Musa-Booth et al. *Afr. J. Clin. Exper. Microbiol.* 2023; 24 (1): 01 - 08 https://www.afrjcem.org

African Journal of Clinical and Experimental Microbiology. ISSN 1595-689X Jan 2023; Vol.24 No.1
AJCEM/2236. https://www.ajol.info/index.php/ajcem

Review Article **Open Access**

A review of the epidemiology, diagnosis, treatment, vaccines and economic impact of human monkeypox (Mpox) outbreaks

[1]Musa-Booth, T. O., [2]Medugu, N., *[2]Adegboro, B., and [3]Babazhitsu, M.

[1]1928 Woodlawn Drive, Woodlawn, Maryland 21207, United States of America
[2]Department of Medical Microbiology and Immunology, Nile University of Nigeria, Abuja, Nigeria
[3]Department of Medical Microbiology and Parasitology, Faculty of Basic Clinical Sciences, College of Health Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria
*Correspondence to: boazadegboro@gmail.com; boaz.adegboro@nileuniversity.edu.ng

Abstract:

The current monkeypox outbreak is a public health emergency of international concern and is coming in the wake of the SARS-CoV-2 pandemic. Human monkeypox is a viral zoonotic infection caused by monkeypox virus, an enveloped double-stranded DNA virus of the genus *Orthopoxvirus* and family *Poxviridae* that also contain smallpox, cowpox, Orf, and vaccinia viruses. Online databases including PubMed, Google Scholar and Web of Science were searched to obtain relevant publications on the epidemiology, treatment, vaccines and the economic impacts of the current monkeypox (Mpox) outbreak.

Keywords: monkeypox, epidemiology, vaccines, treatment, economic impact

Received Nov 1, 2022; Revised Dec 16, 2022; Accepted Dec 18, 2022

Un examen de l'épidémiologie, du diagnostic, du traitement, des vaccins et des impact économiques des épidémies de monkeypox (Mpox) humain

[1]Musa-Booth, T. O., [2]Medugu, N., *[2]Adegboro, B., et [3]Babazhitsu, M.

[1]1928 Promenade Woodlawn, Woodlawn, Maryland 21207, États-Unis d'Amérique
[2]Département de Microbiologie Médicale et d'Immunologie, Université du Nil du Nigéria, Abuja, Nigéria
[3]Département de Microbiologie Médicale et de Parasitologie, Faculté des Sciences Cliniques Fondamentales, Collège des Sciences de la Santé, Université Usmanu Danfodiyo, Sokoto, Nigéria
*Correspondance à: boazadegboro@gmail.com; boaz.adegboro@nileuniversity.edu.ng

Résumé:

L'épidémie actuelle de monkeypox est une urgence de santé publique de portée internationale et survient dans le sillage de la pandémie de SRAS-CoV-2. Le monkeypox humain est une infection zoonotique virale causée par le virus du monkeypox, un virus à ADN double brin enveloppé du genre *Orthopoxvirus* et de la famille des *Poxviridae* qui contient également les virus de la variole, du cowpox, de l'Orf et de la vaccine. Des bases de données en ligne, notamment PubMed, Google Scholar et Web of Science, ont été consultées pour obtenir des publications pertinentes sur l'épidémiologie, le traitement, les vaccins et les impacts économiques de l'épidémie actuelle de monkeypox (Mpox).

Mots clés: monkeypox, épidémiologie, vaccins, traitement, impact économique

Introduction:

Human monkeypox is a viral zoonotic infection caused by monkeypox virus, an enveloped double-stranded DNA virus of the genus *Orthopoxvirus* belonging to the family *Poxviridae* which contains smallpox, cowpox, Orf, and vaccinia viruses (1,2). The virus is made

up of two genetic clades; the Central African (Congo Basin) clade, which is now known as clade 1 and more transmissible and causes more severe disease, and the West African clade (clade 2), which is thought to cause mild disease (1,3).

With the recent increase in monkeypox cases, changes in the geographic location of cases, with majority of infections occurring in regions that have not previously reported cases, and changes in the demography of infected persons, it has become imperative to review the epidemiology, diagnosis, treatment modalities, current vaccines available for prevention and the economic impact of monkeypox outbreak. This will enable researchers to understand the disease trends, shifts in geographical spread and changes in the epidemiological characteristics as a result of evolution of monkeypox virus and adaptation to the human immunity, thereby aiding the development of innovative surveillance systems, diagnostic techniques, treatment modalities and preventive measures including vaccines that will enable prevention and management of future outbreaks. This knowledge will also guide policy makers in making well informed decisions that will positively impact the economy.

The objective of this review is to describe the epidemiology of human monkeypox, diagnosis, available treatment options, current vaccines approved for use, and the economic impacts of the current human monkeypox outbreak.

