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Review Article

MONKEYPOX: WHAT TO KNOW ABOUT THE RE-EMERGING DISEASE FROM WEST AND CENTRAL AFRICA

El Bethel Lalthavel Hmar, YasangamUmbon, Hemanta Kumar Sharma*

Department of Pharmaceutical Sciences, Faculty of Science and Engineering, Dibrugarh University, Dibrugarh 786004, Assam, India

Abstract

Monkeypox virus, a member of the Orthopoxvirus family, is the etiological agent that causes sporadic human infections in Central and West Africa's forested areas. Human infection was first described in Central Africa in 1970. Monkeypox is the most common Orthopoxvirus in humans, at least in endemic regions, and maybe worldwide. Currently Monkeypox virus is known to exist in two separate clades, the West African clade is known to exist from western Cameroon to Sierra Leone, but the Congo Basin clade has been discovered from central and southern Cameroon to the Democratic Republic of the Congo. The most prevalent routes of infection for humans include respiratory, and permucosal percutaneous exposures to infected monkeys, prairie dogs, zoo animals, and humans. This review also elucidates the epidemiology, morphology and genomic organization, transmission, clinical recognition, the possible diagnostic tests, prevention, control and medical countermeasures, and the clinical stages of the monkeypox.

Keywords: monkeypox virus; smallpox; *Orthopoxvirus;* zoonosis; emerging disease

Introduction

The monkeypox virus (MPXV) is a zoonotic illness with public health implications that is developing and re-emerging [1].It's caused by a DNA virus from the *Poxviridae* family's *Orthopoxvirus* genus. When two outbreaks of a pox-like illness occurred in study colonies of monkeys in 1958, the name "monkeypox" was coined. The virus is assumed to spread from wild rodents (such as prairie dogs, Gambian pouched rats, and dormice) to humans or sick individuals [2].However, the illness became common in other African nations, including

*Corresponding author's e-mail: hemantasharma123@yahoo.co.in

Nigeria, Benin, and Liberia, following the discovery of the first human case in the Democratic Republicof the Congo (DRC) in 1970[3][4]. Monkeypox (MPX) is a sylvatic zoonosis that produces occasional human infections in wooded parts of Central and West Africa[1].The variola virus (which causes smallpox), cowpox virus, and vaccinia virus are all members of this genus. MPXV has only been isolated from three African indigenous wild mammals: a Thomas' rope squirrel (*Funisciurusanerythrus*) in the DRC, and a sooty mangabey (*Cercocebus atys atys*) and western chimpanzee (*Pan troglodytes verus*) in Côte d'Ivoire's Ta National Park. Different species of rodents are thought to be potential viral reservoirs (such as *Cricetomys, Graphiurus, Funisciurus* and *Heliosciurus*sp), whereas primates are thought to be accidental hosts. However, empirical evidence to back up these statements is limited, and it is mostly dependent on serological data or DNA amplicons that haven't been sequenced[5][6]. MPX and smallpox have comparable clinical manifestations, with MPX presenting lymphadenopathy early in the disease phase. Smallpox infection results in long-lasting immunity; recurrent smallpox attacks are only approximately 1 in 1000 for the next 15–20 years[7].After small pox, MPX is the second most pathogenic pox viral illness, yet it has never received the attention it deserves to avoid becoming an epidemic[8].May 2022 marks the start of a new global outbreak that is causing concern because it is spreading rapidly across multiple countries, among people who have never travelled, and is now the clinical disease in more than a dozen countries outside of Africa, where this zoonosis is endemic, particularly in the Democratic Republic of the Congo, the Republic of the Congo, and Nigeria[9].

Epidemiology

Monkeypox is caused by the Monkeypox virus (MPXV), belonging to the family *Orthopoxvirus* (OPV). Other OPV's that cause illnesses in humans include Variola (smallpox), vaccinia (used in smallpox vaccine), camelpox, and cowpox virus[1]. Monkeypox is mostly found in West and Central African rain forests. Although antibodies have been found in a variety of small mammal species, the monkeypox virus has only been recovered twice from wild animals, once from a rope squirrel (*Funisciurusanerythrus*) in the Democratic Republic of the Congo and once from a sooty mangabey (*Cercocebusatys*) in Côte d'Ivoire[10]. In 1958, the MPXV was identified as the source of a pox infection in captive monkeys. On September 1, 1970, a nine-month-old child was admitted to the Basankusu Hospital in the Democratic Republic of Congo (DRC), marking the first human MPX case in medical history. MPXV-like virus was identified from the boy's smallpox-like

illness[11]. Human monkeypox cases have been documented in numerous African nations since then, including Benin, Cote d'Ivoire, Cameroon, the Central African Republic, Gabon, Liberia, Sierra Leone, Nigeria, South Sudan, Israel, United States, United Kingdom and Singapore[2][12][13].According to the World Health Organization (WHO), it is most frequent among young people under the age of 40 or 50 (depending on country) as a result of the suspension of smallpox immunisation following the disease's obliteration in 1980[14].

