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Monkeypox Virus: From Origins to On-going Challenges - A Comprehensive Review

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A B S T R A C T

Monkeypox virus, a member of the Orthopoxvirus genus, has emerged as a significant public health concern, primarily within Central and West Africa. This comprehensive review navigates the complex landscape of Monkeypox, delving into its transmission, clinical presentation, diagnosis, treatment, epidemiology, prevention, and on-going research challenges. The review begins with an exploration of the virus's origins, virology, and mechanisms of transmission. It examines the diverse clinical manifestations of Monkeypox, ranging from mild flu-like symptoms to severe cases with extensive skin lesions, highlighting the importance of early diagnosis and differential diagnosis from similar diseases. Epidemiologically, Monkeypox exhibits sporadic outbreaks in endemic regions, with the risk of international spread, necessitating robust surveillance and preparedness efforts. Global collaboration and vaccination strategies are essential in controlling outbreaks and preventing widespread dissemination. Lastly, the article underscores the significance of on-going research in understanding the virus's genetic diversity, host factors influencing susceptibility, and the development of effective Monkeypox vaccines and therapies. The need for a One Health approach, recognizing the interconnectedness of human, animal, and environmental health, is paramount in addressing this emerging infectious disease. In conclusion, this review encapsulates the multifaceted nature of Monkeypox and emphasizes the imperative of continued research, global vigilance, and preparedness to safeguard public health against emerging threats in an interconnected world.

Keywords: Monkeypox virus, Orthopoxvirus, Zoonotic transmission, Clinical presentation, Epidemiology, Emerging infectious disease, Global health

1. Introduction:

Monkeypox was named as this virus forms pox like lesions on skin and was identified from macaque monkeys in 1958(Arita and Henderson 1968). It belongs to poxviridae family, *genus orthopox*, dsDNA, enveloped pleomorphic (brick shaped) virus. It's first human case was reported in 1970 in Democratic Republic of the Congo (DRC)(Tomori and Ogoina 2022). First case was reported of 9 months-old baby, noted signs of monkeypox virus like vesicular rashes on skin which later on developed into crusts and baby recovered within 14 days but on secondary infection this patient died in hospital(Aden, Zaheer et al. 2023). On May 23, 2003 a 3-year-old girl was found infected after being bitten by Prairie dogs. She bought this from animal shop. Animal was ill and died after biting girl within 2 days. Its submandibular lymph nodes were swollen and their sample was submitted to Marshfield Wisconsin laboratories for diagnosis(Reed, Melski et al. 2004). On May 24, 2003 Wisconsin division of Public Health department was reported with the case of 3 year old baby girl. On May 26, 2003 her mother becomes ill. On June 2, 2003 Wisconsin's Marshfield laboratory received case report of her mother.

She died on June 4, 2003 as it was confirmed from her serum sample that she had MPXV, prairie dogs were imported from Ghana. The most largest outbreak of MPV was noted in 2017 in Nigeria(Awadi, Al-Shami et al. 2023). On the basis of phylogenetic it has two different types of clades like Central African clade and West African clade. Central African clade is more disease causative as compared to West African clade, while fatality rate is 10.6% and 3.6% respectively(Velavan and Meyer 2022). Milwaukee health department (MHP) received a case of meat inspector and reported to (DPH).He was bitten by prairie dog March 23, developed clinical signs May 18 later on he died on June 2. Secretary of health department of United States Tommy G. Thompson ordered to ban on the trading of prairie dogs. On July 30, 2003 ≈70 identified cases reported in Wisconsin Indiana. In 1996 almost 72 cases of MPV reported from Zaire village of Africa(Sale, Melski et al. 2006). In 1997 Zairian Ministry of health department team lived in this village for diagnosis purpose and they reported that approximately 88 people infected from diseased people. Afterwards in 2018 it's outbreak was reported in United

Kingdom and patient exposed that he had travelled from Nigeria. While on the other hand a similar case came into view that a person in Israel become infected with this disease who had travelled from Nigeria. Nigerian travellers visited to Singapore and fell victim of MPV on May 19, 2019. WHO reported the 25047 cases of MPV outside Africa on August 2nd, 2022.

