

## Monkey pox virus: A review

Authors - swapnil Sainath Wagh, Asst. prof. Ansar A. shaikh. nandakumar shinde collage of pharmacy.

Date of Submission: 15-11-2024

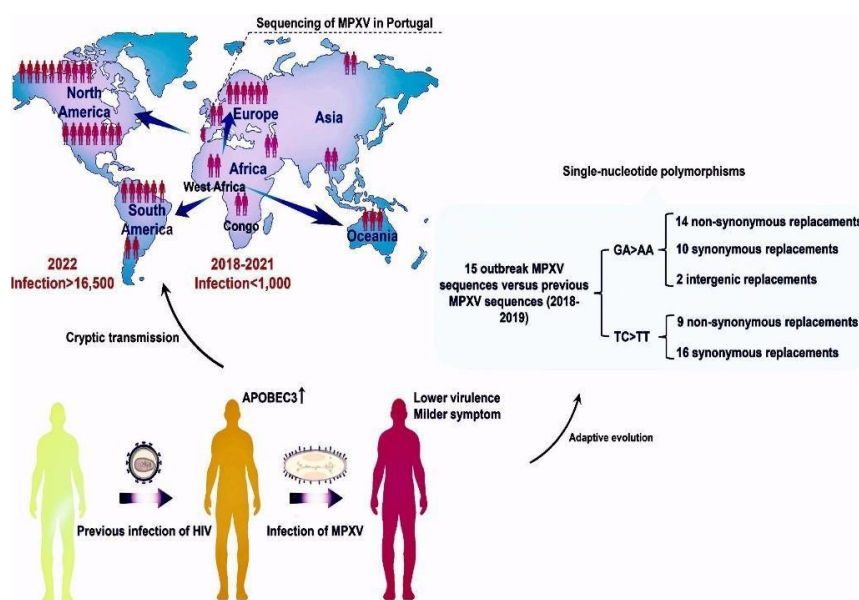
Date of Acceptance: 25-11-2024

### ABSTRACT:

The monkey pox virus, which was formerly only found in Africa, is a rare but significant zoonotic and orthopox virus disease that has drawn increasing attention because of its potential to spread from person to person and because it has recently become more prevalent throughout Europe, North America, and Oceania. The origin of this virus is still unknown, and as the COVID-19 pandemic starts to fade, several countries throughout the world are now dealing with a new outbreak. The virus that causes monkey pox is communicable between humans and animals and is a member of the Orthopox virus genus within the poxviridae family. The 1970s saw an increase in monkey pox cases as a result of the smallpox immunization being discontinued, a development that garnered attention worldwide. The virus was named monkey pox because it was first observed in macaque monkey's. It thought to be transmitted by

several different rodents and small mammals, though the origin of the virus is not known. Unfortunately, there is no definitive cure or treatment for monkey pox, however, supportive care can be offered to improve its symptoms. In several cases, medication like ST-246 may be administered. However, there are no established guidelines for symptom management in monkey pox cases. In this article we have discussed about different aspects of monkey pox virus replication, structure, transmission, vaccination, clinical manifestations, treatment and current recurrence in the world. We will also review the recent outbreak through a Political lens as related to decision making strategies, especially given the lessons learn from COVID-19.

**Keywords:** monkey pox virus, orthopox virus, pandemic, COVID-19 crisis, lessons from COVID-19.



### I. INTRODUCTION:

The monkey pox virus was first described in 1958 during monkey's shipped from Singapore to Denmark, during this decade, additional

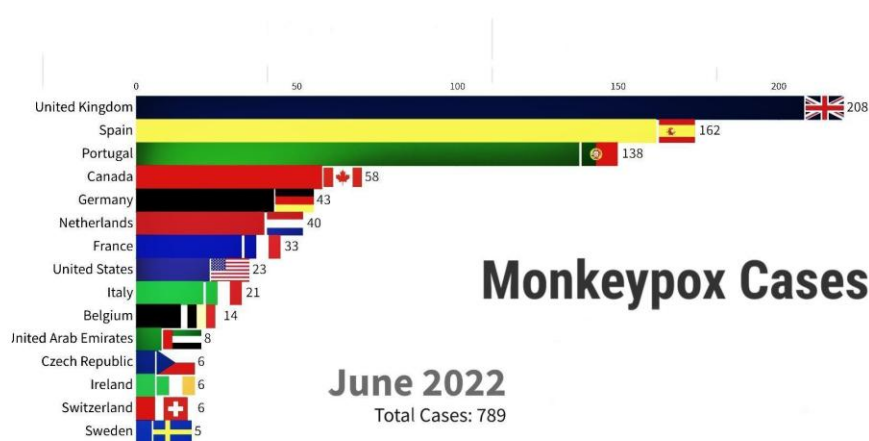
outbreak were reported in the captive monkey's in USA, the Netherlands and France. [ 1 ] [ 2 ] The first human case of monkey pox was recorded in 1970, in what's now the Democratic Republic of

the Congo. In 2022, monkey pox spread around the world. Before that, cases of monkey pox in another place is rare and usually linked to travel or to animals being imported from region where monkey pox virus is endemic [ 3 ]

After the first human case, sporadic outbreak were reported in some countries in west and central Africa, mainly among children in rural, rainforest area. On the basis of clinical presentation and genomic sequencing results, monkey pox virus isolated which classified into two clades. Between 1981 and 2017, monkey pox virus clade 1 cause several outbreak in the democratic republic of Congo, with high fatality rates (1-12%) most of these cases is not laboratory confirmed because of a scarcity of Local diagnostic infrastructure, during this period, very few humans monkey pox virus cases is reported in west Africa But, in 2017, Nigeria had a large outbreak with 122 PCR – confirmed cases of the monkey pox virus. [ 4 ]The progressive rise of cases in the Democratic Republic of the Congo and the re- emergence of monkey pox in Nigeria in 2017 is attributed to the discontinuation of smallpox vaccination in 1980,

there was a global neglect of the African outbreak and dearth of related research. [ 5 ]

Increase global travel and importing of goods from Africa have contributed to sporadic outbreak. Cases have been reported in various countries, including one in Israel in 2018, seven in the United Kingdom (2018-2021), one in Singapore (2019), and two in the United States (2021). However, monkey pox remains prevalent in African countries, as evidenced by the 550 confirmed cases in Nigeria from 2017-16 2022, resulting in nine fatalities.[ 6 ][ 7 ] The number of cases has surged globally, with approximately 50,000 confirmed cases reported across 100 countries as of August 2022, with 13 reported deaths. This alarming increase incases led the World Health Organization to declare the monkey pox outbreak a global health emergency. [ 8 ] While MPV is less fatal and transmissible than the smallpox virus, concerns persist regarding the possibility of it evolving into a more efficient human pathogen. As of October 2022, more than 75,000 cases of MPV were reported across 109 countries, with 34 deaths reported in 12 countries in the year 2022. [ 9 ]



### History:

The monkey pox virus was discovered in Denmark (1958) in monkeys kept for research. The first reported human case of mpox was a nine-month-old boy in the Democratic Republic of the Congo (1970).[ 10 ][ 11 ] in the United States determined that the virus had been introduced through a shipment of animals from Ghana which included monkey pox-infected rodents (2005). These African rodents, imported as exotic pets,

then infected prairie dogs in the United States during transport and holding, humans became infected through contact with the infected prairie dogs. Overall, 72 cases of illness were reported from six Midwestern states, including a young child who developed severe monkey pox encephalitis (2004). [ 12 ]This outbreak highlighted the potential threat of introduction of non-indigenous pathogens from exotic animals, and illustrated the possible emergence of new zoonotic

diseases through animal transport. As a result of this outbreak, new rules and guidelines regarding the shipment and sale of exotic animals have been drafted in the United States and Europe.[ 13 ].

