

A Current Overview of Spreading Mechanism and Treatment of Monkeypox Virus

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ABSTRACT

Outside of Africa, the monkeypox epidemic has returned in 2022. The MPXV spreads from body to body via inhaling droplets, inadvertent contact with contaminated objects, or direct connection with infectious skin. Different epidemiological and clinical characteristics distinguish the illness brought on by the MPXV clades. Comparable to smallpox, the MPXV infection has a lower fatality rate (10%) and a milder form. This virus has developed new features that allow it to spread rapidly. There are currently no specific vaccines or medications that can prevent MPXV infection, despite the fact that smallpox immunization has been found to offer 85% protection against MPXV infection and the promise of 2 anti-smallpox virus treatments for MPXV. The decision to end the national smallpox immunization programs in many nations should thus be given further thought. However, it is highly challenging to establish the disease and identify its cause based solely on clinical symptoms in the absence of reliable diagnostic testing. Strategies for MPXV prevention and treatment, as well as laboratory diagnosis. This study offers the fundamental information needed to stop and manage any further spread of this virus.

KEYWORDS

Monkeypox, smallpox, zoonosis, antiviral drugs, smallpox vaccine

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INTRODUCTION

The advent of zoonotic viral illnesses, which have been responsible for a huge number of epidemics and pandemics. In this series, the uncommon infectious zoonotic illness known as monkeypox is infected by the monkeypox virus (MPXV). Earlier cases of "monkey smallpox" were especially prevalent in Central and West Africa. In MPX similar smallpox-like symptoms are present, although the illness is milder and mostly manifests as headache, fever, lymphadenopathy and systemic pustules and blisters the case mortality rate is between 1 and 10% to the report of Doshi *et al.*¹ and Ogoina *et al.*². On May, 6 2022, the United Kingdom declared an epidemic of monkeypox. This outbreak was traced to a British citizen who visited Nigeria, where the illness is endemic and displayed symptoms corresponding with April 29, 2022, while there on May 4, this individual travelled back to the UK, bringing the outbreak's index case with them.

As of May 21, 2022, 92 cases had been reported from 13 countries where the monkeypox virus (MPXV) is not common. By May 22, 2022, there were confirmed outbreaks in a total of 15 nations.

According to report Hayama *et al.*³ on May 24, the United Arab Emirates revealed the first infection case in all the Arab countries. As of almost two months later, on August 5, 2022, 28,220 persons were infected



with this virus throughout more than 80 different nations. Out of which only the United States of America has suffered 7,509 MPX victims worldwide to date, according to the CDC, whereas Belgium is the first nation to enforce a mandatory 21-day MPX quarantine. The ongoing MPX outbreak has drawn considerable interest from all across the world and can do to pose a risk to larger populations.

So, this MPXV virus prevention is most important to be different. Although the WHO declared the smallpox virus to be extinct in 1980 reported by Jezek *et al.*⁴, the smallpox vaccine has not been used since, despite reports that it offers 85% protection against MPXV, Fine *et al.*⁵. Additionally, MPXV-specific medications and vaccinations are lacking. Therefore, a thorough study of the biological traits and pathogenicity of MPXV is required to stop the spread of MPX outbreaks. Here, this study assessed the state of MPXV research and offered hints for MPX outbreak prevention and control.

FINDING OF MPXV

The smallpox virus, the vaccinia virus and the cowpox virus are all members of the genus *Orthopoxvirus*, which MPXV also belongs to according to Babkin *et al.*⁶. In 1958, MPXV was discovered after vesicular disease struck study monkeys sent from Singapore to Denmark. To whom gave the name was "monkeypox" Magnus *et al.*⁷.