Methodology and Results:

Online electronic databases including PubMed, Google Scholar and Web of Science were searched for primary source articles including original reports, case series studies, case reports, seroprevalence studies and epidemiological reports on human monkeypox. Secondary search was also conducted using references of the primary articles reviewed. Inclusion criteria for selecting studies for the review were studies that provided information on human monkeypox history, diagnosis, clinical features, treatment, vaccination and economic impacts. Search words used include 'human monkeypox' OR 'monkeypox' AND 'monkeypox origin' OR 'history' AND 'monkeypox epidemiology' AND 'monkeypox treatment' AND/OR 'management' AND 'monkeypox vaccines', AND 'monkeypox economic impact'. Studies on reviews and systematic reviews of monkeypox were excluded.

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guide, initial search produced 2310 articles on Google Scholar, 1097 articles from PubMed and 2593 from Web of Science. Following de-duplication, 1090 article titles and abstracts were screened, followed by assessment of 207 full text publications to determine eligibility, and 158 publications were further excluded, leaving 49 eligible articles. A further 28 eligible articles were obtained from secondary searches, giving a total of 77 eligible publications for the review (Fig 1).

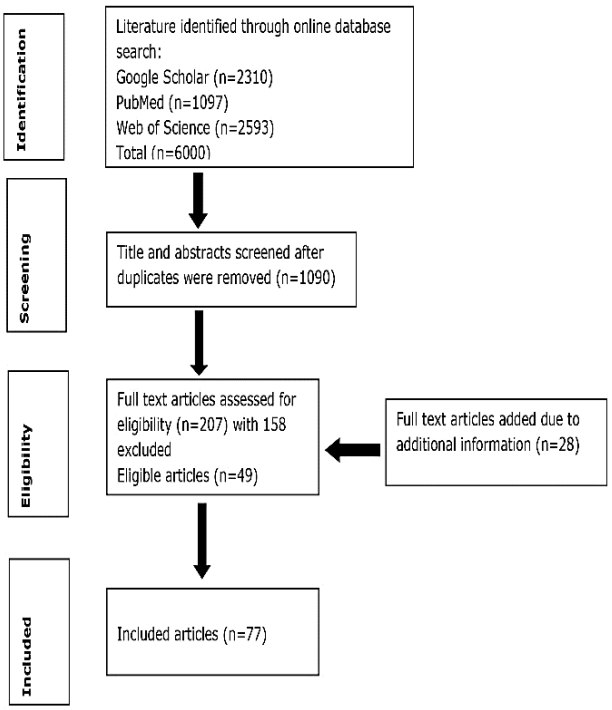

Fig. 1: Process of selection of publications (PRISMA guide) used for the review

Discussion:

Historical background:

Monkeypox was first identified in 1958 in captive monkeys that developed vesicular disease while being transported from Africa to Copenhagen, Denmark for research (4). Although this discovery earned the disease its name, the largest animal reservoirs of the virus are rodents including squirrels and giant pouched rats (4). The World Health Organization (WHO) recently renamed monkeypox as 'Mpox' following reports from countries and individuals of racist and stigmatized language being used in various settings and communities (5). The natural host reservoir is still unknown but the animal hosts are varied and include squirrels, Gambian pouched rats, dormice and non-human primates (1,6-10).

There is plethora of information on monkeypox that remains unknown, which include its mode of transmission from animal to human host, pathogen-host associations, factors that enable the virus to persist in nature, environmental factors that influence the virus

geographical shift are research questions to be answered to help in controlling and preventing monkeypox virus spread. The drivers of transmission to humans are aerosol transmission, documented in animal transmission (11,12) as well as direct and indirect contact with infected live or dead animals (1,13-15). Human-to-human transmission occurs through close contact with respiratory secretions, skin lesions of infected persons and contaminated objects (1,15), placental transmission and close contact during and after birth (1,16). Sexual transmission has not been confirmed and requires further investigation.

Clinical monkeypox virus infections:

Human monkeypox was first diagnosed in the Democratic Republic of the Congo (DRC) in a 9-month-old boy following the cessation of smallpox vaccination, after smallpox eradication in the late 1970s (1,17). The clinical manifestations of human monkeypox are indistinguishable from those of smallpox, but severity and mortality are much lower with monkeypox. The disease is characterized by fever, headache, myalgia, tiredness and marked lymphadenopathy involving the cervical and inguinal lymph nodes, and differs from smallpox and chickenpox in this respect.

The symptoms of monkeypox are milder because of previous immunization with vaccinia virus vaccine during the smallpox eradication programme, at which time individuals developed cross immunity against monkeypox (18). Monkeypox is endemic in Central and West Africa with more cases being seen in rural tropical rainforest regions, where contact with animal hosts is more frequent, although there has been increasing spread to urban areas with urbanization encroaching into the rural areas (7,19). In addition, political instability and insecurity in some of these endemic areas leads to displacement of large numbers of people who then live close to these animal hosts. The practice of many inhabitants hunting wild animals for food, is also a predisposing factor. Other African countries that have reported cases of human monkeypox include Benin, Cameroon, Central African Rep ublic, Côte d'Ivoire, Gabon, Liberia, Nigeria, the Republic of Congo, Sierra Leone and South Sudan.

