

Monkeypox and Monkey fever: Basic understanding for better community participation in disease control

Abstract

Currently, Monkeypox is a threatening viral disease terminology around the world that worries the global community after the Coronavirus pandemic. Beyond the woods of central Africa, where cases were first discovered, the geographic distribution of monkeypox cases has extended to other parts of the world including India, where cases have been imported. Under these circumstances, public confusion is noticed between Monkeypox and Monkey fever across southern parts of India. Monkeypox and Monkey fever (Kyasanur Forest Disease) are categorized as potential emerging or reemerging Zoonotic diseases of humans and are fundamentally having clear-cut differentiation in their causative agent, clinical symptoms, and pathogenesis. Hence, it is important to clarify and eliminate the confusions which would have tremendous and dangerous public health impacts. As defined by the Global Burden of Disease Study, Emerging Infections (EIs) are those that have recently appeared in a population or previously existed but are now gaining in prevalence or geographic spread rapidly. A disease emerges from the interactions between rapidly evolving infectious agents and the environmental changes and changes in human behavior that provide these agents with favorable ecological niches. This review attempts to differentiate between the two emerging infections - Monkeypox and Monkey fever which are affecting a significant group of the population worldwide and provides a comparative picture of both the diseases towards developing adequate awareness among the public and expects to complement the community-based future control measures.

Keywords: Zoonotic diseases, Monkeypox, Monkey fever, Emerging, Reemerging

Introduction

The monkeypox virus (MPXV), is a viral zoonotic pathogen that causes typical illness among humans which are termed monkeypox (MPX). MPXV is categorized under the Orthopoxvirus genus belonging to the Poxviridae family[1]. Monkeypox virus is similar to the virus causing smallpox, chickenpox, and cowpox of the same Orthopoxviridae[2]. On the other hand, Kyasanur Forest Disease (KFD) another popular terminology among public health authorities is an emerging virus zoonosis, is caused by the Kyasanur Forest Disease Virus (KFDV), which belongs to Flaviviridae[3].

Monkeypox virus is a brick-shaped virus enveloped with linear double-stranded DNA of around 197 kb size[4]. KFD virus is a positive-stranded RNA virus[5] that is nearly 11 kb in length [6] According to the EU's "high threat" category of biodefence, MPXV falls under the "biosafety level 3"[7]. KFDV is considered a highly pathogenic agent classified under BSL- 4[8]. As of 2017, KFDV has been classified with Risk Group 4 microorganisms in "Regulations and Guidelines on Biosafety of Recombinant DNA Research and Biocontainment."

A vesico-pustular lesion of an infected cynomolgus monkey was the first instance of Monkeypox being isolated in 1958 from Denmark and Zaire, then known as the Democratic Republic of Congo (DRC), first reported the disease in 1970 in a 9-month-old child[9]. The KFD virus was discovered in 1957 in the Kysanur forest in Soraba, a place coming under the Shimoga district of Karnataka, India isolated from sick black-faced langurs[3].

An epidemic of human monkeypox has recently occurred in the African clime, where it has dominated for decades. Human monkeypox was first isolated in the western hemisphere in 2003[10]. Due to the interaction between humans and monkeypox carrier animals, the disease is spreading more rapidly followed by ecosystem degradation and a high rate of human-to-human transmission[10].

Kysanur forest illness is known as "Monkey fever" because of its close association with monkey fatalities[11]. On the other hand, scientists came up with the name Monkeypox in 1958 after they first detected pox-like symptoms in colonies of monkeys kept for research in a laboratory. Researchers from thirty countries requested the name to be changed in a paper published on June 10 entitled "Urgent need for a nondiscriminatory and non-stigmatizing nomenclature for monkeypox virus". In their opinion, the current name doesn't comply with WHO guidelines that urge against using geographic areas and animal names during nomenclature[12]

Host and Transmission

For Monkeypox, non-human primates, rodents, Gambian pouched rats, rope squirrels, dormice, and tree squirrels are found to be the most substantial reservoirs as they serve as a source of sustenance in some regions of the world[13] and humans are considered the incidental hosts[14] whereas in case of KFD, porcupines, rats, squirrels, mice, shrews, and cattle act as the reservoir host whereas Bonnet monkey with the red face (*Macaca radiata*) and Hanuman langur with black face (*Semnopithecus entellus*) is acting as the amplifying hosts, and humans are considered an accidental host[15]. Fig.1 schematically illustrate the comparison between the spread of Monkey fever and Monkeypox infection.

Infected reservoir creatures are the primary source of Monkeypox transmission. Saliva/respiratory excretions, lesion exudates, and crust residue are believed to be the primary sources of transmission. Viruses shed through feces could also be a transmission source[16]. Human-to-human transmission is possible for monkeypox through pus, skin lesions, and scabs or rashes. The transmission of monkeypox from person to person, including nosocomial and home transmission, is well reported[17]. **Regardless of the fact that human-to-human transmission is less frequent than animal-to-human transmission, it typically includes respiratory droplets and prolonged face-to-face contact or contact**

with an infected patient's lesions [18]. The transmission of monkeypox can be ascribed to intimate contact, although the World Health Organization (WHO) says that it is not yet known whether it is sexually transmitted or not[19]. Some occurrences of genital and crotch lesions have been linked to sexual transmission[20] but there is no conclusive proof that seminal or vaginal fluids can transmit Monkeypox . Fetal fatalities and vertical transmission of the viruses were reported in pregnant women[21]. It has been noted that the disease is more prevalent in men who have sex with men. Monkeypox can be spread by close contact, despite the fact that this is insufficient to classify it as a sexually transmitted illness[22].