The greatest animal reservoirs for the virus are rodents, such as big pouched rats and squirrels, which are hunted for food⁸. When the virus was isolated from a 9-year-old boy in the Democratic Republic of Congo (DRC)s areas which were to was smallpox in August, 1970, which in the first human case identified⁹. Human MPX cases were documented since 1970 in 11 countries in Africa, with a median age of 3¹⁰. Only a few instances have ever been reported outside of Africa. In the present epidemic, the virus was discovered in several individuals for the first time even though they had no obvious connection to West and Central Africa¹¹. The majority of cases that have been reported so far, though not solely, have been found among homosexual and bisexual males aged 20 to 50¹¹, although it is unclear if this is due to sexual practices that make it more contagious or whether it is only a coincidence¹⁰. It has been established that the vaccinia virus, which is used to treat smallpox and offer cross-protection against it, may be transmitted through sexual intercourse reported by Likos *et al.*¹².

SO FAR SITUATION OF MPXV

The two different clades of MPXV are West African and Congo Basin¹. The two MPXV clades that cause the disease have different epidemiological and clinical characteristics. Up to 10% of cases have died in the Congo Basin², compared to only 1% in West Africa, where patients who also have HIV have a greater death rate¹³. The first MPXV case in a human was discovered in the Democratic Republic of the Congo in 1970¹⁴. The MPXV was first discovered in 1958. Since then, MPX has spread to other African countries, mainly those in Central and West Africa and has established itself as an endemic disease in the DRC.

The 38 of the 47 human Monkeypox cases recorded in five Central and West African nations between 1970 and 1979 originated in the Democratic Republic of the Congo, all of which occurred in tropical rain forests and were linked to animal interaction¹⁴. A total of 338 instances of human MPX were discovered in the DRC from 1981-1986 after smallpox was eradicated. Unvaccinated individuals did a death rate as high as 9.8% when it comes to smallpox. The majority of infections in human affect average age group of 4.4 years and comprise 72% of zoonotic transmission cases according to report by Heymann *et al.*¹⁵.

Reports of chronic MPX exposure in humans have declined after the WHO monitoring programme came to an end in 1986. Only 13 instances were documented from 1986 to 1992 and there were none from 1993 to 1995¹⁶. However, there was a sharp rise in the number of human MPXV infection cases recorded in the DRC starting in 1996. By 1997, a total of 88 individuals had been identified as having MPX infection¹⁶. In the US, MPX first appeared in 2003. As a result of marmots brought into the country from Africa

carrying the MPXV, 47 individuals have been diagnosed across five states, making this the first MPX epidemic outside of Africa to be documented by Sale *et al.*¹⁷ and Formenty *et al.*¹⁸. The MPX epidemic in Sudan in 2005 was reported to have resulted in a total of 10 confirmed cases¹⁹. Between 2006 to 2007, the DRC saw the discovery of a fresh case of human MPX infection.

Since the 1980s, MPX transmission has grown 20-fold and is found those who had the smallpox vaccine have a 21-fold reduced chance of infection than those who have not. And in most instances, zoonotic transmission took place. At end of 2017, MPX had been spread throughout Nigeria, where as of November 2019, 183 confirmed cases had been recorded in 18 states. The epidemic was also the worst West African outbreak ever recorded¹⁹⁻²¹.

After that, cases of MPX patients were discovered upon in Singapore²², the United Kingdom²³, Israel²⁴ and other many nations. Up to May, 2022, MPX outbreaks have been reported in a number of nations, which have experts in several nations on high alert²⁵.

MODE OF TRANSMISSION MPXV TO HUMANS

When an individual comes into contact with an infected animal, infected human, or virus-contaminated item, MPXV is spread. By both the animal to human and human to human, MPXV does spread out²⁶. Infection with MPXV in humans is primarily brought about by animal bites or direct contact with the blood, bodily fluids, or lesions of infected animals, eating inadequately prepared infected animals can also result in human infection^{27,28}. Additionally, MPXV can be transmitted through close physical contact, such as kissing, embracing, or touching monkeypox-infected body parts. It can also spread from mother to fetus through the placenta and by direct contact with the virus infected person's bodily fluids or things like clothing and bedding that have come into contact with the virus (Fig. 1). Additionally, in the most recent outbreak, young men who have sex with men (MSM) and have genital lesions that could indicate near contact accounted for the majority of this virus infections to the report of Vivancos *et al.*²⁹.