Monkeypox virus is a member of the Orthopoxvirus genus, which also includes Variola virus (the causative agent of smallpox) and Vaccinia virus (used in smallpox vaccination)(Cheema, Ogedegbe et al. 2022). It is a zoonotic virus, meaning it can be transmitted from animals to humans. Its natural reservoir is believed to be rodents, and sporadic outbreaks in humans occur primarily through contact with infected animals(Simpson, Heymann et al. 2020). Monkeypox can also be transmitted from person to person, leading to human-to-human outbreaks. This is of concern due to the potential for larger-scale transmission. Monkeypox manifests with symptoms similar to smallpox, including fever, rash, and pustules. While it is generally less severe than smallpox, it can still cause significant illness and complications. The virus is mainly found in Central and West Africa, but cases outside of this region have been reported, raising concerns about potential global spread. Monkeypox has gained attention as an emerging infectious disease. Recent outbreaks and cases beyond its historical range suggest changing dynamics(Yinka-Ogunleye, Aruna et al. 2019). Understanding its transmission, treatment, and epidemiology is crucial for preparedness. In an increasingly interconnected world, infectious diseases can spread rapidly. The COVID-19 pandemic has underscored the importance of understanding and managing novel pathogens(Shafqat, Rehman et al. 2022). Monkeypox has the potential to become a global health concern if not properly addressed. The development of effective vaccines against Monkeypox virus is an active area of research. Health systems worldwide need to be prepared to identify, diagnose, and manage Monkeypox cases. There may be recent developments in Monkeypox research, such as genetic sequencing and molecular studies, which can shed light on the virus's evolution and behavior.

2. Outbreaks

First outbreak of MPV was reported in Democratic republic of Congo (DRC) in 1970s, first zoonotic case was confirmed in United State of America (U.S. the case fertility rate was 11% in DRC. It's prevalence was at high level during July 3, 2003 to June 22, 2003. First human outbreak was documented in 2003. While it was reported in February 1996 to 1997 including approximately 6 mortalities. MPV re-emerged in 2017 with 500 suspected cases reported in Nigeria. In United Kingdom (2018-2019) people fell victim of MPV developing skin rashes and pitted scars(Guarner, Del Rio et al. 2022). Prevalence depends upon on travelling history and mostly African states fell victims of MPV due to travelling from Nigeria. In 2021 few cases of MPXV were identified in United States. On May 4, 2022 a person travelled from Nigeria to UK and fell ill. On diagnosis PCR revealed that he has exposed to MPV.MPV has spread in 2022 in ≈49 different countries and six continents and majorly effected countries are England, Germany, Spain and Portugal etc(Rakshit, Meena et al. 2021). Congo basin clade is involved in wide range of mortality and morbidity in western hemisphere. On 12 July 2022 no case fatality of MPV reported in non-infected areas. WHO announced the risk level of MPV in European regions that could be more than ≈79% with new MPV infections globally.

Year	**Cases/Outbreaks**	**References**
1958	MPV identified from macaque monkeys in Denmark	(Begum, Ngangom et al. 2023)
1970	First human case reported in DRC	(Kumar, Singh et al. 2022)
1996-97	MPV outbreak in DRC	(Di Giulio and Eckburg 2004)
2003	Outbreak in US 71 cases no mortality	(Bunge, Hoet et al. 2022)
2017	Re-emergence in Nigeria	(Fowotade, Fasuyi et al. 2018)
2018-19	United Kingdom, DRC and Nigerian confirmed MPV cases	(Karama, Akinola et al. 2023)
2019-2021	Reported in Israel	(Kannan, Ali et al. 2022)
July 14,2021	200 cases reported in united states	(Kumar, Acharya et al. 2022)
May 2022	Outside of Africa reported 25047 cases	(Joshi, Loshali et al. 2022)
May13-21,2022	Cases reported in U.K, Asia, American states etc.	