On 14 July, the State health minister Veena George of Kerala reported a suspected mpox case. [ 14 ]. The patient had been in contact with someone who had tested positive for mpox in the United Arab Emirates and had arrived in India from UAE four days before. India did not have any cases of community transmission or local transmission until July 24, when Delhi reported its first case. The patient had not traveled abroad and had recently been to a party in Himachal Pradesh. Even though government health officials in India did not confirm community transmission of the disease.[ 15 ].

The virus was named after being first seen in macaque monkeys, even though it is not spread by them.[ 14 ]. Prior to 1970, the virus was only found in non-human hosts, with transmission thought to happen among different rodent and small mammal species, although the exact source of the virus is still unknown. Nevertheless, this view changed after the 2003 Monkey pox outbreak in the United States, which showed an enhanced transmissibility among humans and higher viremia levels in infected individuals. In the past, most Monkey pox cases were found in Africa, but now the majority of cases are being reported in the western hemisphere and Europe. The cause of this epidemic is still unknown, and multiple organizations are engaging in contact tracing activities to identify where it started [17][18].

#### Virus structure :

The family **poxviridae** includes viruses groups known for being large in size, having an enveloped structure, and containing double-stranded DNA. These viruses are often present in rodent, rabbit, and non-human primate groups. [ 19 ]. The Poxviridae family is split into two subfamilies: **Entomopoxvirinae** and **Chordopoxvirinae**. The monkey pox virus, known as **Orthopoxvirus** monkeypox, is a virus with an enveloped structure and a double-stranded DNA genome, classified under the **Orthopoxvirus** genus within the Poxviridae family. The Orthopoxvirus category consists of vaccinia virus, cowpox virus, variola virus, and various other animal pathogen poxviruses. [ 20 ]

Poxviruses possess a structure that is either brick-shaped or oval-shaped, with a size ranging from 200 to 400 nm. Each poxvirus

finishes its replication process within the cytoplasm of the cell it has infected[ 21 ]. The genes in the core region of the poxvirus genome are essential for functions like virus transcription and assembly within the cell. At the same time, the genes positioned at the extremities of the genome play a role in the interactions between the virus and its host. All sequenced members of the Poxviridae family have 49 genes in common, while the Chordopoxvirus subfamily has 90 shared genes.



Most of the genes that are preserved are located in the middle part of the genome. Due to their significant size, poxviruses like Monkeypox encounter difficulties in effectively evading host immune responses and quickly multiplying. [ 22 ]. Poxviruses are more prone to trigger a host's immune response because they have greater interaction with the host's immune system. In order to evade detection, poxviruses have developed a set of virulence genes that create substances capable of controlling the host's immune system.[ 23 ]. These proteins can be categorized into two groups depending on their location of action: either intracellular or extracellular. Intracellular proteins consist of virotransducer proteins which block the cell's reaction to the infection and virostealth proteins that decrease the detection of immune recognition markers, such as Major Histocompatibility Complex 1 and CD4.

A viromimic protein is the sole form of extracellular protein. MPXV has a linear DNA genome around 197 kb in size, consisting of approximately 190 nonoverlapping ORFs longer than 180 nucleotides. Just like all other Orthopoxviruses, the central coding region sequence (CRS) located at MPXV nucleotide positions  $\approx 56000$ – $120000$  remains unchanged and is surrounded by variable ends with inverted terminal repeats (ITRs). The Monkeypox virus is a

zoonotic virus that is part of the Orthopoxvirus genus. It is a linear double-stranded DNA virus that belongs to the Poxviridae family and has been included in the WHO's list of diseases with

epidemic or pandemic potential. The subset contains viruses such as Smallpox (variola), Vaccinia, and Cowpox [ 25 ] viruses.

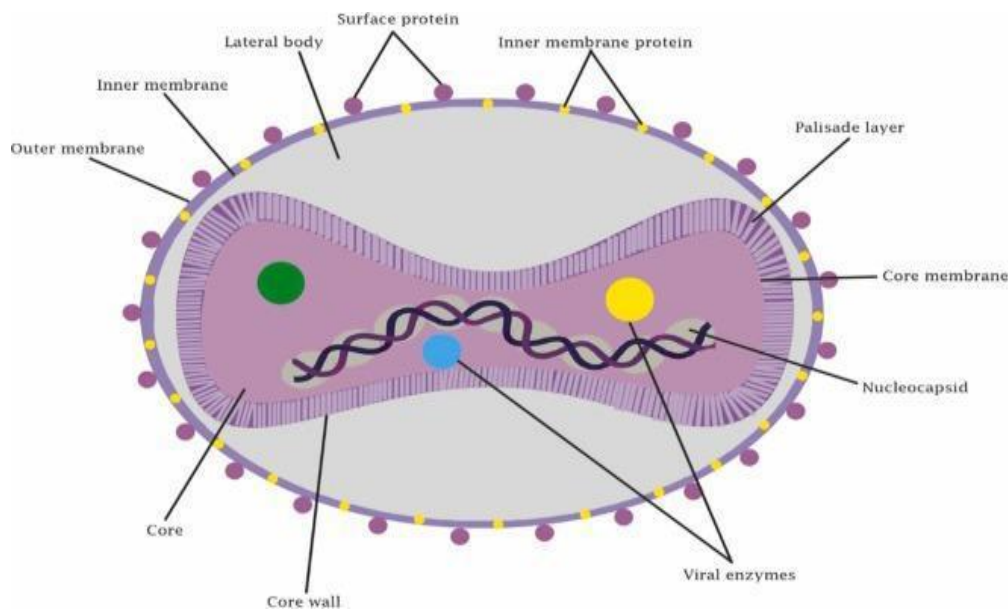


Fig : monkey pox virus structure

**Pathogenesis of viral infection :**

After entering the body through various routes (**mouth, nose, or skin**), the mpox virus multiplies at the site of entry and then travels to nearby lymph nodes. Afterward, a primary viremia triggers the propagation of the virus to other organs.[ 26 ]. This marks the period of incubation, usually lasting between **7 and 14 days**, with a maximum of **21 days**. The monkeypox virus is divided into two primary genetic groups – the Central African (Congo Basin) group and the West African group. The group from the Congo Basin in central Africa has been noted to display increased virulence and lead to more serious disease forms in comparison to the group from West Africa.[ 27 ]



Genetic analysis of monkeypox virus strains from West and central Africa identified certain genes that could explain differences in virulence between the two groups. [ 28 ]. The West African varieties exhibit deletions and fragments in specific open reading frames that can potentially lead to their diminished virulence. Research has shown that the Central African monkeypox virus hinders the activation of T-cells and suppresses the release of inflammation-related cytokines in human cells that are infected.[ 29 ].

The monkeypox virus strain found in Central Africa has demonstrated the ability to impede the activation of T-cells and lower the production of inflammatory cytokines in human cells when infecting them. [ 30 ]. Additionally, this strain appears to specifically weaken the body's defense system by decreasing cell death and blocking the expression of certain genes linked to immunity. It is suspected that the virus can transfer from animals to animals and then to humans, as demonstrated in the 2003 US Midwest outbreak. Pet prairie dogs were infected by rodents imported from Ghana, which were previously infected. [ 31 ]. The main host of the monkeypox virus is still not known, but it is believed that monkeys and humans can sometimes carry it. [ 32 ] The virus likely

originated from certain species of rodents or squirrels in the secondary forests of central Africa. The spread and eventual colonization of monkeypox virus in a host consist of a sequence of occurrences leading to disease development and bodily dysfunction.