However, human-to-human transmission is the mode of transmission during this outbreak. Although the illness isn't typically thought of as a sexually transmitted sickness, intimate contact has been shown to cause inter-human transmission³⁰. As a result, the possibility of communal transmission exists. The MPXV transmission mode is listed in Table 1 from 1970 to 2019 according to Hutson.

COMPLICATION OF MPXV RELATED

Complication of health: Monkeypox cases are typically moderate and self-resolve within a few weeks, but skin lesions frequently leave scars. Serious side effects like blindness, bronchopneumonia,

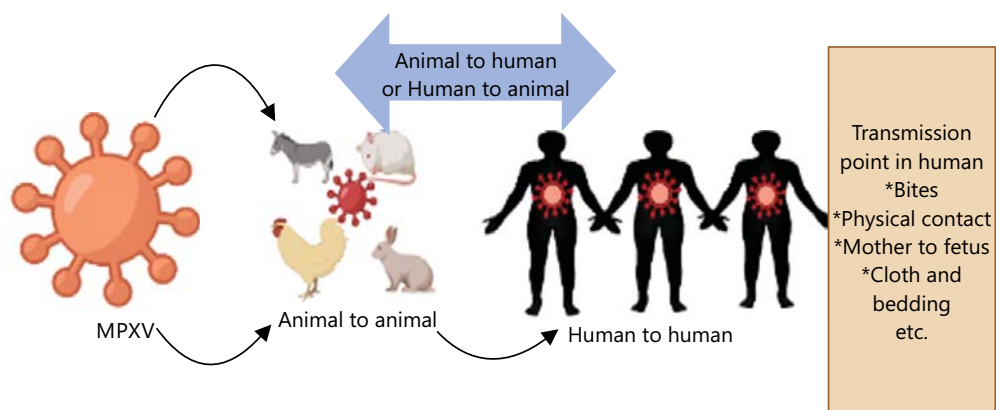


Fig. 1: MPXV spread mode

Table 1: Transmission factors of MPX in previous years

Decades	Central countries	West countries	Another country
1970 to 1979	Cameroon: Unknown DRC: Both	Liberia: Unknown Nigeria: Unknown Nigeria: Human-to-human Sierra Leone: Unknown	
1980 to 1989	CAR: Animal-to-human DRC: Both Gabon: Unknown	Ivory Coast: Unknown	
1990 to 1999	DRC: Both Gabon: Unknown		
2000 to 2009	DRC: Animal-to-human RC: Animal-to-human		
2010 to 2019	CAR: Both DRC: Animal-to-human RC: Unknown	Nigeria: Both Sierra Leone: Unknown Sierra Leone: Animal	Israel: Animal-to-human Singapore: Animal South Sudan: Human-to-human UK: Unknown, human-to-human US: Animal-to-human

CAR: Central African Republic, DRC: Democratic Republic of the Congo and RC: Republic of the Congo

encephalopathy and sepsis can occur less frequently. Similar to smallpox, the most frequent effects of monkeypox are scarring and the emergence of discolored pockmarks, usually on the face and other places where a lot of sebaceous glands.

Complication of laboratory diagnosis: For MPXV testing using nucleic acids might be generic for the *Orthopoxvirus* or particular for the monkeypox virus. Nucleic acid amplification testing employing real-time (RT) or traditional PCR for the identification of viral DNA is required for the definitive diagnosis of monkeypox virus infection. Clinical specimens from skin lesions, such as swabs of the lesion surface or pus, roofs from many lesions, or lesion crusts, as a sample are used for laboratory diagnosis. Pairs of acute and convalescent sera are necessary for serological testing for IgG, which may become detectable 6-8 days after the onset of symptoms. Initial IgM antibodies against the monkeypox virus may be positive during the first three to five days. However, monkeypox should not be diagnosed only using antibody detection in plasma³¹.