3. Host

As it is above mentioned that first documented case was reported from animal to human transmission was due to Macaque monkeys. MPXV is mainly transmitted by Prairie dogs and other small rodents that were imported from Ghana. Non-human primates are involved mostly and are reported. MPXV was isolated from dead sooty mangabey monkey(Hutson, Lee et al. 2007). Another case was reported that Chimpanzee had biten baby girl and she fell

ill and developed clinical signs of MPXV. Apes and monkeys are involved in transmission of MPXV to human beings. Reservoir host are small rodents mainly rope squirrels of Africa are thought to be natural reservoir of MPXV. Incidental host are pet animals like dogs. Different types of African rodents species are involved in transmission of MPXV(Domán, Fehér et al. 2022). Following species are involved in MPXV spread.

Name of host reservoir	
Gambian giant rats (*cricetomys spp)*	Dead sooty mangabey monkey
Rope Squirrels (*Funiscurius spp)*	Colobus monkeys
Cynomolgus monkeys	Zambian baboons
Prairie dogs	Chimpanzees
Wild shrew	Tree squirrels (*Heliosciurus spp)*
Pigs	Dormice (*Graphiusrus spp)*
Chinchillas *(Chinchilla lanigera)*	Jerboa *(Jaculus spp)*

4. Risk factors

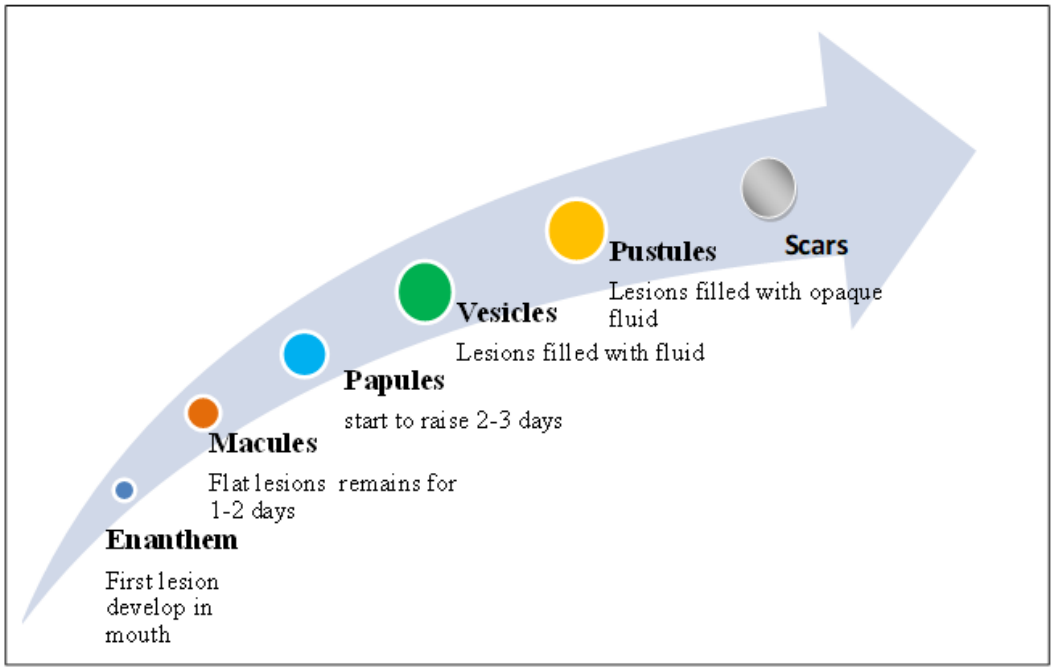
Direct transmission Human to human being was mostly due to females that were not vaccinated against small pox and were involved in taking care of primary cases of MPXV patients. This was due to clade I (Congo basin clade) in democratic republic of Congo (DRC)(Saied, Dhawan et al. 2022). Most important factor is age it is in documented record that mostly children were infected in early outbreaks and after that people of age under 21-40 were infected by clade II (West African clade). Hospital workers and other patients are susceptible to MPXV as it can transits through aerosol droplets while its transmission also depend upon hygienic conditions of hospital, patient room and bedding of patient might cause infection(Organization 2022).