KFDV is transmitted to humans either through tick bites (*Haemaphysalis spinigera*), which serve as reservoirs for the virus, or by coming into contact with a virus-infected animal especially ill or dead monkeys[5]. There have been no reports of transmission from one person to another

In the monkey pox population, mortality rates range from 0-11%, and kids and young individuals who have not been immunized against smallpox are at greater risk[23]. The highest deaths were reported among young children and HIV-positive patients[24]. Researchers found that the majority of monkeypox cases occurred among people under 40, and the average age of the affected people was around 31. The National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Centers for Disease Control and Prevention, states that in Africa, monkeypox causes the death of one in ten who contract it. KFD seems to be deadly with a case fatality of 3-10% every year[25][26].

Molecular characterization

Molecular analysis revealed that the KFD virus' genome codes for a polyprotein that cleaves post-translationally to form three structural proteins (Envelope Glycoprotein M, Envelope Glycoprotein E, and Capsid protein) and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5)[27]. The Envelope protein (E) of the KFD virus is a major causative element of tissue tropism among structural proteins[28]. This protein is accountable for facilitating the virus's entry into the host cell as well as for determining its immunogenetic and phenotypic characteristics, playing an important role in pathogenesis and immune evasion[29]. Monkeypox virus' terminals end contain Vaccinia Virus (VACV) homologs that are primarily involved in immunomodulation, and most have been found to affect pathogenicity and host range determination[4]. Its pathogenesis is essentially the same as smallpox, with the exception that tiny lesions on the skin or oral mucous membranes are most often the entry point for the virus from wildlife sources. Viral entry via the respiratory tract is also possible in rare cases of person-to-person transmission.

Monkeypox and smallpox viruses replicate in lymphoid tissue, but only MPXV causes swelling of lymph nodes. The virus first appears in MNP (mononuclear phagocyte) cells, then spreads through the bloodstream before reappearing in skin cells. KFDV's pathophysiology isn't totally understood. KFDV is reproduced largely in the brain, according to research employing mice models[30]. Other studies have gone further, describing the neurological alterations that occur in diseased species. Scientists revealed that KFDV causes multiplication of glial cells in the infested areas of the central nervous system, inflammation, and necrosis in the brain of KFDV-infected mice. They suggested that KFDV is predominantly a neuropathic disorder with secondary symptoms caused by this aetiology.

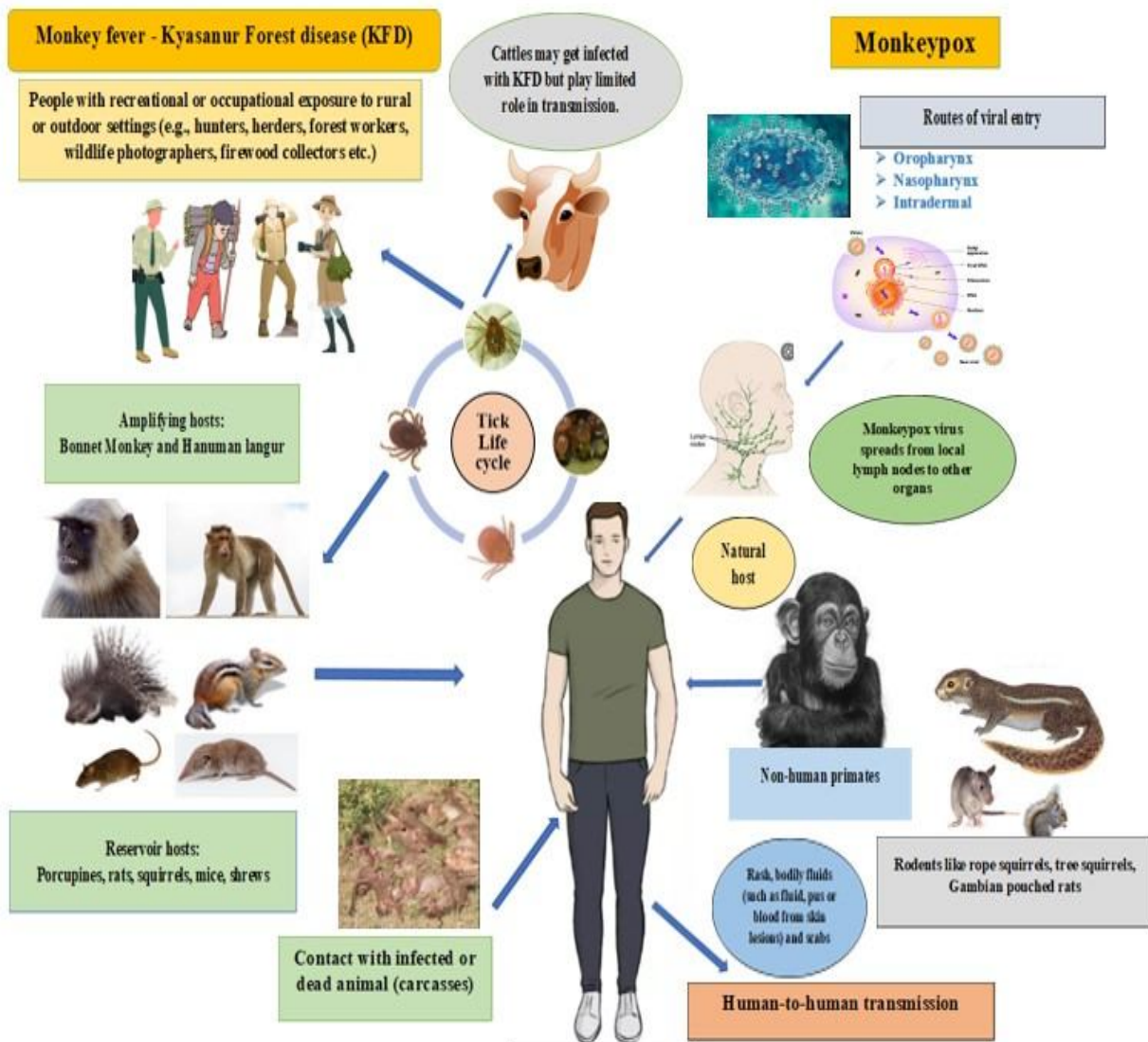


Fig 1: Schematic illustration comparing the spread of Monkey fever and Monkeypox infection