Antiviral drugs: There are currently no antiviral medications specifically prepared for the treatment of MPX. For the MPXV drugs that fight the smallpox virus can be effective against MPXV. Small molecule virus inhibitor tecovirimat (ST-246) possesses potent anti-orthopoxvirus efficacy against smallpox virus, MPXV and cowpox virus. By blocking the primary envelope protein's (F13L) ability to function, it can stop the transmission of viruses by stopping them from exiting infected cells to the findings of Thakur *et al.*³². In 2022, it received approval in Europe for the treatment of MPX³³. Both cidofovir and the brincidofovir derivative (CMX001) work as inhibitors of viral DNA polymerase. An acyclic nucleoside phosphate is cidofovir. The drug's lipid wrap may be broken when CMX001 enters the host cells, releasing free Cidofovir that will then be phosphorylated into cidofovir-diphosphate (CDV-PP). As a substitute matrix, CDV-PP prevents the synthesis of viral DNA polymerase and in end ultimately fend viral DNA synthesis at the DNA polymerase level^{34,35}. Cidofovir and brincidofovir have both shown *in vitro* and *in vivo* that they can prevent MPXV replication³⁶. The nucleoside analogues inhibitor nioch-14 has similar anti-MPXV and anti-VACV properties to tecovirimat and exhibits potent antiviral activity against a variety of *Orthopoxviruses*. Nioch-14 is seen as a potential anti-MPXV medication due to its ease of production according to report of Brown and Leggat³⁷.

Variola virus (VARV) and MPXV are more susceptible to the inosine monophosphate dehydrogenase (IMP) inhibitors ribavirin and tiazofurin, which can decrease the replication of all poxviruses³⁷.

Table 2: Antiviral treatment options for MPXV infection

Therapy	Mechanism of action	Typical dosing	Formulation	Side effects and adverse events
Cidofovir	Blocks viral DNA synthesis through competitive inhibition of DNA polymerase	5 mg kg ⁻¹ once weekly for ≥ 2 doses (with concomitant probenecid)	IV, off-label: Topical, intravesicular	Decreased intraocular pressure, nausea, vomiting
Brincidofovir	Lipid conjugate prodrug of cidofovir	4 mg kg ⁻¹ once weekly for 2 doses (max 200 mg/dose)	Oral	Abdominal pain, vomiting, elevated liver transaminases and bilirubin
Tecovirimat	Inhibits activity of the protein VP37, which prevents creation of virions that can be released from an infected host cell, thereby preventing replication and dissemination within the host	IV: 35 to <120 kg: 200 mg q ⁻¹ 12 hrs ≥ 120 kg: 300 mg q ⁻¹ 12 hrs Oral: 40 to <120 kg: 600 mg q ⁻¹ 12 hrs ≥ 120 kg: 600 mg q ⁻¹ 8 hrs All regimens for 14 days	IV and oral (off-label topical) According to Lederman <i>et al.</i> ⁴⁴	IV: Extravasation at infusion site, headache Oral: Headache, abdominal pain and nausea

Potential anti-MPXV medications include the S-adenosylhomocysteine (SAH) hydrolase inhibitors C-CA3-ADO and C3-NPC A, the DNA polymerase inhibitor HPMA and adenosine N1 oxide (ANO)³⁷. A summary of these treatment options was presented in Table 2.

Vaccines: A vaccine has always worked as a strong weapon for any virus to disseminate or prevention. Although there isn't a specific vaccination available yet to protect against MPXV infection. According to reports, smallpox vaccination offers 85% protection against MPXV to Nasir *et al.*³⁸ and Petersen *et al.*³⁹. Most MPXV cases were born after the smallpox virus eradication program's completion and epidemiological studies showed that almost 90% of verified cases had not been exposed to other poxviruses. This strongly suggested that they had not received the smallpox vaccine according to Nasir *et al.*³⁸.