Epidemiology of monkeypox

There have been several outbreaks of human monkeypox after it was first identified in 1970. The 1970-79 outbreaks affected individuals in DRC, Sierra Leone, Nigeria, Liberia and Ivory Coast resulting in 47 cases, with the majority (n=38) from Zaire and the DRC (20). Although cases are seen all year round, the outbreak occurred most often in the dry season and clustering was noted within families, localities and countries (20,21). Children under 10 years of age (range of 7 months to 35 years) were most affected. The sex ratio was similar with 26 males and 21 females affected. Among females, adult females were more at risk. Incubation period was about 12 days (approximately 7-14 days) (20,22). The onset of symptoms was within 24 hours to five days while onset of rash was between 9 to 17 days. Symptoms ranged from mild to severe and mostly observed among unvaccinated individuals. Mode of transmission was either directly from contact with animals carrying the virus or secondarily through person-to-person transmission (usually milder and atypical) (20).

The DRC had another outbreak between 1981 to 1986 with 338 cases (67% confirmed by virus culture), 182 male and age range of 3 months to 69 years (23). Majority of the cases (86%) were children below 10 years of age and 13% of all cases had vaccination scar. Among cases identified, 72.5% had primary infection and 93 patients were considered to be secondary cases. Attack rates (AR) among unvaccinated persons was 7.47% while AR among unvaccinated individuals living in the same household with cases was 9.3% (7 times higher than AR for vaccinated household contacts) (23). Case fatality rate (CFR) was below 10% which was significantly lower than for smallpox. It was also noted that transmission beyond secondary infection was rare and it was established that repeated reintroduction of the virus was necessary to sustain the disease outbreak (24). In 1984, an outbreak was also reported in the Central African Republic. Six cases were identified among unvaccinated individuals in a pygmy community (25).

A third outbreak occurred in the DRC between 1996-1997. In 1996, Katako-Kombe health zone, Kasai Oriental, DRC was considered the epicenter of the outbreak with 71 cases identified and mode of transmission was predominantly person - to - person (7). From February 1996 to February 1997, 88 clinical cases were identified in nine of 12 villages (AR of 22 per 1000), of which 50 were males. The median age of onset was 10 years (range from 1 month to 62 years). In keeping with its occurrence mainly in the dry season, cases increased from February 1996, peaked in August 1996 and subsequently declined. This trend was the same in 1997 when there was a resurgence in February 1997 with AR being similar in males and females and ranging from 0-105 per 1000 in Akungula (7). By age, children less than 15 years of age were mostly affected (AR of 146 per 1000). As of October 1997, 419 cases were identified; 344 in Katako-Kombe health zone (AR of 1.1 per 1000)

and 75 in Lodja health zone (AR of 0.3 per 1000). Five deaths were reported among children 4 to 8 years of age in Katako-Kombe (1.5% case fatality ratio). Majority of the cases were in individuals less than 16 years and 78% of cases were secondary infections. Among the cases, only 6% had previously received vaccinia vaccine putting the secondary AR at 8% (7). With each outbreak, there have been an increasing number of cases. This has been attributed to the waning cross-immunity among those vaccinated with the smallpox virus, increasing number of young unvaccinated individuals and increasing human contact with small animals that could serve as hosts for monkeypox virus.

In 2003, 11 cases were detected in the Republic of Congo among children below 18 years of age, which resulted in one death and one individual with profound sequelae. It was during this outbreak that sustained person-to-person transmission was initially observed (26). The DRC also experienced an outbreak during this period (2001-2004) with over 2000 suspected cases reported and clinical samples obtained from 136 individuals as a result of the civil unrest which hindered surveillance activities. Fifty-one cases were confirmed from 136 suspected case samples collected, male-to-female ratio was approximately equal and age ranged from 2 months to 54 years with majority of cases occurring in children below 10 years (27). Human monkeypox was also first reported in the United States in 2003 (28). A total of 50 cases were identified in Wisconsin, Illinois, Indiana and New Jersey. Fifty-five percent were females, age ranged between 1 - 59 years (median - 28 years) with most being primary infections from contact with infected prairie dogs. Diagnosis was through culture or DNA amplification of skin lesion samples and antibody neutralization assay. There were no deaths reported during this outbreak (28).

Sudan experienced an outbreak in 2005 with 10 confirmed cases and 9 probable cases (29,30). Surveillance data from the DRC between 2005 to 2007 revealed 760 laboratory-confirmed monkeypox cases with preponderance for people living close to forested areas, males, below 15 years of age and unvaccinated (31). Between 2000 and 2009, the Republic of Congo reported 27 cases while the DRC reported 10,027 suspected cases (32, 33). From 2010 to 2019, 2 cases were reported in Sierra Leone, 6 in Liberia, 3 in Cameroon, 24 in Congo, 61 in Central African Republic, 181 in Nigeria and over 8,700 suspected cases in the DRC (33-46).