The majority of MPX cases, according to the report, occur in people under the age of 40, with a median age of 31. The gender distribution of the illness has also been researched, in addition to the age distribution. MPX cases has been documented in 26 of Nigeria's 36 states (including the Federal Capital Territory), up from 11 states reported in 2017. The male to female ratio (3:1) is confirmed in this data, indicating a larger frequency in the male gender[15][16][17]. As indicated in the graph below, the male gender is more affected than the female gender-

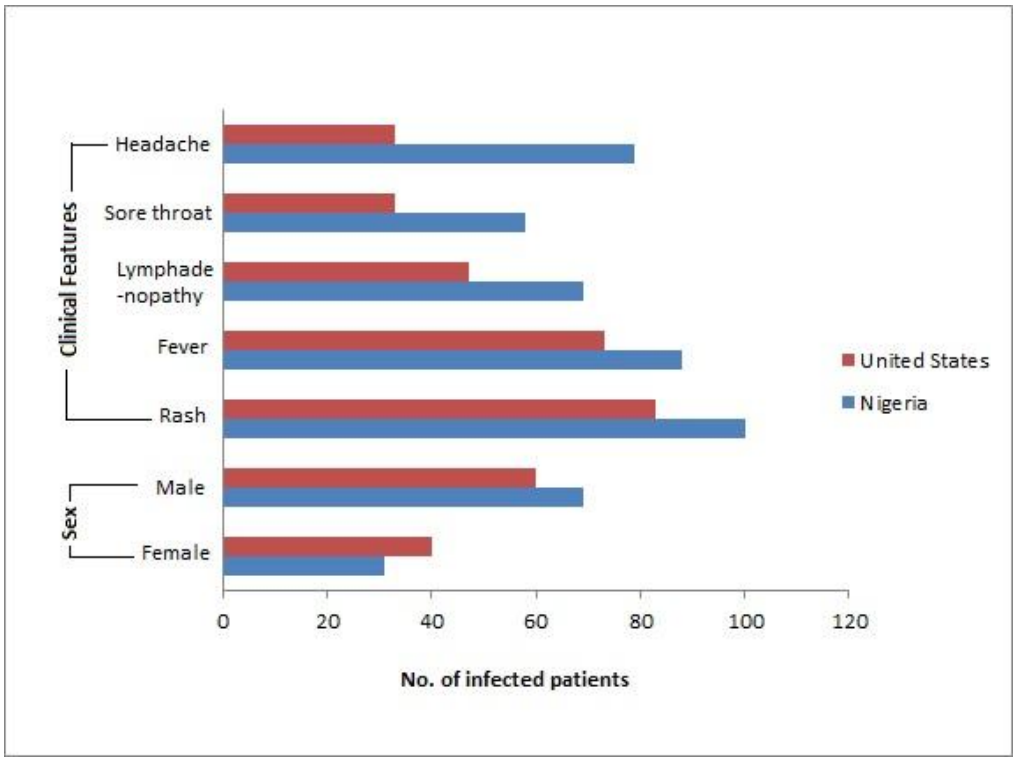

Fig 1: A comparison of the sex distribution and clinical aspects seen in monkeypox patients from two countries

Morphology and Genome organization of MPXV

MPXV is a member of the *Poxviridae* family, as well as the *Chordopoxvirinae* subfamily and the *Orthopoxvirus* genus. MPXV virions are ovoid or brick-shaped particles with a

geometrically corrugated lipoprotein outer membrane and a size range of 200-250 nm, similar to other *Orthopoxviruses* (OPV). The outer membrane protects both the membrane bond and the tightly packed core, which contains enzymes, a double-stranded DNA genome, and transcription factors. The core is described as biconcave, and it contains lateral bodies on either side, due to an electron microscopy fixation artefact[18][19].

The MPXV genome, which is made up of linear double-stranded DNA covalently connected at its ends by palindromic hairpins and inverted terminal repeats (ITRs),which are made up of tandem repeats, hairpin loops, and some open reading frames (ORF) [20].The genome of the MPXV is relatively vast, with 196,858 base pairs encoding 190 open reading frames, which make up the majority of the material required for viral replication in the cytoplasm of cells[21]. Viral entrance into cells is determined by the cell type and viral strain, and occurs when several viral ligands connect with cell surface receptors such chondroitin sulphate or heparan sulphate. [22]. The MPXV genome encodes all the proteins necessary for viral DNA replication, transcription, virion assembly, and egress. Housekeeping genes are highly conserved across OPVs and are found in the central region of the genome, whereas virus–host interaction genes are less conserved and found in the termini area[13]. Vaccinia virus (VACV) homologs to genes discovered in the MPXV genome's terminal ends are mostly engaged in immunomodulation, and the majority of them are expected or known to impact host range tenacity and pathogenicity. Unlike variola virus (VARV), which shortfall ORFs in the ITR region, MPXV has at least four ORFs in the ITR domain[20][23].