Currently, the 2nd generation ACAM 2000 and the third-generation IMVAMUNE (An attenuated modified vaccinia Ankara virus vaccine for smallpox infection) vaccines are authorized for use in preventing both MPXV and smallpox virus. The ACAM 2000 was shown to lessen MPX symptoms during the 2003 MPXV outbreak in the United States³⁸, nevertheless, patients with atopic dermatitis and those with impaired immune systems may experience side effects. In locations where MPXV is endemic, this vaccination is not used and is not accessible to the general public. The IMVAMUNE is a replication-deficient, attenuated, 3rd generation modified vaccinia Ankara (MVA) vaccine that has also received approval from the European Medicine Agency and the FDA for the preclusion of MPXV and smallpox virus in adults and older age in high-risk populations. The IMVAMUNE, in contrast to ACAM 2000, can be taken by people with immunodeficiency and atopic dermatitis⁴⁰. The IMVAMUNE and ACAM2000 have not yet been given the green light for use in the general public. Therefore, it is unknown if certain smallpox vaccines approved for use can prevent MPX illnesses in locations where MPXV is endemic was reported by Brown *et al.*³⁷ and Petersen *et al.*⁴⁰.

FUTURE DIRECTIONS AND LIMITATIONS

Whereas a large number of nations in Europe, South America, the Middle East, Canada and the United States have recorded thousands of cases. Which are young males between the ages of 25 and 35 make up the bulk of cases and many of them self-identify as homosexual, bisexual, or another MSM. Clinical investigations were occasionally characterized by unusual presentations, which are genital, perigenital and perianal lesions, which may have a significant impact on transmission^{41,42}.

Currently, research is being done to determine whether or not monkeypox can be sexually transmitted in the traditional sense. Public health authorities in the UK have advised abstinence during active infection

and for up to eight weeks following recovery as an added precaution until more is studied about the purpose of sexual transmission. Pre-exposure vaccination of gay/bisexual and other MSM and prioritised vaccination of close contacts of case patients are two tactics⁴³⁻⁴⁵ being pushed at the moment in some countries to keep under control this epidemic.

One of the greatest monkeypox outbreaks in recorded history is still running, with numerous nations experiencing chains of transmission outside of areas where the disease is reasoning to be prevailing. The unusually long MPXV incubation period and the initially low index of suspicion displayed by practitioners who were unfamiliar with the virus may have made it possible for local transmission leading to sizable clusters to go unreported for some time⁴⁶.

Although dangerous, the monkeypox scenario today is distinct. The continued outbreaks of monkeypox are not anticipated to cause a pandemic of comparable scope on a worldwide scale. Since MPXV is not a new virus, prior outbreaks have provided insight into how to stop the illness from spreading. However, many professionals are unfamiliar with monkeypox, thus it is understandable that they do not have much expertise in diagnosing or treating instances of the illness. It will be crucial to understand the characteristics of the current outbreak before deciding how to use the tools at our disposal to stop it. The determination of the epidemic's scope and the use of screening procedures in healthcare settings will help identify individuals by utilising developing clinical case definitions. It will be essential to isolate suspected and confirmed cases as soon as possible, closely monitor them and immunise their close contacts and healthcare professionals who have been exposed to high-risk scenarios as necessary in order to avoid new infections and break up transmission chains. It is reasonable to worry that monkeypox may fill new ecological niches in wild animals in places outside of Africa if the current outbreak persists, widening its enzootic and endemic range.

CONCLUSION

The MPX outbreak has spread to be endemic in more than 80 countries to till. According to WHO officers, MPX may not become a pandemic because the virus's infectivity is rather modest. However, this global outbreak with a sporadic high number of cases has alarmed worldwide health officials as it is the greatest and most widespread MPX epidemic to date. Close contact with skin lesions, respiratory secretions and body fluids of infected animals, either directly or indirectly through contaminated fomites, results in the transmission of human monkeypox. Because these viruses spread from human to human, animal to human. Therefore, for these MPX disses proper antiviral drugs for treatment need to be brought to light as soon as possible and vaccines find out get for MPXV are most important and challenging. We must give the scientific organizations a high priority and expand our fundamental studies of zoonotic poxvirus illness. While another side to control the spread of monkeypox, it is serious to strengthen awareness and shadowing and technical worldwide teamwork is essential to decrease the hazard of MPX.