The existence of lymphadenectasis can differentiate Mpox virus infection from infections caused by other orthopoxviruses [ 33 ]. Additionally, having knowledge of how Mpox is transmitted is crucial for implementing successful strategies to fight against the disease. After being in contact with the respiratory secretions or body fluids of Mpox patients, the Mpox virus can infect nearby tissues through mucous membranes like the eyes, nose, mouth, urinary tract, and anus, or through any wounds on the skin. The virus then travels across the body through immune cells in the tissues and lymph nodes that are draining.[ 34 ][ 35 ] This marks the dormant phase of Mpox virus infection, which usually extends for about two weeks. During this time, people with Mpox typically show no symptoms and do not have any sores. After the incubation period, people who have contracted Mpox virus start showing unusual symptoms such as fever, chills, headache, muscle aches, and swollen lymph nodes. The first prodromal signals of Mpox usually persist for a period of three days. Following the fever and lymphadenopathy, a rash starts appearing on the head and face, then spreads gradually across the body. The rash progresses from small bumps to fluid-filled blisters and pus-filled sores, eventually scabbing over and resulting in scars. This advancing rash stage typically continues for a period of 2 to 4 weeks. During the ongoing Mpox outbreak in men who have sex with men (MSM), atypical clinical symptoms have been noted

portraying rashes mainly around the genital or anal region that then spread across the body. Numerous instances of Mpox virus infection can result in complications like hemorrhagic disease, necrotic disease, obstructive disease, inflammation of crucial organs, and septicemia. In non-epidemic areas in 2022, the mortality rate of Mpox was approximately 0.04%. Individuals with compromised immune systems, like children, the elderly, and those with conditions impacting their immune response (such as HIV patients and individuals taking immunosuppressive drugs), are at higher risk of developing these severe symptoms. Furthermore, [ 36 ] Individuals with weakened immune systems are at a higher risk of promoting the development of Mpox, causing it to become more adaptable to human hosts and leading to a widespread spread.[ 37 ].

## Immunology :

### 1. Host immune response :

MPXV is classified under the Orthopoxvirus genus of DNA viruses, along with variola (responsible for smallpox), vaccinia, ectromelia (causes mousepox), and cowpox virus. Orthopoxviruses multiply in monocytes, macrophages, dendritic cells, epithelial cells, and fibroblasts. Viral entry happens when orthopoxviruses attach to host cell-surface glycosaminoglycans and go through endocytosis. Different types of infectious viral particles are produced through viral replication in the cytoplasm of the host cell: enveloped virions associated with the cell, enveloped virions released outside the cell, and mature virions within the cell. Enveloped virions attached to host cells create actin tails to move between cells while still connected to the cell membrane. Extracellular enveloped virions detach from the host cell and spread throughout host tissues. Intracellular mature virions, which are stable viral particles, are released by lysed cells to facilitate transmission among hosts[ 37 ][ 38 ].

### 2. The innate immune response :

The Orthopoxviruses trigger an immune response through various DNA-sensing mechanisms, such as cyclic GMP-AMP synthase, DNA-dependent protein kinase, interferon gamma inducible protein 16, and Toll-like receptor. The activation of the interferon and nuclear factor kappa B signaling pathways is initiated by the activation of STING by DNA sensors. Orthopoxviruses generate double stranded RNA molecules that trigger the activation of protein

kinase R and TLR3. Both PKR and TLR trigger the NF- $\kappa$ B and IFN pathways. Furthermore, PKR blocks mRNA translation by phosphorylating the eukaryotic translation initiation factor 2A complex. [ 39 ].

Natural killer cells play a crucial role in managing MPXV. Research on infected rhesus macaques showed that MPXV infection results in strong growth of every NK cell category in the bloodstream and lymph nodes. While wild mice are very vulnerable to MPXV, most inbred strains of lab mice are immune to orthopoxviruses, even though the specific genes responsible for this resistance are still unidentified. The CAST/EiJ mouse strain is one of the rare laboratory mouse strains highly susceptible to orthopoxviruses because of reduced NK cell counts and an impaired IFN- $\gamma$  reaction. The injection of IL-15 or IFN- $\gamma$  shields the mice from deadly MPXV infection by promoting NK cell proliferation. [ 39 ][ 40 ]

### 3. The adaptive immune response :

Orthopoxviruses trigger the immune system through various DNA-sensing mechanisms such as cyclic GMP-AMP synthase, DNA-

dependent protein kinase, interferon gamma inducible protein 16, and Toll-like receptor 9.[ 41 ]. These sensors stimulate STING, which in turn activates the interferon and nuclear factor kappa B signaling pathways. Orthopoxviruses generate RNA molecules with two strands that can trigger protein kinase R and TLR3. Both PKR and TLR can trigger the NF- $\kappa$ B and IFN signaling pathways. Furthermore, PKR blocks mRNA translation by phosphorylating the eukaryotic translation initiation factor 2A complex.

NK cells play a crucial role in regulating MPXV.[ 42 ]. Research on infected rhesus macaques found that MPXV infection results in strong growth of all NK cell types in the blood and lymph nodes. Even though wild mice are extremely vulnerable to MPXV, the majority of inbred strains of lab mice are immune to orthopoxviruses, with the specific genes responsible for this resistance still unidentified. The CAST/EiJ mouse strain's susceptibility to orthopoxviruses is attributed to low NK cell numbers and a weak IFN- $\gamma$  response. Injecting IL-15 or IFN- $\gamma$  helps mice survive deadly MPXV infection by boosting NK cell replication.[ 43 ].

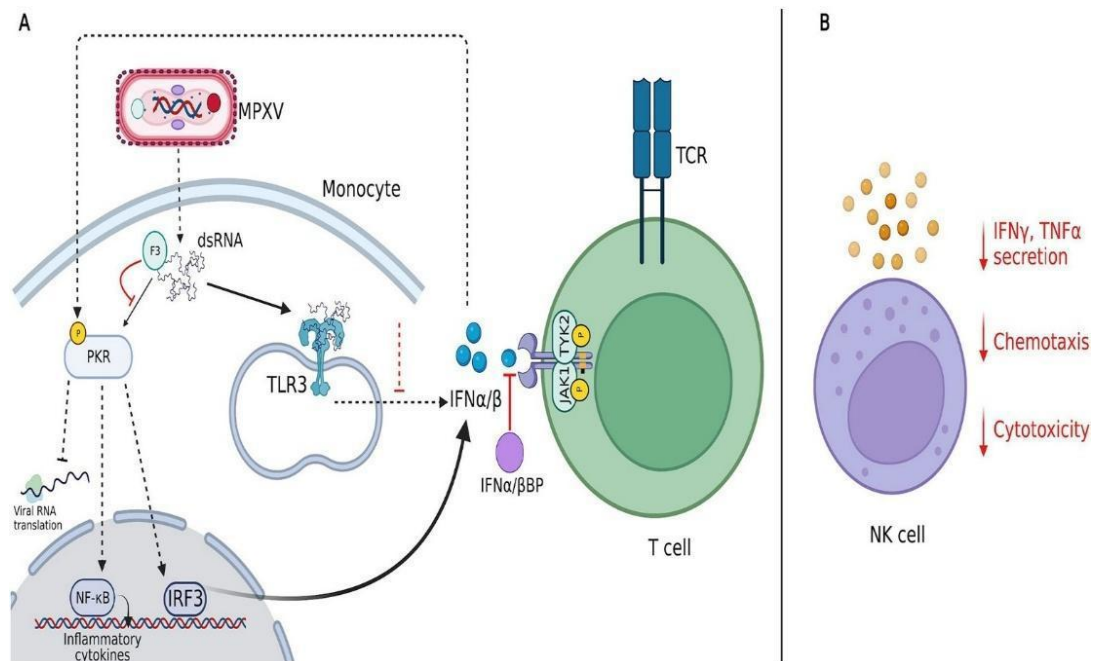


Fig : immunology of MPOX

### Epidemiology :

Surprisingly, monkeypox outbreaks are now happening in regions where the disease was not previously detected, demonstrating that MPXV occurrences beyond its usual areas are not