5. Transmission

It is transmitted by mainly small rodents, mice, rats. There are different routes of transmission of MPXV. Direct contact with infected, dead or sick animals like pet i.e. prairie dogs, monkeys etc. and with infected individual can cause viral spread from animals to human beings(Falendysz, Lopera et al. 2015). Moreover hunting and catching bush meat for food lead to close contact with rodents. Indirect contact i.e. respiratory droplets, eating incomplete cocked food can lead to infection. Moreover direct contact to infected person's blood bodily fluid while ocular discharge of prairie dogs transmits MPXV. Skin to skin contact with infected individual mainly involve in viral spread. It can also be transmitted by sexual contact mostly men sex with men (MSM)(Wang and Lun 2023). Mucocutaneous and aerosol droplets are main routes of viral load transmission. Person to person transmission is mainly noticed and mostly it can be transmitted by close contact with infected person's bedding, cloths, towel etc. MPXV is spread widely through MSM in 2022(Pan, Nazareth et al. 2023). Travelling from Nigeria to other non-endemic countries is also part of viral spread. Nosocomial and vertical transmission is also noticed and is also cause of transmission. However a case study revealed that four pregnant women were found infected with MPXV only one give birth to child with lesions on skin rest undergone miscarriage(Dashraath, Nielsen-Saines et al. 2022). It is very important to discuss that reverse spill over from human to dog transmission was documented first time in the 2022 outbreak of monkey pox. Some cases reported from outside of Africa, which were resulted travelling from infected areas. As WHO reported first travelled case of MPXV on May 7, 2022 has travelling history from Nigeria in April. Another reported case from London indicated that he also travelled from Nigeria. Sometimes it can be transmitted by trying on clothing in shopping malls (low risk level). Health workers who handle bedding and clothing of MPXV patient in hospital might get infection. With infected person sexual intercourse (Semen, or vaginal fluids) can cause infection(Altindis, Puca et al. 2022).

6. Clinical features

Normally incubation period of MPXV is 5-13 days and can last up to ≈21 days. It is self-limiting disease in most or mild cases. When MPXV infect individuals it can leads to High fever, chills, backaches, shortness of breath, back pain, Lymphadenopathy, Nasal congestions, fatigue, sore throat, severe headache(Bothra, Maheswari et al. 2021). Vesicular rashes appear on skin within initial 3 three days of viral infection later on it develops in macules, papules, vesicles, pustules and crusts. Children are more susceptible to this disease. Other complication in its severe form is loss of vision (ocular scarring) infect cornea. Lower trunk areas mainly genital or anus (rashes) develops on hands, feet chest etc(Rasizadeh, Shamekh et al. 2023). However viral transmission accompanied by animal bite. T.cells mediated cytokine response decreased almost 80% even the very low viral load of monkeypox. It can causes mouth, throat ulcers as a result impaired eating for individuals and corneal scarring result in visual loss. It is self-limiting viral infection and sometimes noted long lasting effects. It leads to enteric disturbance like gastrointestinal tract disturbance which result in diarrhoea, vomiting(Domán, Fehér et al. 2022).



Variability in Clinical Manifestations

The clinical presentation of Monkeypox can vary widely from person to person, and some individuals may exhibit atypical or milder symptoms. This variability can include:

i. Mild Disease: In some cases, Monkeypox infection can be relatively mild, resembling a common viral illness with mild fever and a limited rash. These cases often go undiagnosed or misdiagnosed(Harvala and Simmonds 2022).

ii. Severe Disease: Conversely, severe cases can occur, particularly in immuno-compromised individuals. These severe cases may involve extensive rash, organ involvement, and a higher risk of complications. Younger individuals, particularly children and adolescents, tend to have milder forms of the disease compared to adults (Nasir, Fatma et al. 2022).

Severity and Complications

While Monkeypox is generally considered less severe than smallpox, it can still lead to significant complications, especially in severe cases. Complications may include:

i. Secondary Bacterial Infections: Pustules from the rash can become secondarily infected with bacteria, leading to cellulitis or abscess formation(Adnyana 2023).