SIGNIFICANCE STATEMENT

When an individual comes into contact with an infected animal, infected human, or virus-contaminated item, MXV is spread. By both the animal to human and human to human, MXV does spread out. The present work, address recent findings that provide light on the processes underlying monkeypox virus infection and treatment, which will be possible help to be medical field in the future.

ACKNOWLEDGMENT

I would like to thank Sarvepalli Radhakrishnan University Bhopal for their help in this work.

REFERENCES

1. Doshi, R.H., S.A.J. Guagliardo, J.B. Doty, A.D. Babeaux and A. Matheny *et al.*, 2019. Epidemiologic and ecologic investigations of Monkeypox, Likouala Department, Republic of the Congo, 2017. *Emerging Infect. Dis.*, 25: 281-289.
2. Ogoina, D., J.H. Izibewule, A. Ogunleye, E. Ederiane and U. Anebonam *et al.*, 2019. 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. 10.1371/journal.pone.0214229.
3. Hayama, K., H. Ishibashi, S.A. Ishijima, K. Niimi and S. Tansho *et al.*, 2012. A D-octapeptide drug efflux pump inhibitor acts synergistically with azoles in a murine oral candidiasis infection model. *FEMS Microbiol. Lett.*, 328: 130-137.
4. Jezek, Z., L.N. Khodakevich and J.F. Wickett, 1987. Smallpox and its post-eradication surveillance. *Bull. World Health Organ.*, 65: 425-434.
5. Fine, P.E.M., Z. Jezek, B. Grab and H. Dixon, 1988. The transmission potential of monkeypox virus in human populations. *Int. J. Epidemiol.*, 17: 643-650.
6. Babkin, I.V., I.N. Babkina and N.V. Tikunova, 2022. An update of orthopoxvirus molecular evolution. *Viruses*, Vol. 14. 10.3390/v14020388.
7. von Magnus, P., E.K. Andersen, K.B. Petersen and A. Birch-Andersen, 1959. A pox-like disease in cynomolgus monkeys. *Acta Pathologica Microbiol. Scand.*, 46: 156-176.
8. Doty, J.B., J.M. Malekani, L.N. Kalemba, W.T. Stanley and B.P. Monroe, 2017. Assessing monkeypox virus prevalence in small mammals at the human-animal interface in the democratic republic of the Congo. *Viruses*, Vol. 9. 10.3390/v9100283.
9. Marennikova, S.S., E.M. Šeluhina, N.N. Mal'ceva, K.L. Čimiškjan and G.R. Macevič, 1972. Isolation and properties of the causal agent of a new variola-like disease (monkeypox) in man. *Bull. World Health Organ.*, 46: 599-611.
10. Muzny, C.A., R. Nolan, H. King, M. Carrier, L. Mena and P. Byers, 2009. Vulvar vaccinia infection after sexual contact with a smallpox vaccinee. *Am. J. Med. Sci.*, 337: 289-291.
11. Petersen, E., A. Kantele, M. Koopmans, D. Asogun, A. Yinka-Ogunleye, C. Ihekweazu and A. Zumla, 2019. Human monkeypox: Epidemiologic and clinical characteristics, diagnosis, and prevention. *Infect. Dis. Clin. North Am.*, 33: 1027-1043.
12. Likos, A.M., S.A. Sammons, V.A. Olson, A.M. Frace and Y. Li *et al.*, 2005. A tale of two clades: Monkeypox viruses. *J. Gen. Virol.*, 86: 2661-2672.
13. Breman, J.G., Kalisa-Ruti, M.V. Steniowski, E. Zanotto and A.I. Gromyko, 1980. Human monkeypox, 1970-79. *Bull. World Health Organ.*, 58: 165-182.
14. Damon, I.K., 2011. Status of human monkeypox: Clinical disease, epidemiology and research. *Vaccine*, 29: D54-D59.
15. Heymann, D.L., M. Szczeniowski and K. Esteves, 1998. Re-emergence of monkeypox in Africa: A review of the past six years. *Br. Med. Bull.*, 54: 693-702.
16. Reed, K.D., J.W. Melski, M.B. Graham, R.L. Regnery and M.J. Sotir *et al.*, 2004. The detection of monkeypox in humans in the Western hemisphere. *New Engl. J. Med.*, 350: 342-350.
17. Sale, T.A., J.W. Melski and E.J. Stratman, 2006. Monkeypox: An epidemiologic and clinical comparison of African and US disease. *J. Am. Acad. Dermatol.*, 55: 478-481.
18. Formenty, P., M.O. Muntasir, I.K. Damon, V. Chowdhary and M.L. Opoka *et al.*, 2010. Human monkeypox outbreak caused by novel virus belonging to Congo Basin Clade, Sudan, 2005. *Emerging Infect. Dis.*, 16: 1539-1545.
19. Nguyen, P.Y., W.S. Ajisegiri, V. Costantino, A.A. Chughtai and C.R. MacIntyre, 2021. Reemergence of human monkeypox and declining population immunity in the context of urbanization, Nigeria, 2017-2020. *Emerging Infect. Dis.*, 27: 1007-1014.
20. Yinka-Ogunleye, A., O. Aruna, D. Ogoina, N. Aworabhi and W. Eteng *et al.*, 2018. Reemergence of human monkeypox in Nigeria, 2017. *Emerging Infect. Dis.*, 24: 1149-1151.