Monkeypox Virus Variation in Western and Central Africa

There are two distinct clades of monkeypox virus[10], the West African clade is known to exist from western Cameroon to Sierra Leone, but the Congo Basin clade has been discovered from central and southern Cameroon to the Democratic Republic of the Congo[24]. Geographically, these two clades are unique, as are their epidemiological and clinical features. The case fatality rate (CFR) of the West African clade is less than 1%, and no human-to-human transmission has ever been reported. The Congo Basin clade, on the other hand, has a CFR of up to 11% and has been linked to human-to-human transmission in up to six instances[25]. According to studies, the Congo Basin clade (Central Africa clade) is more virulent than the West Africa clade, resulting in more inter-human transmission. Cameroon, the only nation where both viral clades have been detected, has been the site of the geographical split between the two clades thus far[26]. In human cells generated from previously infected monkeypox patients, central African monkeypox blocks T-cell receptor–

mediated T-cell activation, preventing inflammatory cytokine production. These findings imply that monkeypox may release a modulator that inhibits T-cell responses in the host. In the Central African MPXV, several immune evasion possibilities have been found[27].The MPXV inhibitor of complement enzymes, a gene that suppresses complement enzymes and is lacking in West African strains, has been suggested as a crucial immunomodulating component in Central African strains' higher virulence [28][29].Furthermore, as compared to West African monkeypox strains, Central African monkeypox strains preferentially suppress host responses, including apoptosis in the host. In addition, transcriptional investigations have revealed that during an infection, Central African monkeypox appears to preferentially mute transcription of genes implicated in host immunity [30][31].

Transmission

The MPXV may endanger human health. MPXV transmission can occur via two routes: animal-to-human transfer (zoonotic transmission) and human-to-human transmission.[13][32].

Zoonotic transmission

Monkeypox can be induced by ecosystem degradation, which has an influence on human and MPX-infected animals, as well as inadequate nutrition[32]. People can become infected with the monkeypox virus through bites or close contact with diseased animals, especially during meat preparation, with case fatality rates as high as 10%[33].Evidence of MPX infection has been detected in several animals in Africa, including tree squirrels, rope squirrels, dormice, Gambian poached rats, various monkey species, and others. Monkeypox's natural reservoir has yet to be established, while rodents are the most plausible suspect[12].It is believed that the virus enters the body through injured skin, mucosal membranes, or the respiratory system. Indirect contact with lesion material, such as contaminated bedding, can also result in virus transmission[34][35].It's also been observed that monkey poxvirus disseminates by inhalation, with four out of six cynomolgus macaques were killed humanly owing to their critical condition after inhaling it. The monkey pox virus was breathed at a fatal level of 7.8 x 104 pfu lethal dose (LD50) [36].

Human-to-human transmission

According to a survey, small pox vaccination provides 85 % immunity against monkey pox, but humans can only contract the disease by coming into contact with infected animals; there is no transmission of infection from human to human because the virus cannot survive in

humans without vaccination[37]. Due to genetic alterations (gene loss), monkey pox may now survive in humans, and human-to-human transmission is feasible. Because of the MPXV genetic diversity, the virus may survive in humans and propagate between people[20]. Inter-human transmission has been linked to respiratory droplets and contact with bodily fluids ejected from the patient's body or from wounds, a contaminated patient's surroundings or goods, and a skin lesion on an infected individual. The Congo Basin clade (Central African clade) is thought to be more virulent than the West African clade, and hence contributes more to inter-human transmission [13]. Vertical transmission is also discussed. Congenital monkeypox can arise when the virus crosses the placenta. There is no indication of pre-symptomatic transmission, as there is with smallpox; transmission occurs during the rash stage. Observational studies from the mid-1980s revealed that the major infectious phase, comparable to smallpox, occurred during the first week of the rash [35]. What's more unexpected is that incidences have been reported among males who have intercourse with other men (MSM). The significant prevalence of genital and oral ulcers further supports this theory. Close liaison has been embroiled in the virus's transmission, although it's unclear why the Western African clade was designated as the etiological agent [38].In comparison to the Central African clade, which had a greater mortality rate (10.6 %) and known human-to-human transmission, the West African clade had a lower mortality rate (3.6 %) and no direct human-to-human transmission [39].