Epidemiology

Since the first human case was discovered in 1970, the incidence of monkeypox has increased, with high prevalence in Nigeria, the Democratic Republic of the Congo, Cameroon, Liberia, Sudan, Sierra Leone, Gabon, and the Central African Republic [31]. In neoteric years, the disease's swift emergence in countries such as the United States, United Kingdom, Singapore, and Israel, and the incidence has been linked to African origin[32][33]. Travelers play a vital role in spreading Monkeypox infections in new regions globally.

According to CDC National Centre for Emerging Zoonotic Diseases, around 400-500 positive cases of KFD are documented every year among the human population across India.

KFD was first reported in the Shimoga district of Karnataka, a primitive verdant territory in India's Western Ghats. The incidence of this disease was also reported in other districts of Karnataka, including Uttara Kannada, Chikkamagalore, Udupi, and Dakshina Kannada as well as Chamarajanagar and Belagavi (2016).

KFDV was discovered in monkey autopsies from Tamil Nadu's Nilgiris district in 2013. The serological evidence for KFD was detected among humans in other parts of India, namely Gujarat (Kutch and Saurashtra), West Bengal, Goa (North Goa District 2015) Maharashtra (Sindhudurg 2016)[34]and Kerala's Wayanad (2013) and Malappuram (2014)[35].

The smallpox vaccine given to the people before 1980 seemed to protect against the monkeypox virus also[36]. Cross-protective immunity has dwindled since the smallpox immunization campaign was ended[23] and as a result, the younger age group has become more susceptible to infection. However, a younger, non-immune generation coupled with the rise of hunting-dependent populations has resulted in the re-emergence of monkeypox.

Environmental factors influencing the emergence of Infection

According to the studies done, it's been stated that environmental factors play a vital role in the survival of the Monkeypox virus[37] and also the spread of the KFD virus. There is a risk that climate change could alter the geographical distribution and seasonal patterns of infectious diseases, whether directly by altering the pathogen ranges or indirectly by altering vector and reservoir populations[37].The increased interaction between humans and the virus's reservoir hosts has resulted in a greater re-emergence of infection. People moving into previously uncultivated areas increase the risk of cross-species infection as they come into contact with wild fauna and their livestock[38]. Farming, hunting, deforestation, camping, and other modes of habitat destruction have areas created a

new avenue for infectious agents for invading humans[39]. The other reasons for the spreading of these viruses include climate change, demographic changes, population movement, civil wars, deforestation, rainforest exploitation, etc.[40]. Various studies have shown that temperature and light conditions affect the duration the monkeypox virus endures outside a host[37]. As a result of global warming, we can expect more severe rainfalls, droughts, and floods due to the disruption of the hydrologic cycle, contributing to the emergence of infectious diseases. Example is in the 2005 Sudan floods and subsequent monkeypox outbreaks. Due to the expansion of vector populations, food shortages, and effluents introduced in large water resources, the emergence of infectious diseases will be facilitated by these unique environmental conditions. In many places of the world, natural disasters have boosted migration between the states and this has led to the introduction of pathogens to newer areas[41]. The annihilation of natural forests has led to the relocation of animals to newer areas where the human population is there. Trekking causes people to go to deeper areas of the forest with their pet animals and becomes a carrier for these pathogens causing severe illness. KFD is mainly transmitted through ticks and the chance of domestic or other local animals transporting the tick to human settlements again could elevate the extent of the disease spread[42]. Local residents who go to the forest to collect firewood are frequently infected by tick bites that carry and transmit the KFD virus. Mountaineers, hunters, trekkers, farmers, and charcoal makers in Karnataka and other southern states are at high risk of infection due to entertainment or work-related exposure to rural and outdoor settings [43].

Symptoms

Among the earliest signs of monkeypox, which distinguishes it from smallpox, are lymphadenopathy, tiredness, myalgia, fever, and headache. Mouth mucosal lesions appear after 1 to 2 days, followed quickly by skin lesions on the face, extremities, and soles and palms. The total number of lesions can range from a few to thousands, and the rash may or may not spread to the rest of the body[44]. The incubation period of the Monkeypox virus differs from five to twenty-one days and the signs and symptoms experienced during this phase include fever, pharyngitis, rash, swelling of the lymph nodes, respiratory distress, secondary bacterial infection, bronchopneumonia, dehydration, sepsis, gastrointestinal involvement, encephalitis and infection of the cornea resulting in loss of vision[45].

The incubation period of the KFD virus is three to eight days after the bite of an infective hard tick. KFD symptoms appear suddenly after the incubation period, with chills, fever, and headache. Three days after the initial symptom onset, vomiting, gastrointestinal symptoms, severe muscle pain, and bleeding problems may occur. Patients may have unusually low blood pressure as well as low platelet, white blood cell, and RBC counts. Some patients improve without complications after one to two weeks of symptoms. However, at the beginning of the third week, a subset of

patients (about 10 to 20 percent) experiences a subsequent upsurge of symptoms, indicating that the illness is biphasic with fever and brain-related issues. such as severe headaches, mental instabilities, shocks, and vision deficits are among the symptoms. For KFD, the estimated case-fatality rate ranges between 3 and 5%. The clinical spectrum begins with a sudden onset of fever, headache, chills, and generalized myalgia, particularly in the upper and lower back, neck, and extremities[46]. Fig.2 diagrammatically represents the symptoms and complications of KFD and Monkeypox infection .