uncommon.[ 44 ][ 45 ]. Multiple outbreaks have been documented in non-endemic regions, such as the US in 2003 and the UK, Israel, and Singapore in 2017. These outbreaks are mostly associated with travelers coming back from endemic areas or

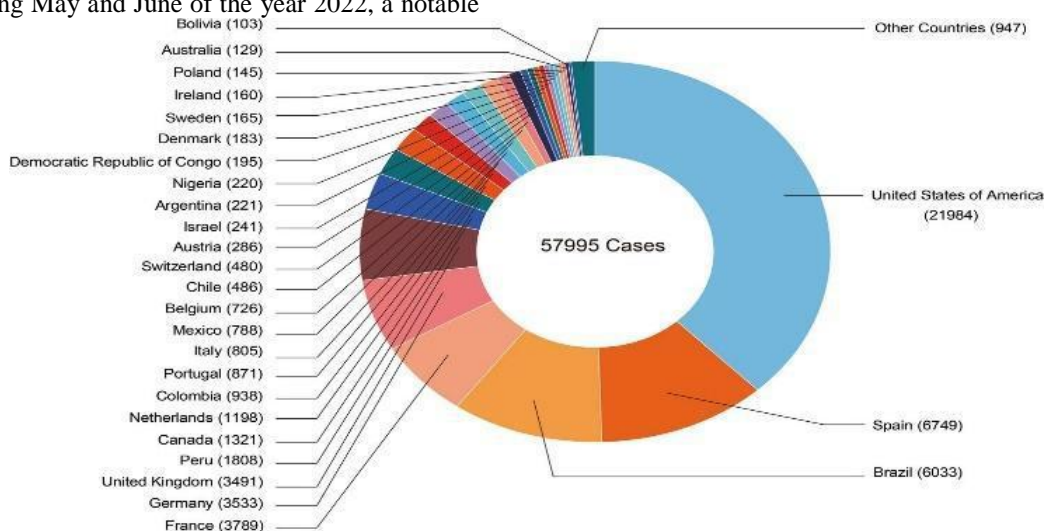
exposure in healthcare settings, like contact with infected rodents. Yet, the scale and speed of the current MPX outbreak [ 46 ] set it apart from previous occurrences. As of August 5, 2022, at least 88 countries or territories had confirmed the spread of the virus through human-to-human contact, a number that was steadily growing. The unexpected increase in MPXV cases in countries where it is usually not found has raised concerns about a possible pandemic. Diagnosing and treating MPXV poses challenges because of its various modes of transmission, including close contact with an infected individual or through droplets. [ 46 ] [ 47 ].

This led to the World Health Organization declaring a Public Health Emergency of International Concern. The recent worldwide spread of monkeypox, a disease that can spread from animals to humans, has raised worries regarding the necessity of current information during a global health crisis. Most instances of monkeypox are concentrated in Europe and the Americas based on the latest transmission data. The initial case of monkeypox outside Africa emerged in Europe in May 2022, and quickly disseminated to additional nations. As of August 5, 2022, a global monkeypox epidemic has been noted with 28,220 confirmed cases in 88 nations and 1685 additional suspected cases. The initial United States case was documented on May 18. And soon after, there were fresh cases of infection reported in Australia, Israel, and Brazil. While; In the course of During May and June of the year 2022, a notable

amount of Monkeypox (MPXV) cases were confirmed, totaling around 6000 cases. [ 48 ].

Nevertheless, in July 2022, there was a notable increase in the number of infected patients, with around 17,000 cases documented. The upward trend of MPX cases persisted in August 2022, with more than 5000 cases documented in the initial five days of the month. Unfortunately, deaths from MPX have been documented in three countries that were not previously known for the disease (Brazil, Spain, and India). [ 49 ]. By 2022, individual cases of Monkeypox in North America and Europe have been linked to the pet industry and travel from areas where the disease is common. During May of the same year, instances of natural MPXV infections were documented in Europe and the United States, mainly affecting males who participate in sexual relations with other males.

There is no known epidemiological link to the Central or West African regions. [ 50 ] Up to September 21, 2022, most MPXV cases have been identified in the United States. A recent study on those impacted by the current global Monkeypox Virus (MPXV) outbreak found that most cases (97.4%) were male, with a median age of 35 years. The sexual orientation of most patients (97.5%) was male who had sex with men, while only 1% identified as bisexual. An investigation in France also validated the existence of asymptomatic MPXV in anorectal samples from male individuals who engage in sexual activity with other men. [ 51. ] [ 52 ].



Most cases of Monkeypox (MPXV) have been documented in Europe and the Americas, with over 90% of confirmed cases reported in 14 countries such as UK, Spain, Germany, France,

Portugal, Italy, Switzerland, Belgium, US, Mexico, Canada, Netherlands, Brazil, and Peru. [ 53 ]. In the meantime, just 345 cases have been documented in seven African nations where MPXV was

previously widespread.[ 54 ] On the other hand, non-endemic countries have reported 27,875 cases. Conversely, Asian nations and countries in the Oceania area have documented lower occurrences of MPXV. Israel reported 160 cases of MPXV, while countries like UAE, Singapore, India, Saudi Arabia, Thailand, Qatar, Taiwan, Japan, South Korea, and the Philippines reported minimal cases. Only Australia had 58 cases, with few Oceania countries reporting a small number of cases. The majority of MPXV cases identified in Europe and America were discovered through local healthcare and sexual health clinics, unrelated to endemic regions in Africa.[ 55 ].

Although there is no previous evidence of MPXV being transmitted sexually, recent findings suggest that most impacted individuals are homosexual. It was also noted that the MPXV virus was found in the semen of patients who were infected. The first human monkeypox case, a 34-year-old woman from Khuzestan province, was revealed by the Iranian Ministry of Health on August 16, 2022. Skin lesions were examined and genetic analysis of the virus confirmed the diagnosis. The virus may have entered Iran from neighboring countries like Qatar, the UAE, Saudi Arabia, Turkey, Pakistan, and Lebanon, as the disease is present in those locations. The human monkeypox viruses found in Iran, as per the Nextstrain database, belong to the B.1 lineage that started in Europe and has now spread worldwide. Many people think that human monkeypox was introduced to Iran from nearby countries in the southwest, but carriers without symptoms also help spread the virus between humans as natural hosts.[ 56 ][ 57 ].

