Adelakun et al. *Afr. J. Clin. Exper. Microbiol.* 2024; 25 (4): 371 – 380 https://www.afrjcem.org

African Journal of Clinical and Experimental Microbiology. ISSN 1595-689X Oct 2024; Vol.25 No.4
AJCEM/2356. https://www.ajol.info/index.php/ajcem



**Review Article** **Open Access**

# Mpox: lessons learnt from previous viral outbreaks applicable to the ongoing outbreak

[1]Adelakun, A. A., [2]Onaolapo, M. C., [2]Olorunsesan, M. D., [2]Oluwole, F., and *[2,3,4]Ajayi, A. F.

[1]Department of Medical Laboratory Sciences, Ladoke Akintola University of Technology, Ogbomoso, Nigeria
[2]Department of Physiology, Ladoke Akintola University of Technology, Ogbomoso, Nigeria
[3]Anchor Biomed Research Institute, Ogbomoso, Nigeria
[4]Department of Physiology, Adeleke University, Ede, Nigeria
*Correspondence to: aajayi22@lautech.edu.ng; Tel: +2348033834495

## Abstract:

Human monkeypox (Mpox) is a zoonotic infection caused by Mpox virus (MPXV) that was first identified in a smallpox suspect in 1970, and presents with smallpox-like symptoms but with less severe manifestations. The infection is initiated through rapid replication at the inoculation site, with early symptoms including fever, chills, and exhaustion. The advent of smallpox vaccines has significantly contributed to its prevention. Due to its zoonotic nature, individuals who consume or handle animals susceptible to the virus are at increased risk and should take appropriate precautions. Both vaccines and non-pharmacological interventions have proven potent in limiting the spread of the infection. This narrative review examines the emergence and spread of Mpox in humans, delving into the epidemiology, clinical manifestations and preventive strategies for Mpox, as well as the transmission dynamics of the two MPXV clades. It also highlights the increase in cases outside Africa, with a particular focus on a UK outbreak linked to travel from Nigeria. The importance of vaccination, especially smallpox vaccines, is underscored, noting recent advancements in vaccine development such as the Vaccinia Ankara vaccine. The review emphasizes the need for robust surveillance, diagnostics, and strategies to control and manage epidemics, drawing lessons from past experiences. It concludes by stressing the clinical similarities between Mpox and smallpox and the growing public health concern posed by Mpox, especially in areas with high human-wildlife interactions.

**Keywords**: Zoonotic; Mpox; Epidemiology; Clades; Vaccine; Smallpox

Received Aug 6, 2024; Revised Sept 25, 2024; Accepted Sept 26, 2024



# Mpox: les leçons tirées des précédentes épidémies virales applicables à l'épidémie actuelle

[1]Adelakun, A. A., [2]Onaolapo, M. C., [2]Olorunsesan, M. D., [2]Oluwole, F., et *[2,3,4]Ajayi, A. F.

[1]Département des Sciences de Laboratoire Médical, Université de Technologie de Ladoke Akintola, Ogbomoso, Nigéria
[2]Département de Physiologie, Université de Technologie de Ladoke Akintola, Ogbomoso, Nigéria
[3]Institut de Recherche Anchor Biomed, Ogbomoso, Nigéria
[4]Département de Physiologie, Université Adeleke, Ede, Nigéria
*Correspondance à: aajayi22@lautech.edu.ng; Tél: +2348033834495

## Résumé:

La variole du singe (Mpox) humaine est une infection zoonotique causée par le virus Mpox (MPXV) qui a été identifié pour la première fois chez un suspect de variole en 1970 et présente des symptômes similaires à ceux de la variole mais avec des manifestations moins graves. L'infection est initiée par une réplication rapide au site d'inoculation, avec des symptômes précoces tels que fièvre, frissons et épuisement. L'avènement des vaccins contre la variole a contribué de manière significative à sa prévention. En raison de sa nature zoonotique, les personnes qui consomment ou manipulent des animaux sensibles au virus courent un risque accru et doivent prendre les précautions appropriées. Les vaccins et les interventions non pharmacologiques se sont avérés efficaces pour limiter la propagation de l'infection. Cette revue narrative examine l'émergence et la propagation

du Mpox chez l'homme, en se penchant sur l'épidémiologie, les manifestations cliniques et les stratégies de prévention du Mpox, ainsi que sur la dynamique de transmission des deux clades du MPXV. L'étude souligne également l'augmentation des cas hors d'Afrique, avec un accent particulier sur une épidémie au Royaume-Uni liée à un voyage en provenance du Nigéria. L'importance de la vaccination, en particulier des vaccins contre la variole, est soulignée, en notant les progrès récents dans le développement de vaccins tels que le vaccin Vaccinia Ankara. L'étude souligne la nécessité d'une surveillance, de diagnostics et de stratégies robustes pour contrôler et gérer les épidémies, en tirant les leçons des expériences passées. Elle conclut en soulignant les similitudes cliniques entre la Mpox et la variole et le problème de santé publique croissant posé par la Mpox, en particulier dans les zones où les interactions entre l'homme et la faune sont élevées.

**Mots-clés:** Zoonotique; Mpox; Épidémiologie; Clades; Vaccin; Variole

## Introduction:

Monkey pox (Mpox) disease in human is a zoonotic infection caused by the Mpox virus (MPXV) (1). It was first discovered in a human smallpox suspect in 1970, presenting with smallpox-like symptoms but with less severity (2). There exist two MPXV classes: West Africa and Congo Basin, with the latter causing grievous diseases (3). The infection is self-constraining, with signs lasting a period of two to four weeks, and a fatality rate of 3-6% (4). The virus invades the host system through oropharyngeal, nasopharyngeal or intradermal route. A rapid replication at the inoculation site promotes establishment of infection, after which it is spread to nearby lymph nodes and other organs. Initial signs of the illness include elevated temperature, chills, and pains in the muscle aches, headaches, and exhaustion. Lesions appear first in the oropharynx and then on the skin. Detection of serum antibodies occur as lesions appear (5,6).