Clinical recognition[4][40]

The clinical course of possible MPX infection is the same as that of conventional smallpox infection. Fever, headaches, backaches, muscle pains, chills, swollen lymph nodes, and exhaustion are all common indications and symptoms. The following are some of the Key characteristic to identifying monkeypox-

a) Lesions are well-defined, deep-seated, and frequently develop umbilication (imitates a dot on the top of the lesion)
b) Lesions on a particular body site have roughly the same size and stage of development (e.g., vesicles on legs or pustules on face)
c) Lesions on palms, soles
d) Fever prior to rash
e) A disseminated rash has a centrifugal effect (additional lesions on the limbs and face)
f) Lymphadenopathy is a prevalent condition.

g) Lesions progress from macules to papules, papules to vesicles, vesicles to pustules, pustules to crusts, and crusts to extensive lesions.
h) The lesions are 0.5cm-1cm in diameter, well confined, umbilicated, and hard.
i) Desquamation takes 2-4 weeks.
j) Lesions are frequently reported as painful until they heal and become itchy (crusts)

Diagnostic Tests for Monkeypox or *Orthopoxvirus*

As the clinical presentation of monkeypox is not very distinctive, scientific approaches like virus isolation, immunohistochemistry, electron microscopy, immunohistochemistry, and PCR(polymerase chain reaction)are necessary to make an unambiguous diagnosis of the infection[41][42]. Some of the most essential diagnostic tests for distinguishing MPXV or *Orthopoxvirus* from clinical specimens are outlined here.

a) Viral culture/isolation

Live virus is generated and described from a patient specimen in this method.

Benefits

Can produce a pure, live viral culture for species classification. *Orthopoxviruses* cause unique "pocks" on chorioallantoic membranes, and various cell-based viral culture techniques are available. Patient specimens from lesions are the most trustworthy for this approach since viremia is not present throughout the disease.

Limitations

It takes many days to finish the test. The presence of microorganisms may impede attempts to culture patient specimens. For viral identification, more characterisation is required. Must be carried out in a large laboratory by competent experts [43][44].

b) Electron microscopy

Under an electron microscope, MPXV appears intracytoplasmic brick-shaped with lateral bodies and a central core of around 200–300 nm, permitting visual identification of a poxvirus different than Parapoxvirus.

Benefits

It can be used to find viral particles in a biopsy sample, vesicular fluid, scab crust, or viral culture. Can tell the difference between an *Orthopoxvirus* and a *Herpesviridae*.

Limitations

Because *Orthopoxviruses* cannot be distinguished morphologically, this approach does not provide a definite diagnosis, but it does provide evidence that the virus pertaining to the *Poxvirida*e family. A big laboratory with competent personnel and an electron microscope must be used[43][45].

c) PCR, including real-time PCR

It's a test that looks for particular DNA markers associated with monkeypox.

Benefits

Using lesion material from a patient, can diagnose a current case. The test relies on viral DNA, which can be kept stable in dark, chilly environments. It's made to target the MPXV only.

Limitations

When contamination is an issue, very sensitive tests are used. These tests necessitate the use of high-priced reagents and equipment. It must be carried out in a reputable laboratory by highly trained experts[42][45].

d) Anti-Orthopoxvirus IgG

It examines the existence of *Orthopoxvirus* antibodies.

Benefits

It's possible to use this test to see if a person has ever been exposed to an *Orthopoxvirus*, along with a pathogen or smallpox immunisation.

Limitations

Blood (serum) collection and a cold chain are required. This test does not detect MPXV. Prior smallpox immunisation will have an impact on the results. The time it takes for a response to appear is vary. It must be carried out in a large laboratory by highly trained workers[14][45][46].

e) Anti-Orthopoxvirus IgM

It examines the existence of *Orthopoxvirus* antibodies.

Benefits

Can be used to assess a recent exposure to an *Orthopoxvirus*, including a pathogen or smallpox

vaccination. This assay could be used as adiagnostic for suspect *Orthopoxvirus* patients with prior smallpox vaccination.

Limitations

Requires the collection of blood (serum) and a cold chain. This assay is not specific for MPXV. Must be performed at a major laboratory with skilled technician[46][47].

f) Immunohistochemistry

Tests forthe presence of *Orthopoxvirus* specific antigens.

Benefits

Antigens in biopsy specimens can be identified using this method. Other questionable agents can be ruled out or identified using this method.

Limitations

This assay is not specific for MPXV. Must be performed at a major laboratory with skilled technician[48].

g) TetracoreOrthopoxBioThreat Alert

Antigens of the *Orthopoxvirus* are detected using this test.