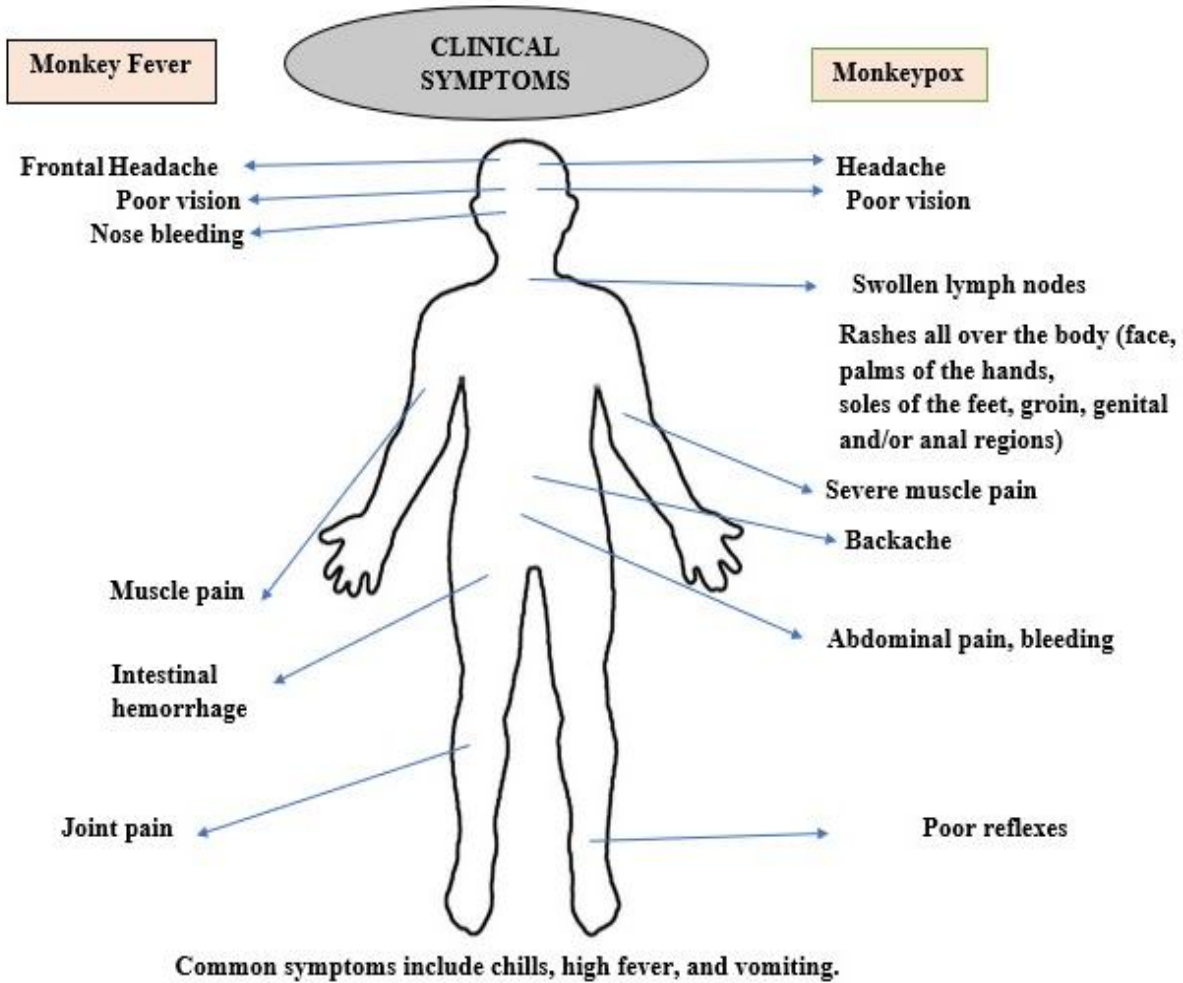


Fig: 2 Diagrammatic representation of symptoms and complications of Kyasanur forest disease (KFD- Monkey fever) and Monkeypox infection

Descriptions	Monkey Fever	Monkeypox
First case reported	Shimoga (Karnataka), India 1957	The Democratic Republic of Congo, 1970
Causative Organism	Kyasanur Forest Disease Virus (KFDV)	Monkeypox Virus (MPXV)
Family	<i>Flaviviridae</i>	<i>Poxviridae</i>
Viral genome	Positive single-stranded RNA	Double-stranded DNA
Host	Reservoir host- Porcupines, rats, squirrels, mice, shrews, and cattle Amplifying host- Red-faced Bonnet monkey (<i>Macaca radiata</i>) and Black-faced Hanuman langur (<i>Semnopithecus entellus</i>) Accidental host- Humans	Reservoir host- Non-human primates, rodents, Gambian pouched rats, rope squirrels, dormice, tree squirrels According to WHO, Uncertainty remains on the natural history of monkeypox virus and further studies are needed to identify the exact reservoir(s) and how virus circulation is maintained in nature.
Incubation period	3-8 days	6-13 but can range from 5-21 days
Mode of transmission	Tick bite, Contact with infected animals.	Contact with infected animals/people through Saliva/respiratory excretions, lesion exudates, and crust residue
Human to Human transmission	Not yet reported	Possible cases are reported
Symptoms	Chills, fever, headache., vomiting, gastrointestinal symptoms, severe muscle pain, bleeding problems, generalized myalgia	Fever, pharyngitis, rash, swelling of the lymph nodes, respiratory distress, secondary bacterial infection, bronchopneumonia, dehydration, sepsis, gastrointestinal involvement, encephalitis, and infection of the cornea resulting in loss of vision
Case Fatality	3-6%	3-5%
Treatment	No specific treatment	Usually self-limited and the recovery occurs in 2-4 weeks. Can be managed by commonly available antiviral drugs.
Vaccine	Chick embryo fibroblast formalin inactivated vaccine.	Smallpox vaccination provides around 80% protection against MPXV.