The outbreak in Nigeria was as a result of the West African clade in 2017-2018 with 122 confirmed cases across 17 States (45). Male individuals were mostly affected (n=84) and the age range of infected persons was between 2 days to 50 years, with median age being 29 years. Seven deaths were reported with a case fatality rate of 6%. Transmission was through primary zoonosis and secondary person-to-person. All the cases had rash and other common symptoms including lymphadenopathy, fever, itching and headache. By January 2019, there were 311 suspected cases across 26 States, of which 132 cases were confirmed. Most cases were between 21 and 40 years (median age of 31 years). Seven deaths were also reported (46). In 2018, three cases were identified in the United Kingdom, two travelled from Nigeria and one was a health worker (46,48). In October of the same year, another case from Nigeria was identified in Israel. In 2019, a case was imported to Singapore while in 2021, another was detected in the USA (49,50,51). In the UK, cases were subsequently detected in 2019, 2021 and 2022 (52,53). The 2021 outbreak in Nigeria was not widespread and the reported number of cases were 32 with no deaths (54).

In 2022, monkeypox became an infection with global impact as it became the largest monkeypox outbreak observed in many countries where it had not previously been seen and declared a public health emergency of international concern (1,55-61). As of September 23 2022, about 106 countries have reported cases, with over 65000 cases globally and majority of cases (approximately 64,800 in 99 locations) have been reported in countries outside Africa (62). The highest numbers have been seen in North America and Europe. Deaths have been equally split between countries where monkeypox is endemic (10 deaths in 3 locations) and locations that have not previously reported cases (10 deaths in 8 locations) (62). Majority (~99%) of cases have been among males, with men who have sex with men (MSM) being disproportionately affected (60,61,66). This has raised the question as to whether it should be termed a sexually transmitted infection (STI) (63-65). Although all age groups are affected, adult males between 26-40 years are worse hit. At the beginning of the outbreak, majority of cases (67%) were seen among Whites but as the outbreak progressed, cases increased among individuals in the minority ethnicity (Hispanics -27% and African Americans-41%) while the number of cases among White reduced (26%) (66). These demographics in the UK were similar (60,61).

While monkeypox is not an STI, it spreads rapidly through sexual and close contact. Person-to-person transmission through close contact with lesions, respiratory droplets, body fluids and contaminated materials are

the major drivers of this outbreak (60,61,66) Other risk factors include eating inadequately cooked infected meat and animal products. Incubation period is from five to 21 days and there are two phases of illness. Invasive (prodrome) phase which is 0-5 days where infected persons experience fever, lymph node enlargement, malaise, headache, itching, chills and myalgia. Lymphadenopathy is a distinguishing sign of monkeypox which differentiates it from other infections with similar signs and symptoms. Skin eruption phase lasts 1-3 days after fever onset and is associated with rash that is predisposed to the face and extremities; 95% of cases have reported facial rash and 75% have experienced rash on the palms of hands and soles of feet (61,62,66). Without treatment, the symptoms usually clear within 2-4 weeks and mortality is between 3-6%, pre dominantly among children and immunocompromised persons.

Diagnosis of monkeypox:

Confirmatory diagnosis of monkeypox has been through polymerase chain reaction (PCR) testing of samples taken from skin lesions because of its high sensitivity and accuracy (60,67). Genomic sequencing is also used as a diagnostic tool (3,68). Serological and antigen detection are not recommended due to cross-reactivity between the different ortho poxviruses.

Treatment of monkeypox:

Treatment of human Monkeypox is mainly symptomatic as there are no drugs developed specifically for monkeypox treatment. Due to the cross sensitivity among the orthopoxviruses, an antiviral drug, tecovirimat, developed for management of smallpox is used in a small percentage of cases, specifically in individuals who have or are prone to developing severe form of the disease including immunocompromised persons and individuals with skin conditions such as eczema (69,70). Cidofovir is also used for treatment in some infected persons (60).

Targeting viral protein p37, a highly conserved domain found in all orthopoxviruses, tecovirimat is able to inhibit the formation of the envelopes of monkeypox virus. It is normally given twice daily as oral capsules for fourteen days. The US FDA has recently approved the intravenous form of the drug (on May 19, 2022), which has been found effective in treating primates (71). The 2022 global monkeypox outbreak is different from previous outbreaks in the mode of transmission, at risk groups and geographic spread, which could well be as a result of viral mutations and waning immunity. People engaging in same sex practices have shown higher incidence in Europe and North America (60,61,62)

Vaccines against monkeypox:

Infection by any of the orthopoxviruses can confer immunity against infection from other species in the family. This is beneficial as people who were immunized with the vaccinia virus vaccine during the smallpox eradication are protected from the smallpox, monkeypox and cowpox diseases. With the eradication of smallpox, immunity has waned leading to resurgence of infections by orthopoxviruses especially among unvaccinated individuals.

There are two vaccines currently approved for prevention of monkeypox. The first is Jynneos (Imvamune or Imvanex), a non-replicating live virus vaccine which is being used to prevent monkeypox and smallpox disease by administration four days before exposure is the primary vaccine approved for use (72). Two doses taken 28 days apart are required to provide optimal immune response. Immunity is conferred 14 days after the second dose. It is approved for use in all ages. Although Jynneos has been shown to be effective in animal and clinical studies, more information is being gathered on its effectiveness, side effects and long-term protective effects. It is also recommended for use in addition to other preventive measures in place. Most common side effects reported include redness, swelling and itching at the injection site, headache, tiredness, muscle aches, chills and nausea (72).