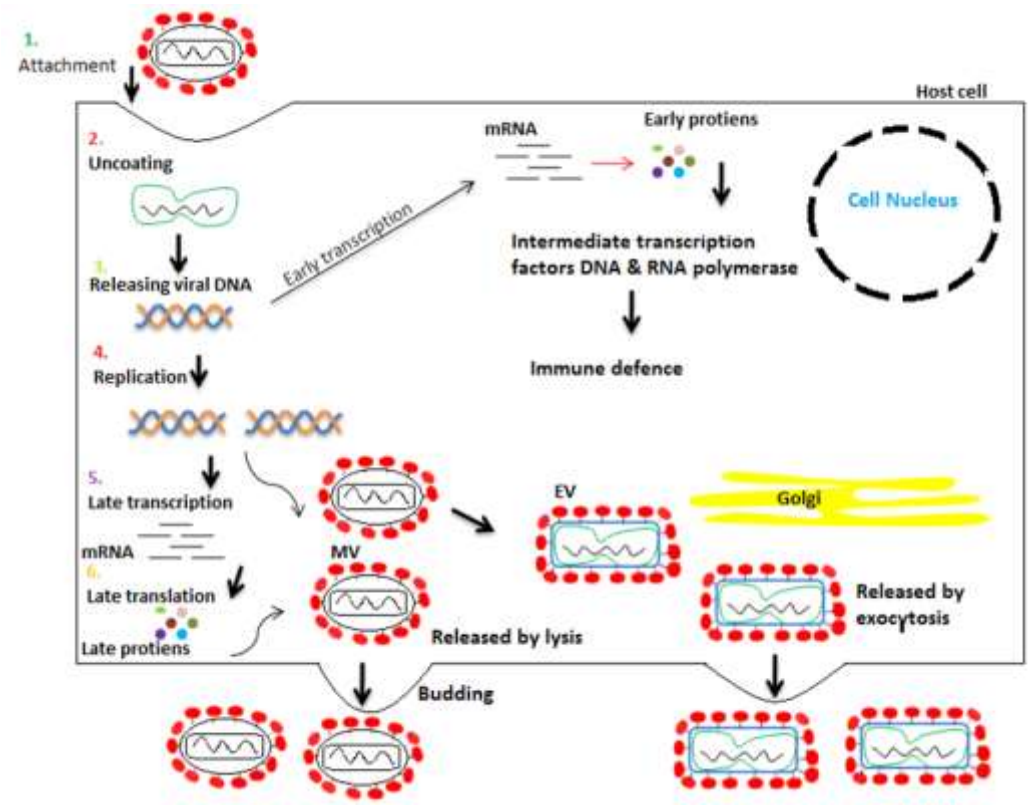
ii. Scarring: The healing of pustules can result in scarring, which can be disfiguring, especially if the face is affected(Chowdhury, Datta et al. 2022).

iii. Eye Involvement: In some cases, the eyes may become involved, leading to conjunctivitis or corneal lesions, which can affect vision.

iv. Pneumonia: Severe cases of Monkeypox can lead to pneumonia, which can be life-threatening(Rebora 2005).

7. Replication

It is observed that MPXV infects the host cell through endosomal pathway or direct fusion. To get entry into host cell viral proteins play role to attach with glycosaminoglycan receptors of host cell. For endosomal pathway entry to target cell pH should low while for direct fusion at plasma membrane pH of target cell should neutral(Rebora 2005). As it gets entry into host cell it's early and transcription is mediated by DNA dependent RNA polymerase after that translation takes place and early and late proteins are formed on the host cell's ribosome. Double stranded DNA is synthesized into cytoplasm and is wrapped by endoplasmic reticulum(Sivan, Weisberg et al. 2016). After that virions assembled and immature viruses retained inside of target cell and released by budding. While on the other hand mature virions get envelope from Golgi complex and released from the cell by exocytosis(Moss 2013).



Mechanisms of Viral Entry and Replication:

1. Attachment and Entry: Monkeypox virus attaches to specific receptors on the surface of host cells, initiating entry. The virus enters the host cell by membrane fusion, allowing it to deliver its genetic material into the host cell's cytoplasm(Aljabali, Obeid et al. 2022).
2. Replication: Once inside the host cell, the virus replicates its DNA and produces viral proteins. It forms viral factories where DNA replication and protein synthesis occur. These factories are essential for generating new viral particles(Harrison, Alberts et al. 2004).
3. Assembly and Release: New virus particles are assembled in the cytoplasm, and they acquire an outer envelope as they bud through the host cell membrane. This process ultimately leads to the release of infectious virions, which can go on to infect other cells (Du Plessis, Maya et al. 2022).