Table.1: Comparison between Monkey Fever and Monkey pox

Diagnosis

Once the patient exhibits any of the following symptoms, such as high-grade fever: Headache, Extreme Weakness, Myalgia, Nausea, Prostration, Diarrhea, Vomiting, or other symptoms like neurological or hemorrhagic complications, KFD is validated by detecting KFDV-specific viral RNA in blood or tissues using RT-PCR (Reverse Transcription Polymerase Chain Reaction) or real-time RT-PCR or by isolating KFDV from blood or tissues in a mouse model or cell culture and by KFD Enzyme-Linked Immunosorbent Assay (ELISA) positive for immunoglobulin M (IgM)[47].

Skin lesions such as vesicles, dry crusts, and pustules, swabs of the lesion surface and/or exudate, roofs from many lesions, or lesion crusts are the preferred specimen type for laboratory confirmation of monkeypox. The collection of an oropharyngeal swab is recommended in addition to a lesion specimen. A negative throat swab specimen should be regarded cautiously because there is limited information on the precision of this specimen type for monkeypox diagnosis. Skin biopsy is also done to collect the samples. Since the present outbreak is still being investigated, collecting additional specimen types for research can be considered provided the relevant ethical review board approves and there is enough laboratory and medical expertise for their secure collection, handling, and storage.

Based on clinical presentation, including the location of lesions, these may include urine, semen, rectal, and/or vaginal swabs. As any viremia occurs early in the course of infection, typically in the prodromal stage and before skin lesions become evident, EDTA blood may help MPXV identification but may not contain the high quantity of virus detected in lesion samples [48]. The virus is visualized through a Transmission Electron Microscope and confirmed by PCR and ELISA, tissue culture, and immunofluorescence assay[49]

Vaccine and Treatment

KFD does not have a specific treatment, however, early hospitalization and supportive therapy are critical. Proper intake of fluids and taking normal precautionary measures for patients with bleeding disorders are all part of supportive care. Monkeypox is usually self-limited and the recovery occurs in 2-4 weeks. According to the Centers for Disease Control and Prevention, monkeypox infection can be managed using the smallpox vaccine, ST-246(Tecovirimat), cidofovir, and Vaccinia Immune Globulin (VIG)[50].

A number of drugs are known to inhibit monkeypox virus replication including brincidofovir, tecovirimat, and intravenous vaccinia immune globulin. However, their efficacy against the monkeypox virus is unknown[51].

Scientific data reveals that the smallpox vaccination offers more than 80% protection from Monkeypox infection[52]. JYNNEOSTM vaccine (also known as Imvanex or Imvamune), has been licensed in the US to prevent monkeypox and smallpox[53].

Formalin inactivated chick embryo fibroblast is used as a vaccine against the Kyasanur Forest Disease Virus for use in KFD endemic areas for people 6 to 65 years of age. Multiple doses of the vaccine are required, and two doses are given to those aged 6 to 65 years at one-month intervals. Since the vaccine only provides temporary immunity, booster doses should be given 6– months after the primary vaccination and every five years after the last confirmed case in the area[54].

Prevention

Since KFD is a tick-borne infection, To prevent tick bites, one can apply tick repellents like N, N-diethyl-metoluamide (DEET), and dimethyl phthalate (DMP) oil. Gamma-hexachlorocyclohexane can be used to treat the forest floor to reduce tick populations[55]. Ivermectin injections given to calves post-monsoon in September and October may lessen the load of ticks on cattle herds [56] In order to prevent the transmission of MPXV in locations where it is endemic, one must limit direct contact with blood and undercooked meat while avoiding all interaction with rodents and primates. During an outbreak, the propagation of the monkeypox virus can be slowed down by isolating the affected and tracking down their contacts for at least six weeks after the last exposure[23]. Precautions should be taken against standard, contact, and droplet hazards for MPXV. Common key preventative measure for both Monkeypox and Monkey fever is to raise knowledge of the illness and the regions where it is endemic among medical professionals. Massive health education efforts are also required to raise public awareness, provide instructions on how to handle potential animal reservoir species (gloves, protective clothes, surgical mask), and warn people to stay away from afflicted people[23].

Conclusion

Monkeypox and monkey fever are two distinct zoonotic infections that are posing grave threats to mankind. The overall comparison between Monkeypox and Monkey fever is given Table.1. Due in part to the skin lesions it creates, monkeypox rarely goes unreported when it infects a person, in contrast to Monkey fever. It would be quite concerning if monkeypox could spread asymptotically as it would make the virus more difficult to detect. Air travel turns the world into a global village in terms of infectious disease because "microbial traffic" follows the human host. As a result, diseases that were long thought to be exotic or tropical are now having a greater influence on