Benefits

A point-of-care diagnostic tool that may quickly diagnose an active case utilising lesion material from a patient. With minimal competence, it can be done at room temperature.

Limitations

This assay is not specific for MPXV. It must be tested in endemic areas. It has a lower sensitivity than PCR.[43][49].

Prevention and control measures[50][51]

The Centers for Disease Control and Prevention (CDC) has produced a list of precautions that can be followed to avoid infection with the monkeypox virus:

a) Avoid coming into contact with any materials that have been in contact with a sick animal, such as bedding.
b) void getting into contact with sick animals, especially those that are unwell or have died in regions where monkeypox occurs.
c) Separate contaminated patients from those who may be at danger of infection.

d) After coming into touch with infectious animals or humans, wash your hands thoroughly. Washing of hands with soap and water or using an alcohol-based hand sanitizer are two examples.
e) When caring for patients, wear personal protective equipment (PPE).
f) The U.S Food and Drug Administration has approved JYNNEOS^{TM}, commonly known as Imvamune or Imvanex, as an attenuated live virus vaccine for the prevention of monkeypox.

Monkeypox medical countermeasures

There has been no established therapy for monkeypox infection over the years, although MPX outbreaks can be managed[4]. The bulk of the time, the therapy is supportive. In the management of MPX epidemics, however, smallpox vaccination, ST-246, cidofovir, and vaccinia immune globulin (VIG) have been advised. Smallpox vaccination should be given within two weeks following monkeypox exposure. Smallpox vaccination, according to scientific research, gives 85 percent protection against the illness [52].

Hatch *et al.,* used Cynomolgus macaques (*Macaca fascularis*) to evaluate the effectiveness of the smallpox vaccinations Imvamune (JYNNEOSTM) and ACAM2000TM against 105 pfu aerosolized MPXV intranasally. Aside from the red patches on all MPXV-challenged animals at the vaccination point, most animals lost weight, notably those mock-vaccinated with TBS (Tris-buffered saline), with 10–18 percent weight loss, and all surviving animals in the vaccination groups gained weight from day 14 post-challenge.[53] This attenuated live virus vaccine (JYNNEOS^{TM}) is approved by the U.S. Food and Drug Administration for the prevention of monkeypox[1][4]. Berhanu*et al*., reported that Tecovirimat (ST-246), an antiviral, gives complete protection against monkeypox when administered alone or in conjunction with the small pox vaccination. In January 2022, it is authorised for the treatment of monkeypox[54][55]. The usefulness of VIG in the treatment of MPX sequelae is unknown. The use of VIG is governed by an Investigational New Drug (IND) and has not been shown to be effective in the treatment of smallpox sequelae. Although it is uncertain if VIG treatment can assist a person with a severe monkeypox infection, it may be explored in such cases.Smallpox vaccination after exposure to MPX is prohibited, thus VIG might be used as a preventative measure in an exposed person with significant immunodeficiency in T-cell function. However, the CDC presently only recommends vaccinia immune globulin (VIG) and cidofovir for the treatment of severe sequelae from smallpox immunisation[4][56].

Clinical stages of monkeypox

a) Incubation period

MPX has an incubation period of 7 to 14 days (from infection to beginning of symptoms), however it can be anywhere from 5 and 21 days. During this time, a person is not infectious, has no symptoms, and may appear healthy [50][57].

b) Prodrome

MPX patients will have an initial round of symptoms (prodrome). During this moment, a person may be infectious. Generalized headache and weariness accompany the early febrile prodrome. Many individuals have maxillary, cervical, or inguinal lymphadenopathy (1–4 cm in diameter) before to and concurrent with the onset of the rash. The presence of lymphadenopathy distinguishes MPX from smallpox [50][58].

c) Rash

Lesions will appear in the mouth and on the body once the prodrome has passed. Before they fall off, lesions go through a number of phases. The rash develops first on the face and then spreads over the body in a centrifugal pattern. The lesions are often macular at first, then papular, vesicular, pustular, then crusted and scabbed over by the end of the second week. Scabs, on the other hand, will last approximately a week until they come off [50][59].

d) Rash resolved

After the scabs have gone off, pitted scars and/or regions of brighter or darker skin may remain. A person is no longer contagious once all scabs have gone off. The entire procedure might take anything from 2-4 weeks. Though a patient who has been infected might spread the illness from one day before to 21 days after the first symptoms or scab falls appear [50][60].