Mpox is native to Central and West Africa (3). A significant source of concern is the rise in the amount of Mpox cases that are spreading to countries outside of Africa (7,8). On May 6, 2022, an Mpox outbreak was reported in the United Kingdom, with the index case associated with previous journey to Nigeria (9). From just a few cases in early May within Europe to greater than 18,000 cases reported in numerous countries by late July, the number of Mpox cases dramatically surged. Urgent attention and concerted efforts are therefore needed by the components of healthcare system to swiftly and effectively control this Mpox menace (10).

Smallpox vaccination has been shown to provide up to 85% protection in the prevention of Mpox illness, and previous studies have also shown the effectiveness of Vaccinia virus-based vaccines against smallpox (11). These vaccines are therefore expected to be effective against Mpox as well due to the protective response of the immune system to Orthopox viruses (12). In 2019, a new vaccine, Vaccinia Ankara, was developed and validated for prevention of Mpox (13). This current vaccine is being modified for clinical use despite its limited availability.

The aim of this review is to highlight the lessons learnt from previous outbreaks of Mpox. The objective is to review the epidemiology and mode of transmission of Mpox, with a view to facilitating identification and management of Mpox and apply the lessons learnt from previous outbreaks to the prevention and management of the ongoing Mpox outbreak

## Historical background:

Mpox virus (MPXV) was first recognized in 1959 in laboratory-held Cynomolgus monkeys (*Macaca fascicularis*) in Copenhagen, Denmark, during research on poliovirus vaccine (14). But, not until 11 years later, in 1970 that the first case in humans was reported in a sick pediatric patient in the former Zaire, now Congo Democratic Republic (15). The zoonotic nature and the occurrence rate of Mpox virus were not detailed enough in part as a result of insufficient research in particular before the 20$^{th}$ century (16). Mpox is rampant in the Central and Western Africa where the virus is classified as endemic, and the disease was not discovered beyond the African region before 2003 (7). However, there are contrasting reports about the real origin because the monkeys initially affected were transported from Singapore and not from Africa. Earlier researches also referred to an outburst in Alto, Uruguay in 1922, and in Brazil among *Mycetesseniculus* and *Cebuscapucinus* monkeys who burst out abscess and resulted in a high mortality in the course of simultaneous pox outburst, which was then thought to be smallpox (17).

The discoveries led to several doubts about the innate origin of Mpox virus in humans and animals. However, two distinct groups of species were discovered in Africa: the West African (WA) group and the Congo Basin or Central African (CA) group (8). A recently concluded analysis revealed a surge in established cases, especially in very endemic areas including Central African Republic (CAR), Republic of Benin, Cameroon, Democratic Republic of Congo (DRC) and the South Sudan. A review conducted globally concluded that the case fatality rate (CFR) was 8.7% (95% CI 7.0-10.8%), with considerable increase in cases from the CA group when put side by side with the WA group [10.6%

(95% CI 8.4-13.3%) vs 3.6% (95% CI 1.7-6.8%)]. However, in children less than 10 years of age, the highest CFR was reported during the period 1970-1990, with a decline reported within the past 20 years (7).

Studies also disclosed that the distribution of Mpox virus in endemic African regions has been below par. Moreover, the differences and population of animal pool are yet to be fully elucidated. Furthermore, the population of *Synanthropes* has drastically increased recently in the African region which subsequently leads to frequent human-rodent interactions and thereby leading to a surge in transmission of Mpox virus (18).

## Epidemiology of Mpox

Similar to humans, monkeys are categorized as disease host. More researches are necessary to deepen our understanding of the mechanisms by which the virus survives and remains present in the natural environment, and to obtain more information on the association between the host and pathogen with the impact of weather and ecological conditions affecting the spread between geographical regions (19). Research has identified rodents, specifically squirrels and giant pouched rats, as the primary animal reservoirs of Mpox virus, which is notable given that these animals are considered food sources in certain areas (20).

**Transmission of monkeypox virus to humans:**

Humans have fed on lower mammals for various socio-economic reasons including financial incapability and war in order to access protein-rich diet thus increasing their proneness to Mpox virus infection (21). The method by which MPXV is transmitted from animal to man is not yet fully understood. Experiments on aerosol transmission have been carried out in animals (22) and can be used to provide a detailed explanation on the nosocomial outburst in the Central African Republic (CAR) (23).

Human MPXV infections are believed to result from close or remote contact with live or dead monkeys (24), and the first reported case in the 9-year-old child in Bukendain village in the Democratic Republic of Congo (formerly known as Zaire) in August 1970 was probably from contact with monkeys. The child presented with blistering skin lesions similar to those of smallpox and the patient was identified during a time of intense surveying for smallpox organized about a year after the WHO had approved the elimination of smallpox in DRC (25). The major route through which the virus proliferates is the oral and nasopharyngeal fluid exchanges and spreads faster at the spots of injection thereafter subsequently extends to the proximal lymph nodes.

**Geographical endemicity and increase in number of Mpox cases:**

Ever since the emergence of Mpox, its endemicity in Central and West Africa regions has been pronounced, with varying number of cases spread among humans from local wildlife. Previous researches identified similar cases between 1970 and 1971 in several regions including Ivory Coast, Liberia, Nigeria and Sierra Leone (26). Further studies which were conducted revealed a higher incidence of Mpox cases in humans. The incidence of human Mpox has been on an exponential increase over the last two decades and have already surpassed the case reported during the first 45 years of its inception (24).

This constant regional increase in the prevalence of Mpox is regarded as the side-effect of declining cross-protective immune responses within the population after smallpox immunization was altered during the early 1980s. The steady decline in immune status is not only associated with ineffective vaccine-induced immunity among patients who were previously vaccinated, but probably and even higher in patients who were vaccine naive. Both conditions contribute to the surge in the number of susceptible individuals in endemic areas of Central and Western Africa (24).

**Mode of transmission and increase in number of cases:**

The precise route by which Mpox is being transmitted is yet to be established. It is believed that MPXV initially infects humans through person to person or indirect contact with infected animals, such as through bites, scratches or touching contaminated surfaces (27). However, close relatives of healthcare workers are more prone to infection because of health workers extended contact with Mpox patients. Nevertheless, findings from research conducted are yet to confirm whether only humans to humans transmission can sustain MPXV infection among humans (28).