the developed world[41]. The present worldwide outbreak of monkeypox virus infection in humans suggests changes in the biological characteristics of the virus, changes in human behavior, or both. Such changes may be triggered by diminishing smallpox immunity, resuming international travel, and sexual encounters associated with huge gatherings[57]. In the current scenario, the increase in KFD cases was associated with improved surveillance and high exposure to the forest due to scanty rainfall. KFD is mostly reported in the dry season when tourists travel to these forest areas for trekking, camping, and other adventurous activity. Hence, we can conclude that the factors like population demographics, climate change, deforestation, pollution, disturbance in the hydrological cycle, etc. influence the emergence and re-emergence of zoonotic viral infections. According to the data and information that have been published, we can draw the conclusion that the spread of monkeypox can be halted by vaccinating the current population against smallpox once again or by using any recently created, regulatory-approved vaccines. Also, the spread of the KFD virus needs to be monitored properly since it is currently declared only as a viral disease endemic to some parts of India but chances are more to be declared a pandemic if spread across the borders of the country. The world must act swiftly and together to fill knowledge gaps and stop the pandemic. Rapid case identification is essential to containment in the absence of readily accessible prophylaxis or treatment. There are various ways that illnesses might present, as is typical in clinical medicine, and monkeypox or monkey fever is no exception. There is a need for targeted health promotion that sensitively encourages improved screening and instruction in vulnerable populations. The recent epidemics and pandemics have tragically taught us that being aware of and prepared for these emergency situations are crucial. The ability to respond simultaneously and swiftly in putting control measures into place is a skill that governments should adapt to. To accomplish a healthy community, the collaborative efforts of multiple disciplines at the local, national, and international levels to achieve people, animals, and the environment's optimal health[58] must be focused on as the health of animals and the environment we share is closely intertwined[59].

References:

- [1] L. Khodakevich, Z. Jezek, and K. Kinzanzka, "ISOLATION OF MONKEYPOX VIRUS FROM WILD SQUIRREL INFECTED IN NATURE," *The Lancet*, vol. 327, no. 8472, pp. 98–99, Jan. 1986, doi: 10.1016/S0140-6736(86)90748-8.
- [2] N. Sklenovská and M. van Ranst, "Emergence of Monkeypox as the Most Important Orthopoxvirus Infection in Humans," *Front Public Health*, vol. 6, Sep. 2018, doi: 10.3389/FPUBH.2018.00241.

- [3] T. H. WORK, F. R. RODERIGUEZ, and P. N. BHATT, "Virological Epidemiology of the 1958 Epidemic of Kyasanur Forest Disease," *Am J Public Health Nations Health*, vol. 49, no. 7, p. 869, 1959, doi: 10.2105/AJPH.49.7.869.
- [4] J. R. Kugelman *et al.*, "Genomic variability of monkeypox virus among humans, Democratic Republic of the Congo.," *Emerg Infect Dis*, vol. 20, no. 2, pp. 232–9, Feb. 2014, doi: 10.3201/eid2002.130118.
- [5] S. Z. Shah *et al.*, "Epidemiology, Pathogenesis, and Control of a Tick-Borne Disease- Kyasanur Forest Disease: Current Status and Future Directions," *Front Cell Infect Microbiol*, vol. 8, May 2018, doi: 10.3389/fcimb.2018.00149.
- [6] P. D. Yadav *et al.*, "Phylogeography of Kyasanur Forest Disease virus in India (1957–2017) reveals evolution and spread in the Western Ghats region," *Sci Rep*, vol. 10, no. 1, Dec. 2020, doi: 10.1038/s41598-020-58242-w.
- [7] D. Tian and T. Zheng, "Comparison and Analysis of Biological Agent Category Lists Based On Biosafety and Biodefense," *PLoS One*, vol. 9, no. 6, p. 101163, 2014, doi: 10.1371/journal.pone.0101163.t001.
- [8] M. Muraleedharan, "Kyasanur Forest Disease (KFD): Rare Disease of Zoonotic Origin.," *J Nepal Health Res Counc*, vol. 14, no. 34, pp. 214–218, Sep. 2016.
- [9] I. D. Ladnyj, P. Ziegler, and E. Kima, "A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo.," *Bull World Health Organ*, vol. 46, no. 5, pp. 593–7, 1972.
- [10] D. B. di Giulio and P. B. Eckburg, "Human monkeypox: an emerging zoonosis.," *Lancet Infect Dis*, vol. 4, no. 1, pp. 15–25, Jan. 2004, doi: 10.1016/s1473-3099(03)00856-9.

- [11] M. Nichter, "Kyasanur Forest Disease: An Ethnography of a Disease of Development," *Med Anthropol Q*, vol. 1, no. 4, pp. 406–423, Dec. 1987, doi: 10.1525/maq.1987.1.4.02a00040.
- [12] "Urgent need for a non-discriminatory and non-stigmatizing nomenclature for monkeypox virus - Monkeypox - Virological." <https://virological.org/t/urgent-need-for-a-non-discriminatory-and-non-stigmatizing-nomenclature-for-monkeypox-virus/853> (accessed Jun. 22, 2022).
- [13] M. E. Wilson, "Re-emerging Diseases: Overview," *International Encyclopedia of Public Health*, pp. 269–277, Oct. 2016, doi: 10.1016/B978-0-12-803678-5.00374-X.
- [14] S. Parker, A. Nuara, R. M. L. Buller, and D. A. Schultz, "Human monkeypox: an emerging zoonotic disease.," *Future Microbiol*, vol. 2, no. 1, pp. 17–34, Feb. 2007, doi: 10.2217/17460913.2.1.17.
- [15] S. ODEND'HAL, "Kyasanur Forest Disease Virus," *The Geographical Distribution of Animal Viral Diseases*, pp. 253–256, 1983, doi: 10.1016/B978-0-12-524180-9.50070-4.
- [16] "Monkeypox Epidemiology." <https://www.news-medical.net/health/Monkeypox-Epidemiology.aspx> (accessed Sep. 24, 2022).
- [17] L. A. Learned *et al.*, "Extended interhuman transmission of monkeypox in a hospital community in the Republic of the Congo, 2003.," *Am J Trop Med Hyg*, vol. 73, no. 2, pp. 428–34, Aug. 2005.
- [18] K. Simpson *et al.*, "Human monkeypox – After 40 years, an unintended consequence of smallpox eradication," *Vaccine*, vol. 38, no. 33, pp. 5077–5081, Jul. 2020, doi: 10.1016/j.vaccine.2020.04.062.
- [19] J. Kaler, A. Hussain, G. Flores, S. Kheiri, and D. Desrosiers, "Monkeypox: A Comprehensive Review of Transmission, Pathogenesis, and Manifestation," *Cureus*, Jul. 2022, doi: 10.7759/cureus.26531.
- [20] D. Ogoina *et al.*, "The 2017 human monkeypox outbreak in Nigeria—Report of outbreak experience and response in the Niger Delta University Teaching Hospital, Bayelsa State, Nigeria," *PLoS One*, vol. 14, no. 4, p. e0214229, Apr. 2019, doi: 10.1371/journal.pone.0214229.