Conclusion

Monkeypox (MPX) is an emerging infectious disease with gradually increasing outbreak frequency and predicted breakout magnitude in human populations. Monkeypox was formerly not transmitted through the respiratory route and could not be sustained in people, but genetic modifications have made this feasible. Monkeypox is no longer a rare illness; it requires greater care. As a result, national and international research efforts should be stepped up in order to identify disease virulence markers, human behaviours that support zoonotic overspill events, host and viral factors that modulate MPXV evolution, asymptomatic contagion surrogates, and virus and host determinants of immunity. The current COVID-19

pandemic has demonstrated to the globe the need of being properly prepared for futurepandemics. Advances in our knowledge of this major zoonosis will aid in the development of improved preventative methods and the mitigation of human sickness.

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References

1. Pal M, Singh R, Gutama KP, Savalia C, Thakur R. Human Monkeypox: An Emerging and Re-emerging Infectious Viral Disease. Acta Sci Microbiol. 2022;(April):146–50.
2. Kozlov M. Monkeypox goes global: why scientists are on alert. Nature [Internet]. 2022;1–3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35595996
3. Otu AA, Ebenso B, Walley J. Comment Global human monkeypox outbreak : atypical presentation demanding urgent public health action. THE LANCET MICROBE. 2022;3(1):1–2.
4. Monkeypox | Poxvirus | CDC [Internet]. Available from: https://www.cdc.gov/poxvirus/monkeypox/index.html
5. Mariën J, Laudisoit A, Patrono L, Baelo P, van Vredendaal R, Musaba P, et al. Monkeypox viruses circulate in distantly-related small mammal species in the Democratic Republic of the Congo. Nat Commun. 2021;PREPRINT:1–12.
6. Khodakevich L, Jezek Z, Messinger D. Monkeypox virus: ecology and public health significance. Bull World Health Organ. 1988;66(6):747–52.
7. Grant R, Nguyen LBL, Breban R. Modelling human-to-human transmission of monkeypox. Bull World Health Organ. 2020;98(9):638–40.
8. Sklenovská N, Van Ranst M. Emergence of Monkeypox as the Most Important Orthopoxvirus Infection in Humans. Vol. 6, Frontiers in Public Health. 2018. p. 1–12.
9. Bonilla-aldana DK, Thormann M, Lopardo G, Rodriguez-morales AJ. Monkeypox virus - Would it arrive in Latin America ? Rev Panam Salud Pública. 2022;5(1):1–3.
10. Leggiadro RJ. Emergence of Monkeypox—West and Central Africa, 1970–2017. Pediatr Infect Dis J. 2018;37(7):721–721.

11. Jezek Z, Gromyko AI, Szczeniowski M V. Human monkeypox. J Hyg Epidemiol Microbiol Immunol. 1983;27(1):13–28.

12. Monkeypox [Internet]. Available from: https://www.who.int/news-room/fact-sheets/detail/monkeypox

13. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox virus in nigeria: Infection biology, epidemiology, and evolution. Viruses. 2020;12(11).

14. Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C, et al. Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infect Dis Clin North Am. 2019 Dec;33(4):1027–43.

15. Joshua J, Nlerum P. A Neuro-Fussy Based Model for Diagnosis of Monkeypox Diseases A Neuro-Fussy Based Model for Diagnosis of Monkeypox Diseases. Int J Comput Sci Trends Technol. 2018;6(2):143–53.

16. Yinka-Ogunleye A, Aruna O, Dalhat M, Ogoina D, McCollum A, Disu Y, et al. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. Lancet Infect Dis. 2019 Aug;19(8):872–9.

17. Faye O, Pratt CB, Faye M, Fall G, Chitty JA, Diagne MM, et al. Genomic characterisation of human monkeypox virus in Nigeria. Vol. 18, The Lancet. Infectious diseases. United States; 2018. p. 246.

18. Cho CT, Wenner HA. Monkeypox virus. Bacteriol Rev [Internet]. 1973 Mar;37(1):1–18. Available from: https://pubmed.ncbi.nlm.nih.gov/4349404

19. Odom MR, Hendrickson RC, Lefkowitz EJ. Poxvirus protein evolution: family wide assessment of possible horizontal gene transfer events. Virus Res. 2009 Sep;144(1–2):233–49.

20. Kugelman JR, Johnston SC, Mulembakani PM, Kisalu N, Lee MS, Koroleva G, et al. Genomic variability of monkeypox virus among humans, Democratic Republic of the Congo. Emerg Infect Dis [Internet]. 2014 Feb;20(2):232–9. Available from: https://pubmed.ncbi.nlm.nih.gov/24457084

21. Shchelkunov SN, Totmenin A V, Safronov PF, Mikheev M V, Gutorov V V, Ryazankina OI, et al. Analysis of the monkeypox virus genome. Virology. 2002 Jun;297(2):172–94.