Immune Response and Pathophysiology

When Monkeypox virus enters the body, the innate immune system recognizes it as foreign. Immune cells such as macrophages and dendritic cells play a role in initiating the immune response. The adaptive immune system, including T cells and B cells, responds to the infection by producing specific antibodies and cytotoxic T cells. These components are critical for controlling the virus(Saghazadeh and Rezaei 2022). Monkeypox virus causes a range of clinical manifestations in infected individuals. The virus can disseminate throughout the body, leading to fever, rash, and the formation of pustules. The severity of disease can vary from mild to severe, with some cases resulting in death, particularly in immuno-compromised individuals(Huang, Howard‐Jones et al. 2022). Monkeypox virus employs various strategies to evade the host immune response, such as inhibiting interferon production and interfering with host cell signalling pathways. These mechanisms contribute to the virus's ability to establish infection and cause disease.

Death: While fatalities are relatively rare, severe Monkeypox infections can be fatal, particularly in individuals with weakened immune systems. It's important to note that the clinical presentation of Monkeypox can mimic other viral infections or skin conditions(Diven 2001),

8. Pathogenesis

It gets entry through respiratory or oral pathways by aerosol inhalation. It infects upper respiratory tract during its primary infection no signs and symptoms develops. MPXV moves towards nearby tissues where immune cells are present, it continues spreading containing antigen-presenting cells like B.cells, dendritic cells, and macrophages(Beeson, Styczynski et al. 2023). On the secondary infection it infects lymph nodes indicating viral infection in lymphoid tissues of neck and throat. This evidence was come into view when a study was conduct on cynomolgus macaque which was infected by aerosol transmission of MPXV and was observed after incubation days of MPXV which showed that viral dissemination takes place into mandibular and neck regions lymph nodes where it replicates(Lum, Torres-Ruesta et al. 2022). In vitro study of nonhuman primates (NHPs) revealed that natural killer cells started accumulation in lymph nodes on the site of MPXV infection. After primary infection it is believed that secondary infection is mediated by infected cells that were infected during primary infection and after lymphoid tissues viral load spreads toward nearby organs like spleen, liver this was studied in

mousepox models(Reynolds 2016). There are different routes of entry of MPXV into its host first it spread in upper respiratory tract and after that on secondary infection proliferate in to systemic infection or infect organs like spleen, liver, lungs etc. It is evidence that to gets entry into blood and destroy blood cells and also infects a skin forming skin lesion which after procession becomes scars. It infect upper skin layer as there is no blood vessels and lymphatic vessels so dendritic cells like Langerhans are proliferated by viral load which is noted by T.cell response (cytotoxic T.cells)(Elsheikh, Makram et al. 2023). While in the upper respiratory infection lesions appear at tongue, trachea, esophagus etc. and it is released through saliva. It was observed that it relocates into lymphatic tissues during skin infection. It causes genital lesions and disseminate up to testies as it is tested and confirmed through semen of infected person. Natural killer cells were isolated from infected lymph nodes of infected model (mousepox) which indicated that they were unable to degranulation and also to secrete TNF (tumor necrotic factors)(Lazar 2022).

9. Diagnosis

Laboratory Methods for Detection:

i. Polymerase Chain Reaction (PCR): PCR is a highly sensitive and specific method for detecting Monkeypox virus genetic material (DNA). It can identify the virus in clinical samples, such as skin lesions, respiratory secretions, or blood. PCR is the most common and reliable diagnostic method(Hu, Wang et al. 2022).

ii. Virus Isolation: The virus can be isolated and grown in cell culture from clinical specimens. Isolation allows for further characterization of the virus and is essential for confirming the diagnosis definitively(Nakhaie, Arefinia et al. 2023).