Only few genomic studies have been carried out on the sources of Mpox outbreaks. Much emphasis has been placed on human-to-human transmission including both primary and secondary cases, and few cases involving serial transmission have also been seen (29). Fig 1 depicts the possible means of transmission of MPXV from animals to humans and from humans to humans.

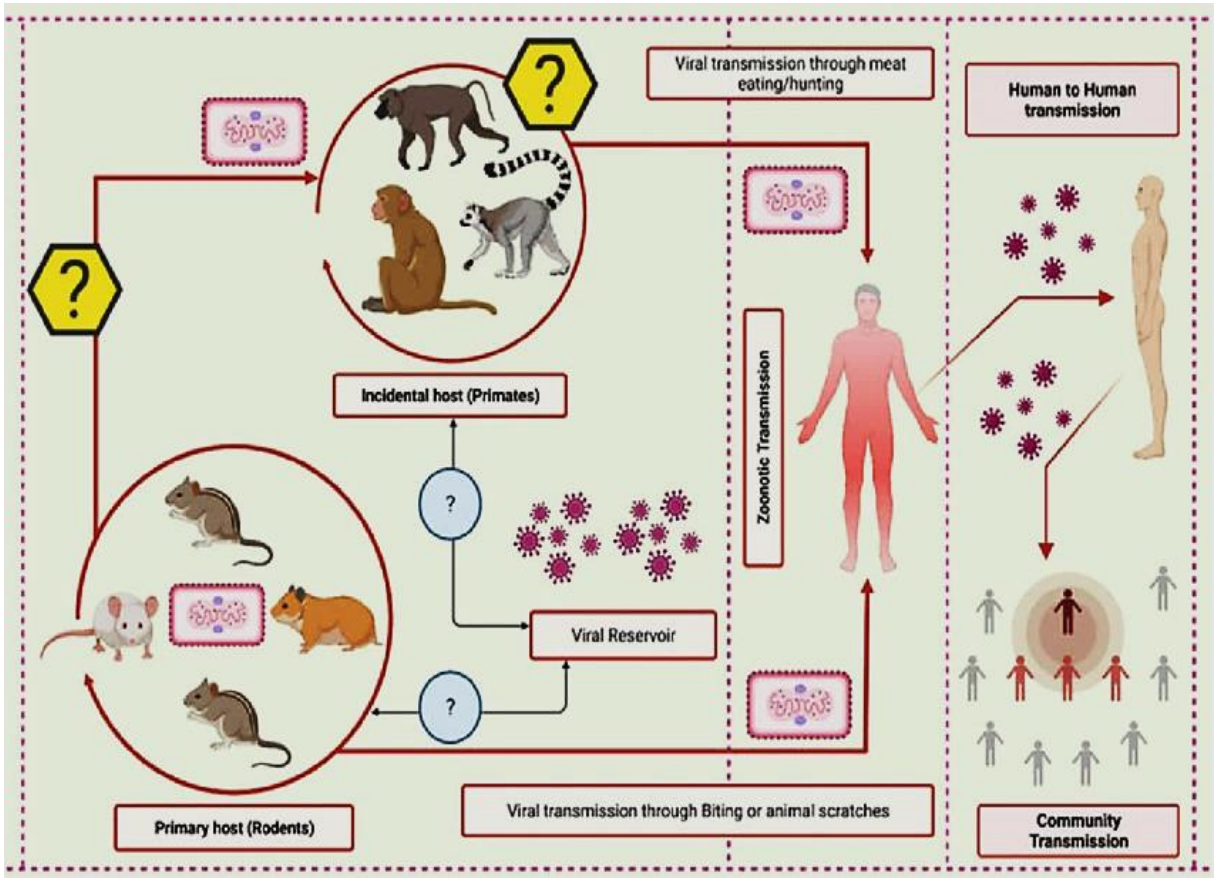


Fig 1. Schematic diagram of the mode of transmission of Mpox virus from animals to humans and from humans to humans.

Amidst the recent Mpox outbreak in Nigeria, genomic studies of MPXV isolated from humans (30) led to the discovery that the index case was not brought in from outside Nigeria. Several studies are still being carried out on the zoonotic sources of the outbreak and is yet to be proven if any environmental or ecologic change might have contributed to the prevalence of Mpox in Nigeria.

The prospect of case clustering has also been explored within several regions but the epidemiologic linkage between them has been null. The discovery of three family clusters of cases suggests that the virus is capable of human-to-human transmission. In a family, the secondary attack rate was approximately 71%, indicating a high rate of transmission among close contacts. However, in most cases, there was no clear connection between patients, such as a common exposure or human-to-human contact, suggesting that the outbreak may have multiple sources or be an endemic disease that has not yet been fully recognized (30).

## Pathogenesis of Mpox:

The steps involved in the pathogenesis of MPXV infection include viral entrance, fusion, replication, and release. This result in the production of two infectious forms of the virus; external enveloped virions (EV) and intracellular mature virions (MV). Unlike MVs, which are single membrane-bound and only released upon host cell lysis, EVs are specialized forms of MVs that are bound by a triple membrane that is antigenically unique. The double membrane is acquired via translocation to Golgi bodies (31,32). It has been proven that antibodies and vaccinations that do not create or target EV antigens offer less protection than those that do (33,34). In the context of Orthopoxviruses, two multi-subunit complexes, COG and GARP, play a crucial role in completing the viral infectious cycle (35).

The GARP complex, responsible for retrograde endosomal transport, consists of four vacuolar protein sorting (VPS) genes (VPS51, VPS52, VPS53, and VPS54), all of which were found to be enriched in both the CA and WA clades, except for VPS53, which was specifically enriched in the CA clade. The significant reduction in extracellular virus (EV) yield in MPXV-infected VPS52 and VPS 54 mutant cells highlights their essential role in viral egress and cell-to-cell dissemination (35). The COG complex, composed of two lobes (A and B) with four subunits each, is necessary for maintaining Golgi structure and regulating intra-Golgi traffic. While COG3 and

COG4 are exclusively enriched in the CA clade, COG7 and COG8 are enriched in both clades, with COG4 and COG7 being the most critical subunits for viral fusion. The two subunits, COG4 and COG7, are regarded to be the most crucial for viral fusion (35).