#### Vaccination :

[ 57 ]. Several vaccines have been created for smallpox and are now being distributed worldwide as medical defenses against the disease. Within the US, only MVA-BN (JYNNEOS) and ACAM2000 vaccines are authorized for preventing both smallpox and monkeypox.



[ 58 ] The two-dose vaccine JYNNEOS can aid in preventing mpox. The second dose is administered 28 days following the initial dose. It is advised for individuals who are at a high risk of mpox or have come into contact with someone who has mpox. Bavarian Nordic's mpox vaccine is the initial one authorized in Europe for individuals under 18 years old. The choice was made one week following the approval of the vaccine for adults by the World Health Organization.[ 59 ][ 60 ].

The preferred route is via subcutaneous administration. Intradermal injection is allowed for adult recipients who wish to receive it through Emergency Use Authorization (EUA). The approved and recommended method for administering the Jynneos vaccine is through subcutaneous injection. CDC guidelines for the correct storage and management of mpox vaccines.[ 60 ][ 61 ].

Clinical trials have observed strong antibody reactions following the initial dose[ 62 ]. An immune response can be detected 14 days post vaccination. Individuals infected with highly potent Orthopoxvirus need a booster dose every 2 years, whereas individuals exposed to less potent strains need one every 10 years. The LC16 vaccine is classified as a third-generation vaccine. Created and approved in Japan, it was later authorized in the United States for treating smallpox, however, it has not been licensed yet for combating monkeypox. This attenuated vaccine, which has restricted replication, was produced through cell culture. The LC16 vaccine originates from the Lister strain and is missing the B5R immunogenic membrane protein. It is given through the skin with a two-pronged needle and can be given to people of any age, including babies and kids, as part of a series of doses. It is essential to assess reactogenicity, safety, and vaccine-related adverse events to determine the most effective vaccine, especially for high-risk and vulnerable populations.



At this moment, multiple vaccines for Orthopoxvirus have been created [62][63].

#### Treatment:

There is no particular cure has been authorized for mpox. Healthcare providers can use antiviral medications like **tecovirimat (TPOXX)** or **brincidofovir (Tembexa)** to treat mpox, a condition that can also be treated with drugs used for **smallpox**. In case the vaccine is not effective for certain individuals, a medical provider could provide vaccinia immune globulin. Using medications like Benadryl and products like calamine lotion or petroleum jelly can assist with relieving itchiness. Taking a warm bath with oatmeal or other bath products purchased without a prescription can help alleviate the dry, itchy feeling that often accompanies a rash. [64][65].

For most people with monkeypox, supportive care and pain control can help them recover. This can include: [66].

- Managing skin damage from the rash
- Drinking enough liquids to keep stool soft
- Taking oral antihistamines like Benadryl
- Applying topical creams like calamine lotion or petroleum jelly
- Taking oatmeal baths
- Resting

#### Symptomatic treatment:

- Pain relief and fever management.
- Isolation: Keeping infected individuals separate to prevent spread.
- Rehydration and nutritional support: Ensuring adequate fluid intake and nutrition.
- Antiviral drugs: Tecovirimat and other medications may be used in severe cases [67].

Research on animals suggests that TPOXX could be beneficial in treating the virus responsible for mpox, and investigations are ongoing to understand its efficacy in treating mpox in humans. Mpox can lead to symptoms that typically emerge within one week, although they may also appear between 1 and 21 days after being exposed. Symptoms usually persist for a period of 2-4 weeks but could extend for a longer duration in individuals with a compromised immune system. Typical signs of mpox include: skin irritation. Antiviral therapy is superior to smallpox vaccination in treating deadly monkeypox virus infection. [68].

In 1970, the first human case of monkeypox was discovered in a 9-month-old child from the Democratic Republic of Congo (previously known as Zaire). Before the recent cases, most information about human monkeypox came from studying outbreaks in Central and West Africa. A vesicular rash can indicate a poxvirus infection like monkeypox, but confirming the diagnosis requires laboratory testing. Multiple laboratory tests can be used to confirm a monkeypox diagnosis, including virus isolation and electron microscopy, polymerase chain reaction testing, enzyme-linked immunosorbent assay tests for IgG and IgM antibodies, immunofluorescent antibody assay, and histopathological analysis. These tests can confirm the existence of the monkeypox virus and assist in diagnosing the infection. To effectively address the spread of viruses, which ignore national borders, it is crucial for the global community to collaborate in promptly addressing any gaps in our knowledge and containing the outbreak. Identifying cases quickly is essential to controlling the disease when treatments or preventative measures are not easily accessible. It is common for the symptoms of monkeypox to differ greatly among individuals in medical settings.



Monkeypox is regarded by the WHO as a resurging illness with the capability of being utilized as biological weapons. This is due to its ability to quickly propagate among a population lacking immunity to the virus. Although monkeypox is not as easily spread or as serious as smallpox or even SARS-CoV-2 (the virus causing the COVID-19 pandemic that quickly spread worldwide), it can still pose a significant risk, especially for individuals with preexisting health conditions. Hence, it is crucial to stay alert in

## II.DISCUSSION :

watching out for any indications of the illness to avoid potential issues.[ 70 ][ 71 ].

Mpox is transmitted through exposure to, or direct interaction with, an infected individual. Mpox may result in a skin irritation, enlarged lymph glands, high temperature, body pains, and additional signs.[ 72 ] Although certain types of mpox can result in serious illnesses, the majority of infections tend to resolve without treatment. Vaccines can protect certain individuals at risk from contracting mpox, which can be transmitted through close contact such as kissing, touching, and various forms of sexual activity with an infectious individual.[ 73 ]. Those individuals who engage in sexual activity with numerous or unfamiliar partners are the most vulnerable.

Nevertheless, African rodents and non-human primates, such as monkeys, are capable of carrying the virus and transmitting it to humans. The initial human case was documented in 1970. Dr. Azar states that the name of the disease has been changed to 'mpox' in order to prevent any racist or discriminatory associations with the original name. Since 2022, there has been a significant increase in both mpox incidences and fatalities in the Democratic Republic of the Congo.[ 72 ][ 73 ]. In certain regions in the country, a recent variation of clade I, known as clade Ib, has been transmitted between individuals. By mid-2024, the clade has been identified in additional countries. Two variations of mpox exist, known as clade 1 and clade 2. Clade 1, which has a fatality rate of 3.6%, is the more aggressive strain that is currently being transmitted in Central and East Africa. The 2022 outbreak originating in West Africa was caused by Clade 2, which had a lower fatality rate of less than 0.2% and milder symptoms.[ 74 ].

### III.CONCLUSION :

Mpox is a viral disease that is closely related to smallpox and primarily found in remote parts of Central and West Africa.[ 75 ]. There is currently no specific vaccine for Mpox, but the smallpox vaccine provides some protection against the disease. However, the smallpox vaccine is no longer routinely administered, and many younger people in Africa may not have received it. Several vaccines are being studied for their potential effectiveness against Mpox, including live-attenuated Mpox vaccines, DNA vaccines, and recombinant vaccines. Synthetic peptide-based prototype vaccines have also shown promise in preclinical studies, and researchers are

investigating the use of mRNA vaccines for booster purposes in those who have received the mRNA vaccine for COVID-19.

Overall, the development of effective vaccines for Mpox is an ongoing area of research, and scientists are working to develop new vaccines that can protect against this rare but potentially serious disease. In regions with a high concentration of the rash, supportive therapy, including the use of moist occlusive dressings, may be used to minimize the risk of complications. Given the ongoing occurrence of monkeypox cases worldwide, organizations need to focus on understanding its sporadic appearance in western hemisphere and Europe, researching for possible treatment ways and examining the long-term effects of the virus to decrease both morbidity and mortality rate in future.[ 76 ][ 77 ].