The second vaccine, called ACAM2000 was developed to protect against smallpox but expected to be effective in preventing monkey pox. Therefore, it is approved as an alternative to Jynneos. ACAM2000 is a live vaccinia virus vaccine (73) and a single dose vaccine administered by giving multiple pricks to the upper arm with a special needle. Special care is needed for the lesion. Optimal immune response is expected 28 days after administration. ACAM2000 is contraindicated in persons with weakened immune system including people with HIV, persons on chemotherapy; pregnant and breastfeeding women; individuals with heart conditions and skin conditions such as psoriasis, eczema, dermatitis; infants below 12 months and individuals who will be unable to self-isolate from persons who have these conditions (73). Unlike Jynneos that can be administered with other vaccines, ACAM2000 cannot be administered with other live injectable vaccines and it is recommended that other vaccines be administered 4 weeks after receiving ACAM2000. Side effects are similar to Jynneos but in addition, a rash may develop and swollen glands may be observed. It is also

associated with more frequent side effects (73).

Other preventive measures recommended include avoiding close or skin-to-skin contact with people who have a rash that looks like monkeypox, avoid touching surfaces, objects and materials used by infected persons and frequent hand washing (74). For those at high risk of infection, limiting activities that increase chances of exposure, limiting number of sex partners and engaging in safer sexual practices (75). Pet animals can be infected and transmit monkeypox therefore, measures should be taken to prevent infection and spread of the virus (76). Preventive measures should also be taken in congregate settings to prevent spread of the virus and in a situation where a monkeypox case is detected, the staff, residents and local authorities should be notified, isolate infected individual and ensure other preventive measures are adhered to so as to avoid the spread of the virus (77).

Economic impacts of monkeypox outbreaks:

With the monkeypox outbreak being a public health emergency of international concern and coming in the wake of SARS-CoV-2 pandemic, the already stretched thin resources have to be further diversified to conduct robust surveillance, research, develop and deploy new vaccines, diagnostic tools and treatment drugs to prevent further spread of the disease. The vaccinia vaccine has proven to be effective but there are limited supplies and production of more vaccines have to be expedited and equitable distribution implemented.

In addition, although monkeypox is regarded as a public health emergency of international concern, it has not affected trade or travel unlike SARS-CoV-2 infection. With the emergence of monkeypox globally at a time the world is still grappling with SARS-COV-2 and with young individuals, that make up the majority of the workforce, being affected, this will negatively impact GDP of different countries in losses due to sick days taken off work, cost of treatment and strain on health care services and personnel.

Conclusion:

The current global pandemic of monkeypox reminds us that infectious diseases know no borders. Responses should therefore protect everyone, leaving no country behind. It is recommended that there should be equitable contributions from countries, with each country taking responsibility for providing solutions to the outbreaks at the national level. By applying resources responsibly, countries where these diseases are endemic can gradually move away from depending on richer countries, and effectively contribute to both national and global efforts to control pandemics.

Contributions of authors:

AB conceived the review idea, designed the outline, reviewed and edited the manuscript. MTO wrote the history, epidemiology, part of the clinical features and treatment, diagnosis, vaccines, economic impact and edited the manuscript. MN wrote part of the clinical features and treatment. BM reviewed and edited the manuscript.

Source of funding:

No funding was received for this study

Conflict of interest:

No conflict of interest is declared

References:

1. World Health Organization (WHO). Monkeypox. 2022. https://www.who.int/news-room/fact-sheets/detail/monkeypox
2. Ladnyj, I. D., Ziegler, P., and Kima, E. A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo. Bull World Health Organ. 1972; 46: 593-597
3. Likos, A. M., Sammons, S. A., Olson, V. A., et al. A tale of two clades: Monkeypox viruses. J Gen Virol. 2005; 86 (10): 2661–2672.
4. Magnus, P. V., Andersen, E. K., Petersen, K. B., and Birch-Andersen, A. A Pox-like Disease in Cynomolgus Monkeys. Acta Pathologica Microbiologica Scandinavica. 1959; 46 (2): 156–76. doi: 10.1111/j.1699-0463.1959.tb00328.x
5. World Health Organization (WHO). WHO recommends new name for monkeypox disease. WHO news release. 2022 https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease#:~:text=Following%20a%20series%20of%20consultations,%E2%80%9Cmonkeypox%E2%80%9D%20is%20phased%20out.
6. 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): 03. doi: 10.3390/v9100283
7. 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 (3): 434–438. doi: 10.3201/eid0703.010311
8. Khodakevich, L., Jezek, Z., and Messinger, D. Monkeypox virus: ecology and public health significance. Bull World Health Organ. 1988; 66 (6): 747–752
9. Jezek, Z., Grab, B., Szczeniowski, M., Paluku, K. M., and Mutombo, M. Clinico-epidemiological features of monkeypox patients with an animal or human source of infection. Bull World Health Organ. 1988; 66 (4): 459–464
10. Reynolds, M. G., Carroll, D. S., Olson, V. A., et al. A silent enzootic of an orthopoxvirus in Ghana, West Africa: Evidence for multi-species involvement in the absence of widespread human dis-