Two unique sections (R1–Open Reading Frame 17 to 32 and R2–Open Reading Frame 179 to 193) of the MPXV CA clade genomes were discovered by bioinformatics research, and their deletion may reduce the virus' pathogenicity (36). Mice mortality and morbidity were reduced after deletion of one or both areas, and viral replication was inhibited (36). The authors were also able to link genes from region R1 to viral replication, while genes from R2 section were linked to viral pathogenicity (36). Researchers found that the most effective way to reduce the virus virulence was to remove both the R1 and R2 genes (36).

According to microarray study, human MPXV causes histone posttranslational modification in the host cell by upregulating core histones while downregulating proteins that control histone expression (36). These modifications may show that host cell histone expression regulates viral DNA compaction and nucleosome formation (37). The researchers additionally observed a downregulation of ion channel expression in cell membranes, accompanied by gene regulation that led to cell cycle arrest in the G2 phase and accelerated progression through the S phase (37).

## Genetics of MPXV clades:

The members of the *Orthopoxvirus* share a high degree of antigenic and genetic similarity, with open reading frames (ORFs) showing >90% sequence commonality (38). The MPXV is evolving in new ways due to gene loss, particularly at the ends of its genome (43). This evolution is likely driven by selective pressure from host species (39). Additionally, variations in gene copy number suggest increased viral fitness for human infection and transmission. The 197 kb genome of the virus contains around 190 non-overlapping ORFs and a highly conserved central coding region sequence (CRS) flanked by variable ends with inverted terminal repeats (ITRs) (40).

The two clades, Congo Basin/Central Africa (CA) and West African (WA), which have been proposed to be renamed Clade 1 (CA) and Clades 2 and 3 (WA) to avoid stigmatizing nomenclature (41). The outbreak in Europe and the Global North was identified as human MPXV B.1 (40). While the WA clade is associated with milder disease and less human-human transmission, the CA clade has a 10% case mortality rate in unvaccinated individuals with common intra-human transmission (7). Studies comparing genomes have found that the two clades differ by 0.55–0.56% nucleotides (42). Compared to the 171 functionally unique genes in the WA clade, the CA clade has 173. The transcriptional regulatory sequences of the two clades shared 170 orthologs at the protein level and were determined to be 99.4% similar, with no obvious differences between them (42,43).

The genes responsible for virulence underwent changes, resulting in 61 conservative, 93 non-conservatives, and 121 silent amino acid substitutions, with 53 of these changes present in both clades (42). Research suggests that variations in the genes encoding virulence proteins, specifically BR-203, BR-209, and COP-C3L, may be responsible for the differences in virulence between the two clades (42,43). These viral proteins play roles in virulence, IL-1 binding and complement inhibition, respectively.

## Clinical presentation of Mpox

Clinically, human Mpox closely resembles smallpox (1). It is a self-limiting illness which exhibit symptoms for a period of 14-28 days, and its fatality rate is about 3-6% of infected humans (4). Prior to the onset of the characteristic rash, most patients experience a prodromal phase, typically lasting 10-14 days, characterized by symptoms such as fever, general feeling of illness, and swollen lymph nodes (1,42). Additional symptoms may include chills or sweating, headache, back pain, sore throat, cough, exhaustion and difficulty breathing, which can be indicative of Mpox.

Lymphadenopathy, which has been shown to occur in 90% of unvaccinated patients and not seen frequently in smallpox, is thought to be one of the main characteristics that distinguish Mpox from smallpox. The sites of lymphadenopathy are the cervical, inguinal and submandibular areas (44), but may expand to other areas (1). Typically, the prodromal phase lasts 1-3 days prior to the classic maculopapular rash appearance. The patient should be kept in isolation for the duration of the first week the rash lasts and until all scabs have separated and the throat swab PCR findings have come back negative.

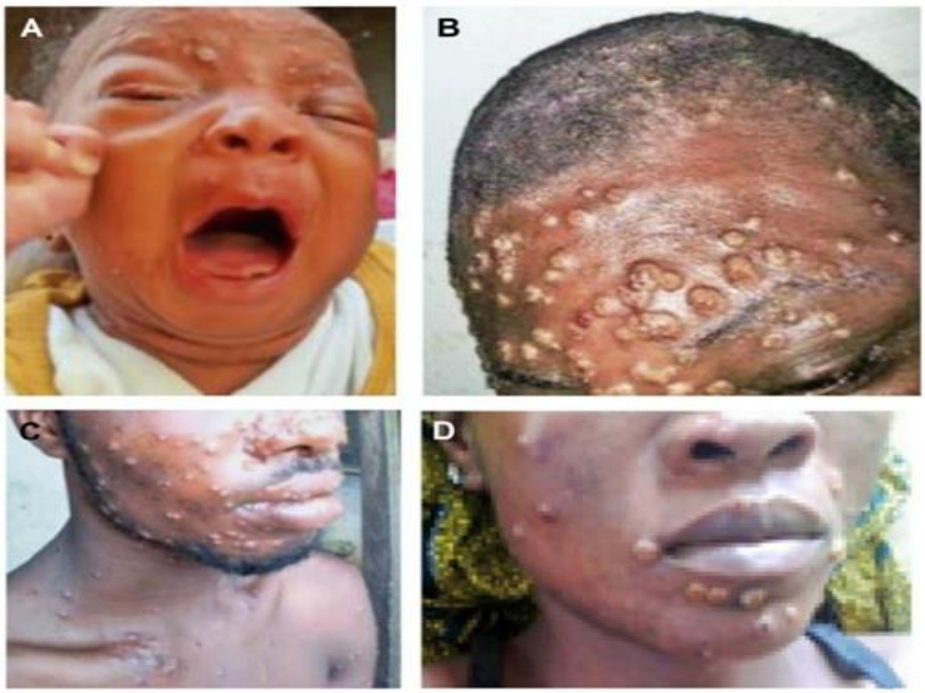


Fig 2. Monkeypox skin lesions on the face, displaying a range of sizes and morphologies, including macules, papules, vesicles, and pustules (Courtesy of Nigeria Center for Disease Control, Abuja, Nigeria).