### REFERENCE:

- [1]. Berche P. Life and death of smallpox. *Presse Med.* 2022 Sep 1;51(3) [PubMed] [Google Scholar]
- [2]. Piot P., Bartos M., Ghys P.D., Walker N., Schwartländer B. The global impact of HIV/AIDS. *Nature.* 2001 Apr;410(6831):968–973. [PubMed] [Google Scholar]
- [3]. Trilla A., Trilla G., Daer C. The 1918 “Spanish flu” in Spain. *Clin. Infect. Dis.* 2008 Sep 1;47(5):668–673. [PubMed] [Google Scholar]
- [4]. Brüßow H., Brüßow L. Clinical evidence that the pandemic from 1889 to 1891 commonly called the Russian flu might have been an earlier coronavirus pandemic. *Microb. Biotechnol.* 2021 Sep;14(5):1860–1870. [PMC free article] [PubMed] [Google Scholar]
- [5]. Mæstad O., Shumbullo E.L. Ebola outbreak 2014–2016: effects on other health services. *CMI Brief.* 2020:2020. 03. [Google Scholar]
- [6]. Sampathkumar P., Temesgen Z., Smith T.F., Thompson R.L. SARS: epidemiology, clinical presentation, management, and infection control measures. *In MayoClin. Proc.* 2003 Jul 1;78(7):882–890. Elsevier. [PMC free article] [PubMed] [Google Scholar]
- [7]. Letafati A., Aghamirmohammadali F.S., Rahimi-Foroushani A., Hasani S.A., Mokhtari-Azad T., Yavarian J. No human respiratory syncytial virus but

- SARS-CoV-2 found in children under 5 years old referred to Children Medical Center in 2021, Tehran, Iran. *J. Med. Virol.* 2022 Jul;94(7):3096–3100. [PMC free article] [PubMed] [Google Scholar]
- [8]. Huang Y.A., Howard-Jones A.R., Durrani S., Wang Z., Williams P.C. Monkeypox: a clinical update for paediatricians. *J. Paediatr. Child Health.* 2022 Sep;58(9):1532–1538. [PMC free article] [PubMed] [Google Scholar]
- [9]. Reed K.D., Melski J.W., Graham M.B., Regnery R.L., Sotir M.J., Wegner M.V. The initial detection of human monkeypox in the western hemisphere: association with infected prairie dogs. *N. Engl. J. Med.* 2004;350(4):342–350. [PubMed] [Google Scholar]
- [10]. Chen N., Li G., Liszewski M.K., Atkinson J.P., Jahrling P.B., Feng Z., Schriewer J., Buck C., Wang C., Lefkowitz E.J., Esposito J.J. Virulence differences between monkeypox virus isolates from West Africa and the Congo basin. *Virology.* 2005 Sep 15;340(1):46–63. [PMC free article] [PubMed] [Google Scholar]
- [11]. Likos A.M., Sammons S.A., Olson V.A., Frace A.M., Li Y., Olsen-Rasmussen M., Davidson W., Galloway R., Khristova M.L., Reynolds M.G., Zhao H. A tale of two clades: monkeypox viruses. *J. Gen. Virol.* 2005 Oct 1;86(10):2661–2672. [PubMed] [Google Scholar]
- [12]. McCollum A.M., Damon I.K. Human monkeypox. *Clin. Infect. Dis.* 2014 Jan 15;58(2):260–267. [PubMed] [Google Scholar]
- [13]. Joklik W.K. The poxviruses. *Bacteriol. Rev.* 1966 Mar;30(1):33–66. [PMC free article] [PubMed] [Google Scholar]
- [14]. Haller S.L., Peng C., McFadden G., Rothenburg S. Poxviruses and the evolution of host range and virulence. *Infect. Genet. Evol.* 2014 Jan 1;21:15–40. [PMC free article] [PubMed] [Google Scholar]
- [15]. Hughes A.L., Irausquin S., Friedman R. The evolutionary biology of poxviruses. *Infect. Genet. Evol.* 2010 Jan 1;10(1):50–59. [PMC free article] [PubMed] [Google Scholar]
- [16]. Appendix2.Monkeypoxvirus. 2009. <https://www.aabb.org/docs/defaultsource/default-document-library/regulatory/aid/130s.pdf> [Google Scholar]
- [17]. Stanford M.M., McFadden G., Karupiah G., Chaudhri G. Immunopathogenesis of poxvirus infections: forecasting the impending storm. *Immunol. Cell Biol.* 2007 Feb;85(2):93–102. [PubMed] [Google Scholar]
- [18]. Moss B. Poxvirus cell entry: how many proteins does it take? *Viruses.* 2012 Apr 27;4(5):688–707. [PMC free article] [PubMed] [Google Scholar]
- [19]. Moss B. Poxvirus DNA replication. *Cold Spring Harbor Perspect. Biol.* 5: a010199. [PMC free article] [PubMed]
- [20]. Upton C., Slack S., Hunter A.L., Ehlers A., Roper R.L. Poxvirus orthologous clusters: toward defining the minimum essential poxvirus genome. *J. Virol.* 2003 Jul 1;77(13):7590–7600. [PMC free article] [PubMed] [Google Scholar]
- [21]. Lefkowitz E.J., Wang C., Upton C. Poxviruses: past, present and future. *Virus Res.* 2006 Apr 1;117(1):105–118. [PubMed] [Google Scholar]
- [22]. Okyay R.A., Bayrak E., Kaya E., Şahin A.R., Koçyiğit B.F., Taşdoğan A.M., Avcı A., Sumbül H.E. Another epidemic in the shadow of covid 19 pandemic: a review of monkeypox. *Proteins.* 2022;7:10. [Google Scholar]
- [23]. Petersen E., Kantele A., Koopmans M., Asogun D., Yinka-Ogunleye A., Ihekweazu C., Zumla A. Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention. *Infect. Dis. Clin.* 2019 Dec 1;33(4):1027–1043. [PMC free article] [PubMed] [Google Scholar]
- [24]. Tolonen N., Doglio L., Schleich S., Locker J.K. Vaccinia virus DNA replication occurs in endoplasmic reticulum-enclosed cytoplasmic mininuclei. *Mol. Biol. Cell.* 2001 Jul 1;12(7):2031–2046. [PMC free article] [PubMed] [Google Scholar]
- [25]. Kieser Q., Noyce R.S., Shenouda M., Lin Y.C., Evans D.H. Cytoplasmic factories, virus assembly, and DNA replication kinetics collectively constrain the formation of poxvirus recombinants. *PLoS One.* 2020 Jan 16;15(1) [PMC free article] [PubMed] [Google Scholar]