21. Erez, N., H. Achdout, E. Milrot, Y. Schwartz and Y. Wiener-Well *et al.*, 2019. Diagnosis of imported monkeypox, Israel, 2018. *Emerging Infect. Dis.*, 25: 980-983.
22. Kozlov, M., 2022. Monkeypox goes global: Why scientists are on alert. *Nature*, 606: 15-16.
23. Ng, O.T., V. Lee, K. Marimuthu, S. Vasoo, G. Chan, R.T.P. Lin and Y.S. Leo, 2019. A case of imported monkeypox in Singapore. *Lancet Infect. Dis.*, Vol. 19. 10.1016/S1473-3099(19)30537-7.
24. Vaughan, A., E. Aarons, J. Astbury, S. Balasegaram and M. Beadsworth *et al.*, 2018. Two cases of monkeypox imported to the United Kingdom, September 2018. *Eurosurveillance*, Vol. 23. 10.2807/1560-7917.ES.2018.23.38.1800509.
25. Alakunle, E., U. Moens, G. Nchinda and M.I. Okeke, 2020. Monkeypox virus in Nigeria: Infection biology, epidemiology, and evolution. *Viruses*, Vol. 12. 10.3390/v12111257.
26. Ellis, C.K., D.S. Carroll, R.R. Lash, A.T. Peterson, I.K. Damon, J. Malekani and P. Formenty, 2012. Ecology and geography of human monkeypox case occurrences across Africa. *J. Wildl. Dis.*, 48: 335-347.
27. Ihekweazu, C., A. Yinka-Ogunleye, S. Lule and A. Ibrahim, 2020. Importance of epidemiological research of monkeypox: Is incidence increasing? *Expert Rev. Anti-Infect. Ther.*, 18: 389-392.
28. Kozlov, M., 2022. Monkeypox outbreaks: 4 key questions researchers have. *Nature*, 606: 238-239.
29. Vivancos, R., C. Anderson, P. Blomquist, S. Balasegaram and A. Bell *et al.*, 2022. Community transmission of monkeypox in the United Kingdom, April to May 2022. *Eurosurveillance*, Vol. 27. 10.2807/1560-7917.ES.2022.27.22.2200422.
30. Hutin, Y.J.F., R.J. Williams, P. Malfait, R. Pebody and V.N. Loparev *et al.*, 2001. Outbreak of human Monkeypox, democratic republic of Congo, 1996 to 1997. *Emerging Infect. Dis.*, 7: 434-438.
31. Yang, G., D.C. Pevear, M.H. Davies, M.S. Collett, T. Bailey, S. Rippen and L. Barone *et al.*, 2005. An orally bioavailable antipoxvirus compound (ST-246) inhibits extracellular virus formation and protects mice from lethal orthopoxvirus challenge. *J. Virol.*, 79: 13139-13149.
32. Thakur, V., P. Thakur, S. Srivastava and P. Kumar, 2022. Monkeypox virus (MPX) in humans a concern: Trespassing the global boundaries-Correspondence. *Int. J. Surg.*, Vol. 104. 10.1016/j.ijsu.2022.106703
33. Magee, W.C., K.Y. Hostetler and D.H. Evans, 2005. Mechanism of inhibition of vaccinia virus DNA polymerase by cidofovir diphosphate. *Antimicrob. Agents Chemother.*, 49: 3153-3162.