22. Alkhalil A, Hammamieh R, Hardick J, Ichou MA, Jett M, Ibrahim S. Gene expression profiling of monkeypox virus-infected cells reveals novel interfaces for host-virus interactions. Virol J. 2010;7:1–19.

23. Shchelkunov SN, Totmenin A V, Babkin I V, Safronov PF, Ryazankina OI, Petrov NA, et al. Human monkeypox and smallpox viruses: genomic comparison. FEBS Lett. 2001 Nov;509(1):66–70.

24. Mauldin MR, McCollum AM, Nakazawa YJ, Mandra A, Whitehouse ER, Davidson W, et al. Exportation of Monkeypox Virus From the African Continent. J Infect Dis. 2022;225(8):1367–76.

25. Jezek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: clinical features of 282 patients. J Infect Dis. 1987 Aug;156(2):293–8.

26. Monkeypox [Internet]. [cited 2022 Jun 1]. Available from: https://www.who.int/news-room/fact-sheets/detail/monkeypox

27. Feng Y. Supporting Information Supporting Informationa. Aldenderfer, Mark S, Craig, Nathan M, Speak Robert Jeff, Popelka-Filcoff, Rachel S. 1997;2(1):1–5.

28. Hudson PN, Self J, Weiss S, Braden Z, Xiao Y, Girgis NM, et al. Elucidating the role of the complement control protein in monkeypox pathogenicity. PLoS One. 2012;7(4):e35086.

29. Estep RD, Messaoudi I, O'Connor MA, Li H, Sprague J, Barron A, et al. Deletion of the monkeypox virus inhibitor of complement enzymes locus impacts the adaptive immune response to monkeypox virus in a nonhuman primate model of infection. J Virol. 2011 Sep;85(18):9527–42.

30. Kindrachuk J, Arsenault R, Kusalik A, Kindrachuk KN, Trost B, Napper S, et al. Systems kinomics demonstrates Congo Basin monkeypox virus infection selectively modulates host cell signaling responses as compared to West African monkeypox virus. Mol Cell Proteomics [Internet]. 2011/12/28. 2012 Jun;11(6):M111.015701-M111.015701. Available from: https://pubmed.ncbi.nlm.nih.gov/22205724

31. Rubins KH, Hensley LE, Relman DA, Brown PO. Stunned silence: gene expression programs in human cells infected with monkeypox or vaccinia virus. PLoS One. 2011 Jan;6(1):e15615.

32. Tosepu R. Early Warning of Monkeypox Disease in Indonesia. Public Heal Indones. 2019;5(2):36–7.

33. Eteng WE, Mandra A, Doty J, Yinka-Ogunleye A, Aruna S, Reynolds MG, et al. Notes from the Field: Responding to an Outbreak of Monkeypox Using the One Health Approach - Nigeria, 2017-2018. MMWR Morb Mortal Wkly Rep. 2018 Sep;67(37):1040–1.

34. Mustaffa F, Adilla N, Zaini B. REVIEW : AN ANALYSIS OF MONKEYPOX DISEASE AND CURRENT SCENARIO IN MALAYSIA. Int J Res - Granthaalayah. 2019;7(9):82–7.

35. Jezek Z, Marennikova SS, Mutumbo M, Nakano JH, Paluku KM, Szczeniowski M. Human monkeypox: a study of 2,510 contacts of 214 patients. J Infect Dis. 1986 Oct;154(4):551–5.

36. Barnewall RE, Fisher DA, Robertson AB, Vales PA, Knostman KA, Bigger JE. Inhalational monkeypox virus infection in cynomolgus macaques. Front Cell Infect Microbiol [Internet]. 2012 Sep 17;2:117. Available from: https://pubmed.ncbi.nlm.nih.gov/23061051

37. Fine PE, Jezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. Int J Epidemiol. 1988 Sep;17(3):643–50.

38. Jain N, Lansiaux E, Simanis R. The New Face of Monkeypox Virus : An Emerging Global Emergency. New Microbes New Infect [Internet]. 2022;1–10. Available from: www.journals.elsevier.com/new-microbes-and-new-infections

39. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox-A potential threat? A systematic review. PLoS Negl Trop Dis. 2022 Feb;16(2):e0010141.

40. Guertin M. A case of monkeypox in the DRC. MSF Paediatr Days. 2021;1–2.

41. Pal M, Mengstie F, Kandi V. Epidemiology, Diagnosis, and Control of Monkeypox Disease: A comprehensive Review. Am J Infect Dis Microbiol [Internet]. 2022 Jun 2;5(2):94–9. Available from: http://pubs.sciepub.com/

42. Li Y, Olson VA, Laue T, Laker MT, Damon IK. Detection of monkeypox virus with real-time PCR assays. J Clin Virol Off Publ Pan Am Soc Clin Virol. 2006

Jul;36(3):194–203.