The clinical progression of the skin lesions is quite related to that of typical smallpox lesions, with a mean diameter of 0.5–1 cm. Lesions develop from macules to papules, vesicles, and pustules during the course of two to four weeks. These changes are followed by umbilication, scabbing, and desquamation (1). The rash typically begins on the trunk but can extend to the palms and soles. Lesions can also appear on mucous membranes, such as the mouth, tongue, and genital area. Figure 2 depicts various sizes and morphologies of Mpox skin lesions on the face. Along with skin lesions, persons infected with MPXV may experience additional symptoms beyond the skin, including secondary infections (19% of cases), lung inflammation (12%), eye problems (4-5%), and brain inflammation (1%) (42). Untreated illness can be fatal, typically in the second week, with a mortality rate of 10% (1,43)

The prevalence of human MPXV infection has been on the increase in several regions of Africa (45), and now considered a threat to public well-being especially in regions where human-animal interactions with wild animal reservoirs is high. However, it is considered less fatal compared to smallpox in terms of the severity of complications and case fatality rate. Awareness has been raised on the uprising of human Mpox in addition to its clinical presentation being similar to smallpox.

## Advances in diagnosis of Mpox

Among various diagnostic modalities for human MPXV the most prominent ones include negative staining of rash using electron microscopy, virus isolation, serological testing with the use of immunoglobulin M (IgM) or immunoglobulin G (IgG), histopathological analysis, and polymerase chain reaction assay (46). Electron microscopy is a highly effective diagnostic tool for identifying poxvirus infections in a laboratory setting and may provide early clues to the cause of an unexplained rash illness. Under electron microscopy, poxvirus virions are expected to display a distinctive morphological structure, characterized by a brick-shaped appearance with round-to-oval inclusions and central sausage-shaped structures, measuring approximately 250µm in size (45). In case of active disease, it is obligatory for laboratories with great contrivance equipment to make a definitive diagnosis for the identification of MPXV using electron microscopy, viral cultures and isolation with characterization by different PCR techniques and sequencing of the PCR amplicons.

In sub-Saharan Africa, the major difficulty is the diagnostic challenge of differentiating between Mpox and varicella. Therefore, it is important to differentiate between Mpox and other poxviruses such as chicken-

pox, varicella and possibly variola to prevent wrong diagnosis that can compromise therapy. In recent years, laboratory diagnosis of MPXV using different real-time PCR assays have been developed, validated and now universally recognized. The most common of these assays are the TaqMan-based assay (E9L-NVAR) and the B6R assay. These assays display 100% specificity and good range of sensitivity for detection of *Orthopoxviruses* and MPXV (47).

## Prevention of Mpox:

The combination of widespread vaccination and intense surveillance led to the successful global elimination of smallpox. Although Mpox cannot be completely eliminated due to its presence in animal reservoirs, vaccination with vaccinia virus (smallpox) vaccine) has been shown to be highly effective in preventing MPXV infection (1). Research has shown that smallpox vaccination offers approximately 85.0% protection against Mpox, making it a valuable tool in preventing the disease. Prior studies showed that formulated vaccines which are developed for prevention of smallpox and Mpox were based on vaccinia virus. This is due to the protective response of the immune system to *Orthopoxviruses*. In 2019, a new version of the vaccine, Vaccinia Ankara, was developed and approved for the prevention of Mpox. This vaccine has been modified for clinical use although its availability remains limited (12).

The major prevention strategy as provided by the World Health Organization is creating awareness about the risk factors when exposed to the virus and enlightening the populace about the measures which can be taken to decrease exposure to the virus (12). In order to minimize the risk of zoonotic transmission, close contact with animal host such as rodents, non-human primates and wild animals, particularly the unhealthy or inactive ones should be reduced. Furthermore, meat should be cooked well, and this is also applicable to all industries producing food containing meat. During disease outbreak, taking control measures is significant. Having close contact with an infected victim is the most noticeable risk factor causing Mpox virus disease, therefore, healthcare workers and those exposed to patients' samples should put into practice standard measures as well as necessary precautions (12).

To prevent future re-emergence of Mpox, the Centers for Disease Control and Prevention strongly advocates that individuals who investigate Mpox cases in animals or humans, healthcare workers caring for patients with suspected or confirmed Mpox, and household members of patients, receive pre-exposure vaccination to protect against the disease. More importantly, animals suspected or infected with Mpox should be placed in isolation, away from other animals to prevent the spread of the disease and observed for Mpox symptoms for a period 30 days. During these periods, the animals should be carefully handled with standard precautions (12).

## Lessons learnt from the previous Mpox outbreaks:

The use of vaccines and non-pharmacological interventions (NPIs), were very essential in the control of the transmission of Mpox virus. Non-pharmacological interventions which include social dissociation, hand washing protocols and the use of face masks are very essential in preventing Mpox outbreak, since most human-to-human transmission of Mpox virus is by coming in contact with scabs, sores, respiratory droplets of an infected person (39). The Mpox outbreaks have taught us a crucial lesson; the vital importance of maintaining primary healthcare services during a crisis, as well as the need to provide emotional and professional support to healthcare workers to mitigate the psychological toll of working in a pandemic environment.

Moreover, it is essential to harness the knowledge and experience gained during the outbreak to inform the training and development of healthcare workers, ensuring they are better equipped to handle future pandemics (40). Previous Mpox outbreak also exposed the essence of halting an outbreak before its spread becomes rampant and this must always be a top priority when signs are looming. Unveiling several cases of Mpox in several countries without any obvious reason should serve as warning to government and law makers and efficient strategies must be employed in tackling the outbreak (41).