34. Magee, W.C., K.A. Aldern, K.Y. Hostetler and D.H. Evans, 2008. Cidofovir and (S)-9-[3-hydroxy-(2-phosphonomethoxy)propyl]adenine are highly effective inhibitors of vaccinia virus DNA polymerase when incorporated into the template strand. *Antimicrob. Agents Chemother.*, 52: 586-597.
35. Delaune, D. and F. Iseni, 2020. Drug development against smallpox: Present and future. *Antimicrob. Agents Chemother.*, Vol. 64. 10.1128/AAC.01683-19
36. Baker, R.O., M. Bray and J.W. Huggins, 2003. Potential antiviral therapeutics for smallpox, monkeypox and other orthopoxvirus infections. *Antiviral Res.*, 57: 13-23.
37. Brown, K. and P.A. Leggat, 2016. Human monkeypox: Current state of knowledge and implications for the future. *Trop. Med. Infect. Dis.*, Vol. 1. 10.3390/tropicalmed1010008.
38. Nasir, I.A., A. Dangana, I. Ojeamiren and A.U. Emeribe, 2018. Reminiscing the recent incidence of monkeypox in Nigeria: Its ecologic-epidemiology and literature review *Port Harcourt Med. J.*, 12: 1-9.
39. Petersen, B.W., J. Kabamba, A.M. McCollum, R.S. Lushima and E.O. Wemakoy *et al.*, 2019. Vaccinating against monkeypox in the Democratic Republic of the Congo. *Antiviral Res.*, 162: 171-177.
40. Petersen, E., I. Abubakar, C. Ihekweazu, D. Heymann and F. Ntumi *et al.*, 2019. Monkeypox-Enhancing public health preparedness for an emerging lethal human zoonotic epidemic threat in the wake of the smallpox post-eradication era. *Int. J. Infect. Dis.*, 78: 78-84.
41. Antinori, A., V. Mazzotta, S. Vita, F. Carletti and D. Tacconi *et al.*, 2022. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. *Eurosurveillance*, Vol. 27. 10.2807/1560-7917.ES.2022.27.22.2200421.
42. Noe, S., S. Zange, M. Seilmaier, M.H. Antwerpen and T. Fenzl *et al.*, 2023. Clinical and virological features of first human monkeypox cases in Germany. *Infection*, 51: 265-270.

43. Brabec, J.L., J. Wright, T. Ly, H.T. Wong and C.J. McClimans *et al.*, 2020. Arsenic disturbs the gut microbiome of individuals in a disadvantaged community in Nepal. *Heliyon*, Vol. 6. 10.1016/j.heliyon.2020.e03313.
44. Lederman, E.R., W. Davidson, H.L. Groff, S.K. Smith and T. Warkentien *et al.*, 2012. Progressive vaccinia: Case description and laboratory-guided therapy with vaccinia immune globulin, ST-246, and CMX001. *J. Infect. Dis.*, 206: 1372-1385.
45. Verma, S., S. Haque and S. Singh, 2022. A rumination on highly resistant the SARS-CoV-2 (Omicron) of mutation, spread, and vaccinations to new challenges. *Ambient Sci.*, 9: 79-82.
46. Verma, S. and S. Singh, 2022. Microorganisms' effects and mechanisms in ocular infections: A systematic review. *J. Res. Appl. Sci. Biotechnol.*, 1: 13-25.