- [21] P. K. Mbala *et al.*, "Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo," *BRIEF REPORT The Journal of Infectious Diseases*®, vol. 824, pp. 824–832, 2017, doi: 10.1093/infdis/jix260.
- [22] ramazan azim okyay, "Another Epidemic in the Shadow of Covid 19 Pandemic: A Review of Monkeypox," *Eurasian J Med Oncol*, 2022, doi: 10.14744/ejmo.2022.2022.
- [23] E. Petersen *et al.*, "Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention.," *Infect Dis Clin North Am*, vol. 33, no. 4, pp. 1027–1043, 2019, doi: 10.1016/j.idc.2019.03.001.
- [24] Eloy José Tarín-Vicente *et al.*, "Clinical presentation and virological assessment of confirmed human monkeypox virus cases in Spain_ a prospective observational cohort study _ LANCET," *www.thelancet.com* , vol. August 8, 2022, doi: [https://doi.org/10.1016/S0140-6736\(22\)01436-2](https://doi.org/10.1016/S0140-6736(22)01436-2).
- [25] M. R. Holbrook, "Kyasanur forest disease.," *Antiviral Res*, vol. 96, no. 3, pp. 353–62, Dec. 2012, doi: 10.1016/j.antiviral.2012.10.005.
- [26] P. Rajaiah, "Kyasanur Forest Disease in India: innovative options for intervention," *Human Vaccines and Immunotherapeutics*, vol. 15, no. 10. Taylor and Francis Inc., pp. 2243–2248, Oct. 03, 2019. doi: 10.1080/21645515.2019.1602431.
- [27] C. B. Jonsson *et al.*, "Epidemiology, Pathogenesis, and Control of a Tick-Borne Disease- Kyasanur Forest Disease: Current Status and Future Directions," *Frontiers in Cellular and Infection Microbiology* | *www.frontiersin.org*, vol. 1, p. 149, 2018, doi: 10.3389/fcimb.2018.00149.
- [28] D. Lin *et al.*, "Analysis of the complete genome of the tick-borne flavivirus Omsk hemorrhagic fever virus," *Virology*, vol. 313, no. 1, pp. 81–90, Aug. 2003, doi: 10.1016/S0042-6822(03)00246-0.

- [29] W. C. Barker, R. Mazumder, S. Vasudevan, J.-L. Sagripanti, and C. H. Wu, "Sequence signatures in envelope protein may determine whether flaviviruses produce hemorrhagic or encephalitic syndromes," *Virus Genes*, vol. 39, no. 1, pp. 1–9, Aug. 2009, doi: 10.1007/s11262-009-0343-4.
- [30] B. Sawatsky, A. J. McAuley, M. R. Holbrook, and D. A. Bente, "Comparative pathogenesis of Alkhumra hemorrhagic fever and Kyasanur forest disease viruses in a mouse model.," *PLoS Negl Trop Dis*, vol. 8, no. 6, p. e2934, Jun. 2014, doi: 10.1371/journal.pntd.0002934.
- [31] N. A. Hoff *et al.*, "Evolution of a Disease Surveillance System: An Increase in Reporting of Human Monkeypox Disease in the Democratic Republic of the Congo, 2001-2013," *Int J Trop Dis Health*, vol. 25, no. 2, p. 35885, 2017, doi: 10.9734/IJTDH/2017/35885.
- [32] A. Vaughan *et al.*, "Two cases of monkeypox imported to the United Kingdom, September 2018," *Eurosurveillance*, vol. 23, no. 38, 2018, doi: 10.2807/1560-7917.
- [33] N. Erez *et al.*, "Diagnosis of imported monkey pox, Israel, 2018," *Emerging Infectious Diseases* • www.cdc.gov/eid •, vol. 25, no. 5, 2019, doi: 10.3201/eid2505.190076.
- [34] P. Pattnaik, "Kyasanur forest disease: An epidemiological view in India," *Rev Med Virol*, vol. 16, no. 3, pp. 151–165, 2006, doi: 10.1002/rmv.495.
- [35] D. T. Mourya and P. D. Yadav, "Recent Scenario of Emergence of Kyasanur Forest Disease in India and Public Health Importance," *Current Tropical Medicine Reports*, vol. 3, no. 1. Springer Verlag, pp. 7–13, Mar. 01, 2016. doi: 10.1007/s40475-016-0067-1.
- [36] E. M. Bunge *et al.*, "The changing epidemiology of human monkeypox-A potential threat? A systematic review.," *PLoS Negl Trop Dis*, vol. 16, no. 2, p. e0010141, 2022, doi: 10.1371/journal.pntd.0010141.