The key strategic steps to employ include public enlightenment and sensitization on disease manifestation, transmission and prevention. Also, it is important to provide adequate means of protection to health care workers either through the provision of personal protective equipment (PPE) or through the use of vaccines especially in rural areas. Efforts should also be increased towards research on the unparalleled and global spread of the virus. It is also very important to identify the root of the diseases if the virus is to be tackled effectively before it becomes

fatal. Countries who have experienced outbreaks should also implement the use of vaccines to limit the effect of Mpox virus (12).

## A new outbreak of Mpox:

The World Health Organization recently declared the current outbreak of Mpox a Public Health Emergency of International Concern (PHEIC) due to a significant rise in cases across several countries, especially in Africa (48). This new wave has affected countries such as the DRC, Cameroon, Nigeria, and others. Nigeria, for instance, has seen a rise in cases alongside 15 other African Union (AU) member states, which have reported over 26,000 cases as of September 2024 (49). The rapid increase in cases and the appearance of a new strain of the virus have prompted a coordinated global response, including the provision of vaccines (50).

The Africa Mpox crisis has worsened in 2024, with a 177% increase in cases compared to the previous year, and nations such as Rwanda and the DRC have begun vaccination campaigns to combat the outbreak (49). Outside Africa, countries in Asia and Europe have also reported cases, highlighting the global nature of this health threat. The resurgence of Mpox calls for continued surveillance, vaccination efforts, and international collaboration to bring the outbreak under control (50).

## Discussion:

The symptoms of human Mpox progress in a similar way to smallpox, with skin lesions typically measuring between 0.5 and 1cm in diameter. The incidence and geographic range of human Mpox virus have increased in several African countries, posing a growing public health threat, particularly in Central and West Africa, where human contact with wild animals is common. The decline in cross-protective immunity in the populace, as a result of the cessation of smallpox vaccination in the early 1980s, has contributed to the ongoing surge in cases in these regions. The gradual deterioration of immune function is linked to insufficient vaccine-induced immunity not just in patients who had vaccinations first, but also, and possibly more importantly, in patients who did not receive vaccinations. Both circumstances increase the number of persons who are susceptible to the disease in endemic regions, particularly in the Central and West Africa regions.

The recent rapid expansion and spread of Mpox outside of Africa, however, is very concerning on a worldwide scale, and this has underlined the necessity for ongoing, diligent surveillance as well as the creation of cutting-edge preventative and treatment approaches. It is therefore recommended that to control the ongoing Mpox outbreak, the healthcare sector and the public must adhere to standard and transmission-based precautions.

Appropriate precautions such as isolation and contact tracing should be used. Also, the specific path and mode of transmission of MPXV should be identified. In addition, it is critical to give healthcare personnel proper safety, particularly in remote regions, by giving them access to vaccines or personal protective equipment (PPE). Also, a lot more studies are required to understand the virus unusual global spread. In order to properly combat the virus before it becomes lethal, it is also crucial to pinpoint the source of the disease. Countries that have experienced outbreaks should employ vaccinations as well to lessen the impact of MPXV.

The resurgence of Mpox in recent years has significantly challenged global health, especially in Africa. The geographic distribution of MPXV infections has notably increased, which has attracted the global health community. The World Health Organization and other global health bodies have declared the current Mpox outbreaks a Public Health Emergency of International Concern (PHEIC), a decision bordering on the gravity of the situation and the global effort needed to control it.

## Conclusion and recommendation:

Mpox continues to pose a significant public health threat, particularly in regions where it is endemic. The ongoing global outbreak underscore the need for vigilance, preparedness, and international cooperation in addressing emerging infectious diseases. While vaccines and NPIs remain critical tools in controlling Mpox, challenges such as limited vaccine availability and inadequate surveillance systems must be addressed. By learning from past outbreaks and implementing comprehensive public health strategies, the global community can prevent future Mpox outbreaks and mitigate their impact on public health.

To prevent future Mpox outbreaks, it is essential to address both the zoonotic and human-to-human transmission routes. This requires a multifaceted approach that includes strengthening surveillance systems, improving public health education, expanding vaccine access, and investing in research to better understand the virus transmission dynamics and pathogenesis.

**Strengthening surveillance systems**:

Enhanced surveillance is critical for early detection of Mpox cases and preventing large-scale outbreaks. In endemic regions,

surveillance systems must be integrated with global disease monitoring platforms to facilitate real-time data sharing and coordinated responses. Increased funding for laboratory capacity and training of healthcare workers in Mpox diagnosis is also essential.

**Public health education**:

Raising awareness about the risks of Mpox transmission and promoting safe practices, such as avoiding contact with wildlife and properly cooking bushmeat, is essential in endemic regions. Public health campaigns must also target non-endemic regions to reduce stigma and misinformation about the virus.

**Expanding vaccine access**:

Global efforts to increase the availability of Mpox vaccines must be prioritized. International organizations such as WHO, the Africa CDC, and GAVI must work together to ensure equitable vaccine distribution, particularly in low-and-middle-income countries that are disproportionately affected by the virus.

**Investing in research**:

Continued research into Mpox virus is needed to develop more effective vaccines and antiviral treatments. Studies on the virus transmission dynamics, animal reservoirs, and genetic evolution will provide valuable insights for controlling future outbreaks.

**Preparedness plans**:

Countries must develop preparedness and response plans for Mpox and other emerging infectious diseases. These plans should include the stockpiling of vaccines and personal protective equipment (PPE), training healthcare workers, and establishing isolation and treatment facilities.

## Contributions of authors

AAA and AFA conceived the study idea; AAA, MCO, OMD, and OF wrote the initial manuscript draft; AFA managed the study and handled correspondence. All authors reviewed and approved the final version.

## Source of funding:

Authors received no external funding.

## Conflict of interest:

No conflict of interest is declared.