43. States M, States M, Regulations IH, States M, States M, Office WHOR, et al. Laboratory testing for the monkeypox virus. World Heal Organ. 2022;1–6.

44. Kulesh DA, Loveless BM, Norwood D, Garrison J, Whitehouse CA, Hartmann C, et al. Monkeypox virus detection in rodents using real-time 3'-minor groove binder TaqMan assays on the Roche LightCycler. Lab Invest. 2004 Sep;84(9):1200–8.

45. Reed KD, Melski JW, Graham MB, Regnery RL, Sotir MJ, Wegner M V, et al. The Detection of Monkeypox in Humans in the Western Hemisphere. N Engl J Med [Internet]. 2004 Jan 22;350(4):342–50. Available from: https://doi.org/10.1056/NEJMoa032299

46. Leendertz SAJ, Stern D, Theophil D, Anoh E, Mossoun A, Schubert G, et al. A Cross-Sectional Serosurvey of Anti-Orthopoxvirus Antibodies in Central and Western Africa. Viruses. 2017 Sep;9(10).

47. Vora NM, Li Y, Geleishvili M, Emerson GL, Khmaladze E, Maghlakelidze G, et al. Human infection with a zoonotic orthopoxvirus in the country of Georgia. N Engl J Med [Internet]. 2015 Mar 26;372(13):1223–30. Available from: https://pubmed.ncbi.nlm.nih.gov/25806914

48. McCollum AM, Damon IK. Human Monkeypox. Clin Infect Dis [Internet]. 2014 Jan 15;58(2):260–7. Available from: https://doi.org/10.1093/cid/cit703

49. Townsend MB, MacNeil A, Reynolds MG, Hughes CM, Olson VA, Damon IK, et al. Evaluation of the Tetracore Orthopox BioThreat® antigen detection assay using laboratory grown orthopoxviruses and rash illness clinical specimens. J Virol Methods. 2013 Jan;187(1):37–42.

50. Monkeypox | Poxvirus | CDC [Internet]. [cited 2022 Jun 1]. Available from: https://www.cdc.gov/poxvirus/monkeypox/index.html

51. PEDRO N. ACHA BS. ZOONOSES AND COMMUNICABLE DISEASES COMMON TO MAN AND ANIMALS. Vol. 1, Pan American Health Organization (PAHO), Washington, D.C.USA. 2001. 16–21 p.

52. Russo AT, Berhanu A, Bigger CB, Prigge J, Silvera PM, Grosenbach DW, et al. Co-administration of tecovirimat and ACAM2000™ in non-human primates: Effect of

tecovirimat treatment on ACAM2000 immunogenicity and efficacy versus lethal monkeypox virus challenge. Vaccine. 2020 Jan;38(3):644–54.

53. Hatch GJ, Graham VA, Bewley KR, Tree JA, Dennis M, Taylor I, et al. Assessment of the protective effect of Imvamune and Acam2000 vaccines against aerosolized monkeypox virus in cynomolgus macaques. J Virol. 2013 Jul;87(14):7805–15.

54. Berhanu A, Prigge JT, Silvera PM, Honeychurch KM, Hruby DE, Grosenbach DW. Treatment with the smallpox antiviral tecovirimat (ST-246) alone or in combination with ACAM2000 vaccination is effective as a postsymptomatic therapy for monkeypox virus infection. Antimicrob Agents Chemother. 2015 Jul;59(7):4296–300.

55. Monkeypox - PAHO/WHO | Pan American Health Organization [Internet]. Available from: https://www.paho.org/en/topics/monkeypox

56. Shearer JD, Siemann L, Gerkovich M, House R V. Biological activity of an intravenous preparation of human vaccinia immune globulin in mouse models of vaccinia virus infection. Antimicrob Agents Chemother [Internet]. 2005 Jul;49(7):2634–41. Available from: https://pubmed.ncbi.nlm.nih.gov/15980330

57. Monkeypox (MPX) | Australian Government Department of Health [Internet]. Available from: https://www.health.gov.au/health-topics/monkeypox-mpx

58. Damon IK. Status of human monkeypox: clinical disease, epidemiology and research. Vaccine. 2011 Dec;29 Suppl 4:D54-9.

59. Di Giulio DB, Eckburg PB. Human monkeypox: an emerging zoonosis. Lancet Infect Dis. 2004 Jan;4(1):15–25.

60. Monkeypox: Stages of rash progression, how long it lasts; know from expert | Health - Hindustan Times [Internet]. Available from: https://www.hindustantimes.com/lifestyle/health/monkeypox-how-the-rash-progresses-for-how-long-it-lasts-know-from-expert-101653393046909.html

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