- [37] H. A. Thomassen *et al.*, "Pathogen-Host Associations and Predicted Range Shifts of Human Monkeypox in Response to Climate Change in Central Africa," *PLoS One*, vol. 8, no. 7, Jul. 2013, doi: 10.1371/JOURNAL.PONE.0066071.
- [38] R. A. Weiss and A. J. McMichael, "Social and environmental risk factors in the emergence of infectious diseases," *Nat Med*, vol. 10, no. S12, pp. S70–S76, Dec. 2004, doi: 10.1038/nm1150.
- [39] J. , S. R. E. & O. S. C. eds Lederberg, *Emerging Infections: Microbial Threats to Health in the United States*. National Academy Press, Washington DC, 1992.
- [40] A. S. Fauci, "Emerging and reemerging infectious diseases: the perpetual challenge.," *Acad Med*, vol. 80, no. 12, pp. 1079–85, Dec. 2005, doi: 10.1097/00001888-200512000-00002.
- [41] D. L. Church, "Major factors affecting the emergence and re-emergence of infectious diseases," *Clin Lab Med*, vol. 24, no. 3, pp. 559–586, Sep. 2004, doi: 10.1016/j.cll.2004.05.008.
- [42] M. v. Murhekar, G. S. Kasabi, S. M. Mehendale, D. T. Mourya, P. D. Yadav, and B. v. Tandale, "On the transmission pattern of Kyasanur Forest disease (KFD) in India," *Infect Dis Poverty*, vol. 4, no. 1, Aug. 2015, doi: 10.1186/s40249-015-0066-9.
- [43] CDC National center for emerging zoonotic diseases, "CDC Fact Sheet," Page last reviewed: December 23, 2013 Content source: Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID). Accessed: May 22, 2022. [Online]. Available: <https://www.cdc.gov/vhf/kyasanur/pdf/factsheet.pdf>
- [44] A. M. McCollum and I. K. Damon, "Human Monkeypox," *Clinical Infectious Diseases*, vol. 58, no. 2, pp. 260–267, Jan. 2014, doi: 10.1093/cid/cit703.
- [45] E. Petersen *et al.*, "Human Monkeypox," *Infect Dis Clin North Am*, vol. 33, no. 4, pp. 1027–1043, Dec. 2019, doi: 10.1016/j.idc.2019.03.001.

- [46] R. R. S. P. D. Y. R. V. & D. T. M. Ashok Munivenkatappa1, "Clinical & epidemiological significance of Kyasanur forest disease," *Indian J Med Res*, vol. 148, no. August 2018, pp. 145–150, 2018, doi: 10.4103/ijmr.IJMR_688_17.
- [47] "Kyasanur forest disease: A public health concern."
<https://ncdc.gov.in/WriteReadData/l892s/62082401691532083718.pdf> (accessed Sep. 24, 2022).
- [48] "Laboratory testing for the monkeypox virus." Accessed: Oct. 25, 2022. [Online]. Available: <https://apps.who.int/iris/bitstream/handle/10665/354488/WHO-MPX-Laboratory-2022.1-eng.pdf?sequence=1&isAllowed=y>
- [49] M. G. Reynolds, D. S. Carroll, and K. L. Karem, "Factors affecting the likelihood of monkeypox's emergence and spread in the post-smallpox era," *Curr Opin Virol*, vol. 2, no. 3, pp. 335–343, Jun. 2012, doi: 10.1016/J.COVIRO.2012.02.004.
- [50] M. J. Oladoye, "Monkeypox: A Neglected Viral Zoonotic Disease," *European Journal of Medical and Educational Technologies*, vol. 14, no. 2, p. em2108, May 2021, doi: 10.30935/ejmets/10911.
- [51] M. E. Wilson, J. M. Hughes, A. M. Mccollum, and I. K. Damon, "EMERGING INFECTIONS Human Monkeypox," *Clinical Infectious Diseases*, vol. 58, pp. 260–267, 2014, doi: 10.1093/cid/cit703.
- [52] S. Com Sciep, V. Kandi, M. Pal, and F. Mengstie, "Epidemiology, Diagnosis, and Control of Monkeypox Disease: A comprehensive Review," *American Journal of Infectious Diseases and Microbiology*, vol. 5, no. 2, pp. 94–99, 2017, doi: 10.12691/ajidm-5-2-4.
- [53] C. Potter, L. Warmbrod, R. A. Vahey, and A. Browett, "Factsheet: Monkeypox," 2022, Accessed: Sep. 24, 2022. [Online]. Available: https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/fact_sheets/monkeypox.pdf

- [54] G. S. Kasabi *et al.*, "Coverage and Effectiveness of Kyasanur Forest Disease(KFD) Vaccine in Karnataka, South India, 2005–10," *LOS Neglected Tropical Diseases* | www.plosntds.org 4 January 2013 | Volume 7 | Issue 1 | e2025, pp. 2005–2015, doi: 10.1371/journal.pntd.0002025.
- [55] A. Munivenkatappa, R. Sahay, P. Yadav, R. Viswanathan, and D. Mourya, "Clinical & epidemiological significance of Kyasanur forest disease," *Indian Journal of Medical Research*, vol. 148, no. 2, p. 145, 2018, doi: 10.4103/ijmr.IJMR_688_17.
- [56] S. Ghosh, P. Azhahianambi, and M. P. Yadav, "Upcoming and future strategies of tick control: a review.," *J Vector Borne Dis*, vol. 44, no. 2, pp. 79–89, Jun. 2007.
- [57] J. P. Thornhill *et al.*, "Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022," *New England Journal of Medicine*, Jul. 2022, doi: 10.1056/NEJMoa2207323.
- [58] B. A. Ruscio, M. Brubaker, J. Glasser, W. Hueston, and T. W. Hennessy, "One Health Á a strategy for resilience in a changing arctic," *Int J Circumpolar Health*, p. 74, 2015, doi: 10.3402/ijch.v74.27913.
- [59] "One Health Basics | One Health | CDC." <https://www.cdc.gov/onehealth/basics/index.html> (accessed Jun. 04, 2022).