## References:

1. Nalca, A., Rimoin A. W., Bavari, S., and Whitehouse, C. A. Reemergence of Monkeypox: Prevalence, Diagnostics, and Countermeasures. Clin Infect Dis. 2005; 41(12):1765-71. doi: 10.1086/498155.
2. McCollum, A. I., Damon. Human monkeypox. Clin Infect Dis. 2013; 58 (2): 260–267. doi: 10.1093/cid/cit703.
3. Minhaj, F., Ogale, Y., Whitehil, F., Schultz, J., Foote, M., and Davidson W. Monkeypox Outbreak - Nine States, Centers for Disease Control and Prevention. 2022; 719 (23): 764-769
4. Saxena, S., Ansari, S., Maurya, V., et al. Re-emerging human monkeypox: a major public-health debacle. J Med Virol. 2023; doi: 10.1002/jmv.27902
5. Hutson, C. L., Carroll, D. S., Gallardo-Romero, N., et al. Comparison of Monkeypox Virus Clade Kinetics and Pathology within the Prairie Dog Animal Model Using a Serial Sacrifice Study Design. Biomed Res Int. 2015: 965710. doi: 10.1155/2015/965710
6. Kumar, N., Acharya, A., Gendelman, H., Byrareddy, S. The 2022 outbreak and the patho biology of the monkeypox virus. J Autoimmun. 20221; 31: 102855. doi: 10.1016/j.jaut.2022.102855.
7. Bunge, E., Hoet, B., Chen, L., Lienert, F., Weidenthaler, H., and Baer, L. The changing epidemiology of human monkeypox—a potential threat? A systematic review. PLoS Negl Trop Dis 16(2): e0010141. https://doi.org/10.1371/journal.pntd.0010141
8. Leon-Figueroa, D., Bonilla-Aldana, D., Pachar, M., et al. The never-ending global emergence of viral zoonoses after COVID-19? The rising concern of monkeypox in Europe, North America and beyond. Travel Med Infect Dis. 2022; 49:102362. doi: 10.1016/j.tmaid.2022.102362.
9. Hraib, M., Jouni, S., Albitar, M., Alaidi, S., and Alshehabi, Z. The outbreak of monkeypox 2022: an overview. Ann Med Surg. 2022; 79:104069. doi: 10.1016/j.amsu.2022.104069
10. Zaheer, A.B., Ali, T., Ashfaq, A., and Jabeen, A. Monkeypox outbreak amidst COVID-19 re-emergence in the European Region: Challenges, efforts, and recommendations. Ann Med Surg. 2022; 82: 104657. doi: 10.1016/j.amsu.2022.104657
11. Walsh, S. R., and Dolin, R. Vaccinia viruses: vaccines against smallpox and vectors against infectious diseases and tumors. Expert Rev Vaccines. 2011; 10 (8): 1221-1240. doi: 10.1586/erv.11.79
12. World Health Organization. Facts on monkeypox. 2022. https://www.who.int/news-room/fact-sheets/detail/monkeypox
13. Farahet, R. A. Human Monkeypox disease (MPX). Infect Med. 2022; 30 (3): 372-391. doi: 10.53854/liim-3003-6
14. Magnus, P., Anderson, E. K., Petersen, K. B., and Birch-Andresen, A. A pox-like disease in cynomolgus monkeys. Acta Pathol Microbiol Scan. 1959; 4 (2): 156-176. https://doi.org/10.1111/j.1699-0463.1959.tb0 0328.x
15. Cho, C. T., and Wenner, H. A. Monkeypox virus. Bacteriol Rev. 1973; 37: 1-18. doi: 10.1128/br.37.1.1-18.1973
16. Cheng, K., Guo, Q., Zhou, Y., and Wu, H. Concern over monkeypox outbreak: What can we learn from the top 100 highly cited articles in monkeypox research? Travel Med Infect Dis. 2022; 102371. doi: 10.1016/j.tmaid.2022.102371
17. Bonilla-Aldana, D. K., and Rodriguez-Morales, A. J. Is monkeypox another reemerging viral zoonosis with many animal hosts yet to be defined? 2022; Vet Q. 1-5. doi: 10.1080/01652176.2022.2088881
18. Haider, N., Guitian, J., Simons, D., et al. Increased outbreaks of monkeypox highlight gaps in actual disease burden in Sub-Saharan Africa and in animal reservoirs. Int J Infect Dis.