ease. Am J Trop Med Hyg. 2010; 82 (4): 746–754. doi: 10.4269/ajtmh.2010.09-0716.
11. Prier, J. E., and Sauer, R. M. A pox disease of monkeys. Ann N Y Acad Sci. 1960; 85: 951-959.
12. Wenner, H. A., Macasaet, D., Kamitsuka, P. S., et al. Monkeypox I. Clinical, virologic and immunologic studies. Am J Epidemiol, 1968; 87: 551-566
13. 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
14. Sklenovská, N., and Van Ranst, M. Emergence of monkeypox as the most important orthopoxvirus infection in humans. Front Publ Health. 2018; 6: 241
15. UK Health Security Agency. Monkeypox: background information. 2018 https://www.gov.uk/guidance/monkeypox#transmission)
16. Mbala, P. K., Huggins, J. W., Riu-Rovira, T., et al. Maternal and fetal outcomes among pregnant women with human monkeypox infection in the Democratic Republic of Congo. J Infect Dis. 2017; 216: 824-828.
17. Marennikova, S. S., Seluhina, E. M., Malceva, N. M., and Ladnyj, I. D. Poxviruses isolated from clinically ill and asymptomatically infected monkeys and a chimpanzee. Bull World Health Organ. 1972; 46 (5): 613–620.
18. Nguyen, P. Y., Ajisegiri, W. S., Costantino, V., Chughtai, A. A., and MacIntyre, C. R. Re-emergence of Human Monkeypox and Declining Population Immunity in the Context of Urbanization, Nigeria, 2017-2020. Emerg Infect Dis. 2021;27 (4):
19. Centers for Disease Control and Prevention (CDC). Human monkeypox -- Kasai Oriental, Democratic Republic of Congo, February 1996-October 1997. MMWR Morb Mortal Wkly Rep. 1997; 46 (49): 1168-1171.
20. Breman, J. G., Kalisa-Ruti, Steniowski, M. V., Zanotto, E., Gromyko, A. I., and Arita. I. Human monkeypox, 1970-79. Bull World Health Organ. 1980; 58 (2): 165-82.
21. Jezek, Z., Gromyko, A. I., and Szczeniowski, M. V. Human monkeypox. J Hyg Epidem Microbiol Immunol. 1983; 27 (1): 13-28.
22. Arita, I., and Henderson, D. A. Monkeypox and whitepox viruses in West and Central Africa. Bull World Health Organ. 1976; 53 (4): 347-353.
23. Jezek, Z., Grab, B., Szczeniowski, M. V., Paluku, K. M., and Mutombo, M. Human monkeypox: secondary attack rates. Bull World Health Organ. 1988; 66 (4): 465-470
24. Jezek, Z., Grab, B., Paluku, K. M., and Szczeniowski, M. V. Human monkeypox: disease pattern, incidence and attack rates in a rural area of northern Zaire. Trop Geogr Med. 1988; 40 (2): 73-83.
25. Khodakevich, L., Widy-Wirski, R., Arita, I., et al. Monkey pox virus infection in humans in the Central African Republic. Bull Soc Pathol Exot Filiales, 1985; 78: 311-320
26. Learned, L. A., Reynolds, M. G., Wassa, D. W., et al. Extended interhuman transmission of monkey pox in a hospital community in the Republic of the Congo, 2003. Am J Trop Med Hyg. 2005; 73 428-434
27. Rimoin, A. W., Kisalu, N., Kebela-Ilunga, B., et al. Endemic human monkeypox, Democratic Republic of Congo, 2001-2004. Emerg Infect Dis. 2007; 13: 934-937
28. Centers for Disease Control and Prevention (CDC). Update: multistate outbreak of monkeypox–Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003. MMWR Morb Mortal Wkly Rep. 2003; 52 (27) 642-646.
29. Formenty, P., Muntasir, M. O., Damon, I., et al. Human monkeypox outbreak caused by novel virus belonging to Congo Basin clade, Sudan, 2005. Emerg Infect Dis. 2010 16 (10): 1539–1545. http://dx.doi.org/10.3201/eid1610.100713