- [26]. Katsafanas G.C., Moss B. Colocalization of transcription and translation within cytoplasmic poxvirus factories coordinates viral expression and subjugates host functions. *Cell Host Microbe*. 2007 Oct 11;2(4):221–228. [PMC free article] [PubMed] [Google Scholar]
- [27]. Monkeypox. 2022 <https://www.who.int/news-room/factsheets/detail/monkeypox> [Google Scholar]
- [28]. Reynolds M.G., Damon I.K. Outbreaks of human monkeypox after cessation of smallpox vaccination. *Trends Microbiol*. 2012 Feb 1;20(2):80–87. [PubMed] [Google Scholar]
- [29]. Hammarlund E., Dasgupta A., Pinilla C., Norori P., Früh K., Slifka M.K. Monkeypox virus evades antiviral CD4+ and CD8+ T cell responses by suppressing cognate T cell activation. *Proc. Natl. Acad. Sci. USA*. 2008 Sep 23;105(38):14567–14572. [PMC free article] [PubMed] [Google Scholar]
- [30]. Simpson K., Heymann D., Brown C.S., Edmunds W.J., Elsgaard J., Fine P., Hochrein H., Hoff N.A., Green A., Ihekweazu C., Jones T.C. Human monkeypox—After 40 years, an unintended consequence of smallpox eradication. *Vaccine*. 2020 Jul 14;38(33):5077–5081. [PMC free article] [PubMed] [Google Scholar]
- [31]. Bartlett JG. Review of Literature: General Infectious Diseases.
- [32]. Weinstein R.A., Nalca A., Rimoin A.W., Bavari S., Whitehouse C.A. Reemergence of monkeypox: prevalence, diagnostics, and countermeasures. *Clin. Infect. Dis*. 2005 Dec 15;41(12):1765–1771. [PubMed] [Google Scholar]
- [33]. Hutson C.L., Olson V.A., Carroll D.S., Abel J.A., Hughes C.M., Braden Z.H., Weiss S., Self J., Osorio J.E., Hudson P.N., Dillon M. A prairie dog animal model of systemic orthopoxvirus disease using West African and Congo Basin strains of monkeypox virus. *J. Gen. Virol*. 2009 Feb 1;90(2):323–333. [PubMed] [Google Scholar]
- [34]. [a] Moore M.J., Rathish B., Zahra F. *InStatPearls* [internet] StatPearls Publishing; 2022. Monkeypox. Oct 8 [PubMed] [Google Scholar][b] Ježek Z., Szczeniowski M., Paluku K.M., Mutombo M. Human monkeypox: clinical features of 282 patients. *J. Infect. Dis*. 1987 Aug 1;156(2):293–298. [PubMed] [Google Scholar]
- [35]. Ježek Z., Szczeniowski M., Paluku K.M., Mutombo M. Human monkeypox: clinical features of 282 patients. *J. Infect. Dis*. 1987 Aug 1;156(2):293–298. [PubMed] [Google Scholar]
- [36]. Di Giulio D.B., Eckburg P.B. Human monkeypox: an emerging zoonosis. *Lancet Infect. Dis*. 2004 Jan 1;4(1):15–25. [PMC free article] [PubMed] [Google Scholar]
- [37]. Afshar Z.M., Rostami H.N., Hosseinzadeh R., Janbakhsh A., Pirzaman A.T., Babazadeh A., Aryanian Z., Sio T.T., Barary M., Ebrahimipour S. The reemergence of monkeypox as a new potential health challenge: a critical review. *Authorea Preprints*. 2022 Jun 5 [Google Scholar]
- [38]. Reynolds M.G., McCollum A.M., Nguete B., ShongoLushima R., Petersen B.W. Improving the care and treatment of monkeypox patients in low-resource settings: applying evidence from contemporary biomedical and smallpox biodefense research. *Viruses*. 2017 Dec 12;9(12):380. [PMC free article] [PubMed] [Google Scholar]
- [39]. Stagles M.J., Watson A.A., Boyd J.F., More I.A., McSeveney D. The histopathology and electron microscopy of a human monkeypox lesion. *Trans. R. Soc. Trop. Med. Hyg*. 1985 Jan 1;79(2):192–202. [PubMed] [Google Scholar]
- [40]. Patel A.R., Romanelli P., Roberts B., Kirsner R.S. Herpes simplex virus: a histopathologic study of the depth of herpetic wounds. *Int. J. Dermatol*. 2009 Jan;48(1):36–40. [PubMed] [Google Scholar]
- [41]. Magnus P.V.O.N., Andebson E.K., Petebson K.B., Andebson A.B. A pox-like disease in cynomolgus monkeys. *ActaPathol. Microbiol. Scand*. 1959;46:156–176. [Google Scholar]
- [42]. Silenou B.C., Tom-Aba D., Adeoyo O., Arinze C.C., Oyiri F., Suleman A.K., Yinka-Ogunleye A., Dörrbecker J., Ihekweazu C., Krause G. Use of

- surveillance outbreak response management and analysis system for human monkeypox outbreak, Nigeria. *Emerg. Infect. Dis.* 2020 Feb;26(2):345. 2017–2019. [PMC free article] [PubMed] [Google Scholar]
- [43]. Ogoina D., Izibewule J.H., Ogunleye A., Ederiane E., Anebonam U., Neni A., Oyeyemi A., Etebu E.N., Ihekweazu C. 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.* 2019 Apr 17;14(4) [PMC free article] [PubMed] [Google Scholar]
- [44]. Sabeena S. The changing epidemiology of monkeypox and preventive measures: an update. *Arch. Virol.* 2023 Jan;168(1):31. [PubMed] [Google Scholar]
- [45]. Foster S.O., Brink E.W., Hutchins D.L., Pifer J.M., Lourie B., Moser C.R., Cummings E.C., Kuteyi O.E., Eke R.E., Titus J.B., Smith E.A. Human monkeypox. *Bull. World Health Organ.* 1972;46(5):569. [PMC free article] [PubMed] [Google Scholar]
- [46]. Ladnyj I.D., Ziegler P., Kima E. A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo. *Bull. World Health Organ.* 1972;46(5):593. [PMC free article] [PubMed] [Google Scholar]
- [47]. Alakunle E.F., Okeke M.I. Monkeypox virus: a neglected zoonotic pathogen spreads globally. *Nat. Rev. Microbiol.* 2022 Sep;20(9):507–508. [PMC free article] [PubMed] [Google Scholar]
- [48]. Mahase E. Monkeypox: what Do We Know about the Outbreaks in Europe and North America?. [PubMed]
- [49]. DiGiulio D.B., Eckburg P.B. Monkeypox in the western hemisphere. *N. Engl. J. Med.* 2004 Apr 1;350(17):1790. [PubMed] [Google Scholar]
- [50]. Simpson K., Heymann D., Brown C.S., Edmunds W.J., Elsgaard J., Fine P., Hochrein H., Hoff N.A., Green A., Ihekweazu C., Jones T.C. Human monkeypox—After 40 years, an unintended consequence of smallpox eradication. *Vaccine.* 2020 Jul 14;38(33):5077–5081. [PMC free article] [PubMed] [Google Scholar]
- [51]. Weaver, J.R.; Isaacs, S.N. Monkeypox virus and insights into its immunomodulatory proteins. *Immunol. Rev.* 2008, 225, 96–113. [Google Scholar] [CrossRef]
- [52]. Huhn, G.D.; Bauer, A.M.; Yorita, K.; Graham, M.B.; Sejvar, J.; Likos, A.; Damon, I.K.; Reynolds, M.G.; Kuehnert, M.J. Clinical Characteristics of Human Monkeypox, and Risk Factors for Severe Disease. *Clin. Infect. Dis.* 2005, 41, 1742–1751. [Google Scholar] [CrossRef] [PubMed]
- [53]. Nigeria Centre for Disease Control and Prevention. Available online: <https://ncdc.gov.ng/diseases/sitreps/?cat=8&name=An%20Update%20of%20Monkeypox%20Outbreak%20in%20Nigeria> (accessed on 27 September 2023).
- [54]. Kraemer, M.U.G.; Tegally, H.; Pigott, D.M.; Dasgupta, A.; Sheldon, J.; Wilkinson, E.; Schultheiss, M.; Han, A.; Oglia, M.; Marks, S.; et al. Tracking the 2022 monkeypox outbreak with epidemiological data in real-time. *Lancet Infect. Dis.* 2022, 22, 941–942. [Google Scholar] [CrossRef] [PubMed]
- [55]. Hirani, R.; Rashid, D.; Lewis, J.; Hosein-Woodley, R.; Issani, A. Monkeypox outbreak in the age of COVID-19: A new global health emergency. *Mil. Med. Res.* 2022, 9, 55. [Google Scholar] [CrossRef] [PubMed]
- [56]. Kimball, S. CNBC. WHO Declares Rapidly Spreading Monkeypox Outbreak a Global Health Emergency. 2022. Available online: <https://www.cnn.com/2022/07/23/who-declares-spreading-monkeypox-outbreak-a-global-health-emergency.html> (accessed on 27 September 2023).
- [57]. Bhalla, N.; Payam, A.F. Addressing the Silent Spread of Monkeypox Disease with Advanced Analytical Tools. *Small* 2023, 19, 2206633. [Google Scholar] [CrossRef]
- [58]. Chen, N.; Li, G.; Liszewski, M.K.; Atkinson, J.P.; Jahrling, P.B.; Feng, Z.; Schriewer, J.; Buck, C.; Wang, C.; Lefkowitz, E.J.; et al. Virulence differences between monkeypox virus isolates from West Africa and the Congo basin. *Virology* 2005, 340, 46–63. [Google Scholar] [CrossRef]