2022; 122: 107-111. doi: 10.1016/j.ijid.2022.05.058
19. Radonić A, Metzger S, Dabrowski PW, et al. Fatal monkeypox in wild-living sooty mangabey, Côte d'Ivoire, 2012. Emerg Infect Dis. 2014; 20(6):1009-1011.doi:10.3201/eid2006.13-1329
20. Thomassen, H. A., Fuller, T., Asefi-Najafabady, S., et al. Pathogen-host associations and predicted range shifts of human monkeypox in response to climate change in central Africa. PLoS One. 2013; 8: e66071. https://doi.org/10.1371/journal.pone.0066071
21. Doty, J. B., Malekani, J. M., Kalemba, L. N., et al. Assessing Monkeypox Virus Prevalence in Small Mammals at the Human-Animal Interface in the Democratic Republic of the Congo. Viruses. 2017; 9(10):283. doi:10.3390/v9100283
22. Quiner, C. A., Moses, C., Monroe, B. P., et al. Presumptive risk factors for monkeypox in rural communities in the Democratic Republic of the Congo. PLoS One. 2017; 12: e0168664. https://doi.org/10.1371/journal.pone.0168664
23. Prier, J. E., and Sauer, R. M. A pox disease of monkeys. Ann N Y Acad Sci. 1960; 85: 951-959. doi: 10.1111/j.1749-6632.1960.tb50015.x.
24. Nakoune, E., Lampaert, E., Ndjapou, S. G., et al. A nosocomial outbreak of human monkeypox in the Central African Republic. Open Forum Infect Dis. 2017; 4: ofx168. doi: 10.1093/ofid/ofx168
25. Durski, K. N., McCollum, A. M., Nakazawa, Y., et al. Emergence of monkeypox—West and Central Africa, 1970-2017. MMWR Morb Mortal Wkly Rep. 2018; 67: 306–310. doi: 10.15585/mmwr.mm6710a5
26. Marennikova, S. S., Seluhina, E. M., Malceva, N. N. et al. Isolation and properties of the causal agent of a new variola-like disease (monkeypox) in man. Bull World Health Organ 1972; 46: 599–611.
27. Fine, P. E., Jezek, Z., Grab, B., et al. The transmission potential of monkeypox virus in human populations. Int J Epidemiol. 1988; 17: 643–650. doi: 10.1093/ije/17.3.643.
28. Hutin, Y, J., Williams. R. J., Malfait, P., et al. Outbreak of human monkeypox, Democratic Republic of Congo, 1996 to 1997. Emerg Infect Dis. 2001; 7: 434. doi: 10.3201/eid0703.010311
29. Learned, L. A., Reynolds, M. G., Wassa, D. W., et al. Extended interhuman transmission of monkeypox in a hospital community in the Republic of the Congo, 2003. Am J Trop Med Hyg. 2005; 73: 428–434
30. Nolen, L. D., Osadebe, L., Katomba, J., et al. Extended human-to-human transmission during a monkeypox outbreak in the Democratic Republic of the Congo. Emerg Infect Dis. 2016; 22: 1014–1021. doi: 10.3201/eid2206.150579
31. Realegeno, S., Priyamvada, L., Kumar, A., et al. Conserved Oligomeric Golgi (COG) complex proteins facilitate orthopoxvirus entry, fusion and spread. Viruses. 2020; 12 (7): 707. doi: 10.3390/v12070707
32. Mucker, E. M., Thiele-Suess, C., Baumhof, P., and Hooper, J. W. Lipid nanoparticle delivery of unmodified mRNAs encoding multiple monoclonal antibodies targeting poxviruses in rabbits. Mol Ther Nucleic Acids. 2022a; 28: 847–858. doi: 10.1016/j.omtn.2022.05.025
33. Golden, J. W., Zaitseva, M., Kapnick, S., et al. Polyclonal antibody cocktails generated using DNA vaccine technology protect in murine models of orthopoxvirus disease. Virol J. 2011; 8: 441. doi: 10.1186/1743-422X-8-441
34. Lustig, S., Fogg, C., Whitbeck, J. C., Eisenberg, R. J., Cohen, G. H., and Moss, B. Combinations of polyclonal or monoclonal antibodies to proteins of the outer membranes of the two infectious forms of vaccinia virus protect mice against a lethal respiratory challenge. J Virol. 2005; 79 (21): 1345–1346. doi: 10.1128/JVI.79.21.13454-13462.2005.
35. Realegeno, S., Puschnik, A. S., Kumar, A., et al. Monkeypox virus host factor screen using haploid cells identifies essential role of GARP complex in extracellular virus formation. J Virol. 2017; 91 (11): e00011-17. doi: 10.1128/JVI.00011-17.
36. Lopera, J. G., Falendysz, E. A., Rocke, T. E., and Osorio, J. E. Attenuation of monkeypox virus by deletion of genomic regions. Virol. 2015; 475: 129–138. doi: 10.1016/j.virol.2014.11.009
37. Alkhalil, A., Hammamieh, R., Hardick, J., Ichou, M.A., Jett, M., and Ibrahim, S. Gene expression profiling of monkeypox virus-infected cells reveals novel interfaces for host-virus interactions. Virol J. 2010; 7: 173. doi.org/10.1186/1743-422X-7-173
38. Faye, O., Pratt, C. B., Faye, M., et al. Genomic characterisation of human monkeypox virus in Nigeria. Lancet Infect Dis. 2018; 18: 246. doi : 10.1016/S1473-3099(18)30043-4
39. Calle-Prieto, F., Munoz, M. E., Ramirez, G., et al. Treatment and prevention of monkeypox. Enferm Infect Microbiol Clin. 2022. doi:10.1016/j.eimce.2022.12.010
40. Rawaf, S., Allen, L. N., Stigler, F. L., Kringos, D., Quezada, Y. H., and van Weel, C. Global Forum on Universal Health Coverage and Primary Health Care. Lessons on the COVID-19 pandemic, for and by primary care professionals worldwide. Eur J Gen Pract. 2020; 26 (1): 129-133. doi: 10.1080/13814788.2020.1820479
41. Kozlov, M. Monkeypox goes global: why scientists are on alert. Nature. 2022 : 724 https://doi.org/10.1038/d41586-022-01421-8
42. Di Giulio, D. B., and Eckburg, P. B. Human monkeypox: an emerging zoonosis. Lancet Infect Dis. 2004; 4: 15–25. doi: 10.1016/s1473-3099(03)00856-9.
43. Frey, S. E., and Belshe, R. B. Poxvirus zoonose-putting pocks into context. N Engl J Med. 2004; 350: 324–327. doi: 10.1056/NEJMp038208.
44. Alder, H., Gould, S., Hine, P., Snell, L. B., and Wong, W. Clinical features and management of human monkeypox: a retrospective observational study in the UK. The Lancet Infect Dis. 2022; 22(8): 1153-1162. doi: 10.1016/S1473-3099(22)00228-6
45. Petersen, E., Kantele, A., Koopmans, M., et al. Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infect Dis Clin North Am. 2019; 33(4):1027-1043. doi: 10.1016/j.idc.2019.03.001
46. Brown, K., and Leggat, P. A. Human monkeypox: current state of knowledge and implications for the future. Trop Med Infect Dis. 2016; 1 (1): 8. doi: 10.3390/tropicalmed1010008.
47. Li, Y., Olson, V. A., Laue, T., Laker, M. T., and Damon, I. K. Detection of monkeypox virus with real-time PCR assays. 2006, 36 (3): 194-203. doi: 10.1016/j.jcv.2006.03.012
48. Adepoju, P. Mpox declared a public health emergency. The Lancet. 2024:404(10454) e1-e2. doi: 10.1016/S0140-6736(24)01751-3.
49. World Health Organization. WHO invites mpox vaccine manufacturers to submit dossiers for emergency evaluation? https://www.who.int/news/item/09-08-2024-who-invites-mpoxvaccine-manufacturers-to-submitdossiers-for-emergency-evaluations. (Accessed August 12, 2024)
50. World Health Organization. Multi-country outbreak of Mpox. WHO international documents. https://www.who.int/docs/default-source/coronaviruse/situationreports/20240812_mpox_external-sitrep_35.pdf. (Accessed Aug 12, 2024)