30. Damon, I. K., Roth, C. E., and Chowdhary, V. Discovery of monkeypox in Sudan. N Engl J Med. 2006; 355: 962–963 doi: 10.1056/NEJMc060792
31. Rimoin, A. W., Mulembakani, P. M., Johnston, S. C., et al. Major increase in human monkeypox incidence 30 years after smallpox vaccination campaigns cease in the Democratic Republic of Congo. PNAS. 2010; 107 (37): 16262-16267
32. The New Humanitarian. Congo: Monkeypox infects 60 in north [press release]. Reliefweb, 25 September 2007. https://reliefweb.int/report/congo/congo-monkeypox-infects-60-north
33. Hoff, N. A., Doshi, R. H., Colwell, B., et al. Evolution of a disease surveillance system: An increase in reporting of human monkeypox disease in the Democratic Republic of the Congo, 2001–2013. Int J Trop Dis Health. 2017; 25 (2). doi: 10.9734/IJTDH/2017/35885.
34. Doshi, R. H., Guagliardo, S. A. J., Doty, J. B., et al. Epidemiologic and ecologic investigations of monkeypox, Likouala Department, Republic of the Congo, 2017. Emerg Infect Dis. 2019; 25 (2): 281–289. doi: 10.3201/eid2502.181222. pmid:30666937
35. Berthet, N., Nakouné, E., Whist, E., et al. Maculopapular lesions in the Central African Republic. Lancet. 2011; 378 (9799): 1354. doi: 10.1016/S0140-6736(11)61142-2.
36. Besombes, C., Gonofio, E., Konamna, X., et al. Intrafamily transmission of monkeypox virus, Central African Republic, 2018. Emerg Infect Dis. 2019; 25 (8): 1602–1604. doi: 10.3201/eid2508.190112.
37. Kalthan, E., Dondo-Fongbia, J. P., Yambele, S., Dieu-Creer, L. R., Zepio, R., and Pamatika, C. M. Twelve cases of monkeypox virus outbreak in Bangassou District (Central African Republic) in December 2015. Bull Soc Pathol Exot. 2016; 109 (5): 358–363. doi: 10.1007/s13149-016-0516-z.
38. Kalthan, E., Tenguere, J., Ndjapou, S. G., et al. Investigation of an outbreak of monkeypox in an area occupied by armed groups, Central African Republic. Med Mal Infect. 2018; 48 (4): 263–268. doi: 10.1016/j.medmal.2018.02.010.
39. 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 (4): ofx168. doi: 10.1093/ofid/ofx168.
40. Reynolds, M. G., Emerson, G. L., Pukuta, E., et al. Detection of human monkeypox in the Republic of the Congo following intensive community education. Am J Trop Med Hyg. 2013; 88 (5): 982–985. doi: 10.4269/ajtmh.12-0758.
41. Reynolds, M. G., Wauquier, N., Li, Y., et al. Human monkeypox in Sierra Leone after 44-Year absence of reported cases. Emerg Infect Dis. 2019; 25 (5): 1023–1025. doi: 10.3201/eid2505.180832.
42. Ye, F., Song, J., Zhao, L., et al. Molecular evidence of human monkeypox virus infection, Sierra Leone. Emerg Infect Dis. 2019; 25 (6): 1220–1222. doi: 10.3201/eid2506.180296.
43. Monkeypox confirmed in Liberia [press release]. April 11, 2018 http://outbreaknewstoday.com/monkeypox-confirmed-liberia-57035/
44. World Health Organization. Regional Office for Africa, Health Emergencies Programme. 2018. Weekly Bulletin on Outbreaks and other Emergencies: Week 1: 30 December 2017–5 January 2018 https://apps.who.int/iris/handle/10665/259809
45. Yinka-Ogunleye, A., Aruna, O., Ogoina, D., et al. Re-emergence of human monkeypox in Nigeria, 2017. Emerg Infect Dis. 2018; 24.