- [59]. Reed, K.D.; Melski, J.W.; Graham, M.B.; Regnery, R.L.; Sotir, M.J.; Wegner, M.V.; Kazmierczak, J.J.; Stratman, E.J.; Li, Y.; Fairley, J.A.; et al. The Detection of Monkeypox in Humans in the Western Hemisphere. *N. Engl. J. Med.* 2004, 350, 342–350. [Google Scholar] [CrossRef]
- [60]. Isidro, J.; Borges, V.; Pinto, M.; Sobral, D.; Santos, J.D.; Nunes, A.; Mixão, V.; Ferreira, R.; Santos, D.; Duarte, S.; et al. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. *Nat. Med.* 2022, 28, 1569–1572. [Google Scholar] [CrossRef]
- [61]. Kaler, J.; Hussain, A.; Flores, G.; Kheiri, S.; Desrosiers, D.; Kaler, J.; Hussain, A.; Flores, G.; Kheiri, S.; Desrosiers, D. Monkeypox: A Comprehensive Review of Transmission, Pathogenesis, and Manifestation. *Cureus* 2022, 14, e26531. Available online: <https://www.cureus.com/articles/100707-monkeypox-a-comprehensive-review-of-transmission-pathogenesis-and-manifestation> (accessed on 2 October 2023). [CrossRef]
- [62]. Moss, B. Poxvirus Cell Entry: How Many Proteins Does it Take? *Viruses* 2012, 4, 688–707. [Google Scholar] [CrossRef]
- [63]. Rampogu, S.; Kim, Y.; Kim, S.W.; Lee, K.W. An overview on monkeypox virus: Pathogenesis, transmission, host interaction and therapeutics. *Front. Cell Infect. Microbiol.* 2023, 13, 1076251. Available online: <https://www.frontiersin.org/articles/10.3389/fcimb.2023.1076251> (accessed on 2 October 2023). [CrossRef]
- [64]. Moss, B. Poxvirus DNA Replication. *Cold Spring Harb. Perspect. Biol.* 2013, 5, a010199. [Google Scholar] [CrossRef]
- [65]. Sklenovská N. Monkeypox Virus. In *Animal-Origin Viral Zoonoses*; Malik, Y.S.; Singh, R.K.; Dhama, K. (Eds.) *Livestock Diseases and Management*; Springer: Singapore, 2020; pp. 39–68. [Google Scholar] [CrossRef]
- [66]. Bray, M.; Buller, M. Looking Back at Smallpox. *Clin. Infect. Dis.* 2004, 38, 882–889. [Google Scholar] [CrossRef] [PubMed]
- [67]. Roberts, K.L.; Smith, G.L. Vaccinia virus morphogenesis and dissemination. *Trends Microbiol.* 2008, 16, 472–479. [Google Scholar] [CrossRef]
- [68]. Xiang, Y.; White, A. Monkeypox virus emerges from the shadow of its more infamous cousin: Family biology matters. *Emerg. Microbes Infect.* 2022, 11, 1768–1777. [Google Scholar] [CrossRef] [PubMed]
- [69]. Ježek, Z.; Szczeniowski, M.; Paluku, K.M.; Mutombo, M. Human Monkeypox: Clinical Features of 282 Patients. *J. Infect. Dis.* 1987, 156, 293–298. [Google Scholar] [CrossRef]
- [70]. Weinstein, R.A.; Nalca, A.; Rimoin, A.W.; Bavari, S.; Whitehouse, C.A. Reemergence of Monkeypox: Prevalence, Diagnostics, and Countermeasures. *Clin. Infect. Dis.* 2005, 41, 1765–1771. [Google Scholar] [CrossRef]
- [71]. Mitjà, O.; Ogoina, D.; Titanji, B.K.; Galvan, C.; Muyembe, J.J.; Marks, M.; Orkin, C.M. Monkeypox. *Lancet* 2023, 401, 60–74. [Google Scholar] [CrossRef] [PubMed]
- [72]. McCollum, A.M.; Damon, I.K. Human Monkeypox. *Clin. Infect. Dis.* 2014, 58, 260–267. [Google Scholar] [CrossRef] [PubMed]
- [73]. Patrocinio-Jesus, R.; Peruzzo, F. Monkeypox Genital Lesions. *N. Engl. J. Med.* 2022, 387, 66. [Google Scholar] [CrossRef]
- [74]. Antinori, A.; Mazzotta, V.; Vita, S.; Carletti, F.; Tacconi, D.; Lapini, L.E.; D’Abramo, A.; Cicalini, S.; Lapa, D.; Pittalis, S.; et al. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. *Eurosurveillance* 2022, 27, 2200421. [Google Scholar] [CrossRef]
- [75]. Mbala, P.K.; Huggins, J.W.; Riu-Rovira, T.; Ahuka, S.M.; Mulembakani, P.; Rimoin, A.W.; Martin, J.W.; Muyembe, J.-J.T. Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo. *J. Infect. Dis.* 2017, 216, 824–828. [Google Scholar] [CrossRef]
- [76]. Dashraath, P.; Nielsen-Saines, K.; Rimoin, A.; Mattar, C.N.Z.; Panchaud, A.; Baud, D. Monkeypox in pregnancy: Virology, clinical presentation, and obstetric

- management. *Am. J. Obstet. Gynecol.* 2022, 227, 849–861.e7. [Google Scholar] [CrossRef] [PubMed]
- [77]. Satapathy, P.; Mohanty, P.; Manna, S.; Shamim, M.A.; Rao, P.P.; Aggarwal, A.K.; Khubchandani, J.; Mohanty, A.; Nowrouzi-Kia, B.; Chattu, V.K.; et al. Potentially Asymptomatic Infection of Monkeypox Virus: A Systematic Review and Meta-Analysis. *Vaccines* 2022, 10, 2083. [Google Scholar] [CrossRef] [PubMed]