbonate, uveitis, neutropenia, nephrotoxicity	Have not reported	Not recommended in pregnant and breast-feeding women.
NOTE:-		BID twice a day, IV intravenous, PO per os (orally), CrCl creatinine clearance, and DNA deoxyribonucleic acid.					

Challenges and Future Directions

Several challenges remain in controlling monkeypox, including underreporting in endemic regions, limited access to diagnostic tools, and the lack of widespread vaccine availability. The recent outbreaks in non-endemic regions highlight the need for improved surveillance, rapid diagnostics, and international cooperation in monitoring and controlling the disease.

In addition, further research is needed to better understand the virus's reservoir hosts, modes of transmission, and mechanisms of immune evasion. The development of more effective vaccines and treatments remains a priority in preventing future outbreaks.

Conclusion

Monkeypox, once a neglected tropical disease confined to certain regions of Africa, has emerged as a global health concern. While the disease is less severe than smallpox, its potential for spread and significant morbidity, especially in vulnerable populations, requires sustained efforts in surveillance, vaccination, and treatment development. With the increasing threat of zoonotic diseases due to human-wildlife interaction, the global health community must remain vigilant in addressing monkeypox outbreaks and preventing further escalation.

As of 2024, the global epidemiology of mpox (monkeypox) continues to show regional variations with significant cases reported in both Africa and other parts of the world. From 2022 to mid-2024, over 102,000 confirmed cases were documented across 121 countries, with 219 deaths globally. The virus remains concentrated in certain clusters, with Africa, particularly the Democratic Republic of Congo (DRC) and neighboring nations, reporting a significant share of cases, particularly of Clade I. Other regions, including Europe and the Americas, continue to report sporadic cases of Clade II, but at a much lower rate than during the initial outbreak of 2022-2023.

The virus's evolution has been relatively stable, with minimal genetic changes observed in Clade IIb, particularly lineage B.1, the primary variant involved in the global spread outside of Africa. Despite a decrease in cases in some regions in 2024, ongoing surveillance remains critical to monitor any potential resurgence or mutations that could impact transmission dynamics.

In the U.S., the CDC continues to focus on improving detection systems, particularly for clade I cases, and enhancing vaccination efforts for high-risk groups. In Africa, outbreaks remain concerning, with mortality rates as high as 2.9% in affected regions .

A progressive loss of smallpox immunity may account for part of the increase in monkeypox prevalence in some endemic locations of the illness. However, the current Pandemic is a pertinent reminder that the development of viruses is an ongoing, limitless occurrence that is oftentimes unexpected in its beginning, purpose, and scope. There is need to gain a deeper comprehension of immunization.

This review provides an overview of the monkeypox virus, including its virology, epidemiology, clinical features, and strategies for prevention and control.

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