doi: 10.3201/eid2406.180017
46. Nigeria Centre for Disease Control. Nigeria monkeypox monthly situation report. December 2019. https://reliefweb.int/sites/reliefweb.int/files/resources/5a1a9820f21136842ba43f186b8d09e7.pdf
47. Public Health England. Cases of monkeypox confirmed in England https://www.gov.uk/government/news/monkeypox-case-in-england.
48. Vaughan, A., Aarons, E., Astbury, J., et al. Two cases of monkeypox imported to the United Kingdom, September 2018. Euro Surveill. 2018; 23 (38). doi; 10.2807/1560-7917
49. Ministry of Health, State of Israel. Monkeypox patient diagnosed https://www.health.gov.il/English/News_and_Events/Spokespersons_Messages/Pages/12102018 1.aspx
50. Yong, S. E. F., Ng, O. T., Ho, Z. J. M., et al. Imported monkeypox, Singapore. Emerg Infect Dis. 2020; 26 (8): 1826–1830. doi: 10.3201/eid2608.191387.
51. Center for Disease Prevention and Control (CDC) Newsroom. CDC and Texas Confirm Monkeypox in U.S. Traveller [press release]. July 16, 2021. https://www.cdc.gov/media/releases/2021/s0716-confirm-monkeypox.html
52. Public Health England. Monkeypox case confirmed in England 2019 https://www.gov.uk/government/news/monkeypox-case-confirmed-in-england.
53. Monkeypox—United Kingdom of Great Britain and Northern Ireland (Nigeria) [press release]. 11 June 2021 https://www.who.int/emergencies/disease-outbreak-news/item/monkeypox---united-kingdom-of-great-britain-and-northern-ireland-ex-nigeria
54. Nigeria Centre for Disease Control. Monkeypox Situation Report in Nigeria. May 31, 2021. https://reliefweb.int/sites/reliefweb.int/files/resources/An%20Update%20of%20Monkeypox%20Outbreak%20in%20Nigeria_210521_21.pdf
55. Chen, Y., Li, M., and Fan, H. The monkeypox outbreak in 2022: adaptive evolution associated with APOBEC3 may account for. Sig Transduct Target Ther. 2022; 7: 323 https://doi.org/10.1038/s41392-022-01181-x
56. European Centre for Disease Prevention and Control. Risk assessment: monkeypox multi-country outbreak https://www.ecdc.europa.eu/en/publications-data/risk-assessment-monkeypox-multi-country-outbreak, 2022.
57. European Centre for Disease Prevention and Control. Epidemiological update: monkeypox multi-country outbreak https://www.ecdc.europa.eu/en/news-events/epidemiological-update-monkeypox-multi-country-outbreak, 2022.
58. Kraemer, M. U. G., Tegally, H., Pigott, D. M., et al. Tracking the 2022 monkeypox outbreak with epidemiological data in real-time. Lancet Infect Dis. 2022; 22: 941-942 https://doi.org/10.1016/S1473-3099(22)00359-0.
59. UK Health Security Agency. Guidance: monkeypox: background information https://www.gov.uk/guidance/monkeypox, 2022.
60. Thornhill, J. P., Barkati, S., Warmsley, S., et al. Monkeypox virus infection in humans across 16 countries - April-June 2022. N Engl J Med. 2022; 387: 679-691 https://doi.org/10.1056/NEJMoa2207323 (2022).
61. Girometti, N., Bryne, R., Bracchi, M., et al. Demographic and clinical characteristics of confirmed human monkeypox virus cases in individuals attending a sexual health centre in London, UK: an observational analysis. Lancet Infect Dis. 2022; 22: 1321-1328 https://doi.org/10.1016/S1473-3099(22)00411-X (2022)
62. Center for Disease Prevention and Control (CDC). Monkeypox: 2022 Global map and case count. 2022. https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html
63. Heskin, J., Belfield, A., Milne, C., et al. Transmission of monkeypox virus through sexual contact—a novel route of infection. J Infect. 2022; 85: 334-363 https://doi.org/10.1016/j.jinf.2022.05.028
64. Vivancos, R., Anderson, C., Blomquist, P., et al. Community transmission of monkeypox in the United Kingdom, April to May 2022. Euro Surveill. 2022; 27: 22.
65. Perez Duque, M., Ribeiro, S., Martins, J. V., et al. Ongoing monkeypox virus outbreak, Portugal, 29 April to 23 May 2022. Euro Surveill. 2022; 27: 22.
66. Center for Disease Prevention and Control (CDC). Monkeypox: Case demographics and symptoms. 2022. https://www.cdc.gov/poxvirus/monkeypox/response/2022/demographics.html
67. Antinori, A., Mazzotta, V., Vita, S., et al and the INMI Monkeypox Group. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill. 2022;27 (22): pii=2200421 https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421
68. Yinka-Ogunleye, A., Aruna, O., Dalhat, M., et al. Outbreak of human monkeypox in Nigeria in 2017-18: a clinical and epidemiological report. Lancet Infect Dis. 2019; 19 (8): 872-879 https://doi.org/10.1016/S1473-3099(19)30294-4.
69. Grosenbach, D. W., Honeychurch, K., Rose, E. A., et al. Oral tecovirimat for the treatment of smallpox. N Engl J Med. 2018; 379: 44-53.
70. Center for Disease Prevention and Control (CDC). Monkeypox: Patient's guide to TPOXX. 2022. https://www.cdc.gov/poxvirus/monkeypox/if-sick/treatment.html
71. World Health Organization (WHO). Clinical Management and Infection Prevention and Control for Monkeypox. Interim Rapid Response Guide, 10 June 2022.
72. Center for Disease Prevention and Control (CDC). Monkeypox vaccines: JYNNEOS. 2022 https://www.cdc.gov/poxvirus/monkeypox/vaccines/jynneos.html
73. Center for Disease Prevention and Control (CDC). Monkeypox vaccines: ACAM2000. 2022 https://www.cdc.gov/poxvirus/monkeypox/vaccines/acam2000.html.
74. Center for Disease Prevention and Control (CDC). Monkeypox Prevention steps. 2022 https://www.cdc.gov/poxvirus/monkeypox/prevention/protect-yourself.html
75. Center for Disease Prevention and Control (CDC). Monkeypox safer sex and social gatherings. 2022. https://www.cdc.gov/poxvirus/monkeypox/prevention/sexual-health.html
76. Center for Disease Prevention and Control (CDC). Monkeypox: pets and monkeypox. 2022 https://www.cdc.gov/poxvirus/monkeypox/prevention/pets-in-homes.html
77. Center for Disease Prevention and Control (CDC). Monkeypox: congregate settings. 2022. https://www.cdc.gov/poxvirus/monkeypox/community/congregate.html.