iii. Serology: Serological tests detect antibodies produced by the immune system in response to Monkeypox infection. Enzyme-linked immuno sorbent assay (ELISA) and immunofluorescence assays are commonly used serological methods. However, serology may not be as reliable in the early stages of infection(Oliveira, Longhi et al. 2008).

iv. Immunohistochemistry: In cases where skin lesions are present, immunohistochemistry can be used to identify Monkeypox virus antigens in skin biopsy samples. This method is particularly useful for confirming the diagnosis when other tests are inconclusive(Nakhaie, Arefinia et al. 2023).

v. Electron Microscopy: Electron microscopy can visualize the virus particles directly in clinical specimens, although it is less commonly used than PCR or virus isolation due to its lower sensitivity(Curry, Appleton et al. 2006).

Differential Diagnosis from Other Similar Diseases:

Monkeypox shares clinical features with several other infectious diseases, which can complicate diagnosis. Differential diagnosis includes:

Smallpox	**Chickenpox (Varicella):**	**Herpes Simplex Virus (HSV) Infections**	**Impetigo**	**Other Viral Exanthemas**
Historically, Monkeypox was often mistaken for smallpox due to their similar clinical presentations. However, smallpox has been eradicated, so it is extremely rare. PCR and serological testing can distinguish between the two.	Chickenpox also presents with a vesicular rash, fever, and malaise. However, Monkeypox typically has a higher fever and more pronounced lymphadenopathy. Laboratory tests can differentiate between the two.	HSV infections can cause painful skin lesions, but they usually lack the severe systemic symptoms seen in Monkeypox. Laboratory testing for HSV can confirm the diagnosis.	Impetigo is a bacterial skin infection that can cause pustules similar in appearance to Monkeypox lesions. Bacterial culture can identify the causative organism.	Other viral infections, such as measles, rubella, and hand-foot-and-mouth disease, can produce rashes. Clinical and epidemiological factors, along with laboratory tests, can help differentiate these from Monkeypox.

Accurate diagnosis of Monkeypox is crucial to ensure appropriate patient care, isolate infected individuals, and implement public health measures to prevent further transmission. It often requires a combination of clinical assessment and laboratory testing, especially PCR for confirmation.

10. Treatment

Antiviral Therapies and Their Efficacy:

i. Cidofovir: Cidofovir is an antiviral medication that has shown some effectiveness against Monkeypox virus in vitro (in the laboratory) and in a limited number of clinical cases. It is administered intravenously and is considered one of the primary antiviral options for severe Monkeypox cases(Frenois-Veyrat, Gallardo et al. 2022).

ii. Brincidofovir: Brincidofovir is another antiviral drug that has shown promise against orthopoxviruses, including Monkeypox, in laboratory studies. It is administered orally and is being investigated as a potential treatment option(Khani, Afsharirad et al. 2023).

iii. Vaccinia Immune Globulin (VIG): VIG is a product derived from the blood plasma of individuals vaccinated against smallpox. It contains antibodies against orthopoxviruses and has been used in some Monkeypox cases, especially in severe or complicated infections. It's important to note that while these antiviral therapies have shown some efficacy, their use is often reserved for severe or complicated cases, and more research is needed to establish their effectiveness definitively. Additionally, antiviral treatment should ideally be initiated early in the course of the disease to be most effective(Fowotade, Fasuyi et al. 2018).

Supportive Care and Management of Symptoms:

i. Isolation and Infection Control: Infected individuals should be isolated to prevent further transmission. Infection control measures, such as proper hand hygiene and the use of personal protective equipment, are crucial for healthcare workers and caregivers.

ii. Fever Management: Fever is a common symptom in Monkeypox. Over-the-counter antipyretic medications (e.g., acetaminophen) can help reduce fever and alleviate discomfort(Roomi 2022).

iii. Pain Management: Pain from skin lesions and muscle aches can be managed with pain relievers, such as non-steroidal anti-inflammatory drugs (NSAIDs).

iv. Fluids and Nutrition: Maintaining proper hydration and nutrition is essential, especially in severe cases. Intravenous fluids may be necessary for individuals who are unable to maintain oral intake(Mansour, Houston et al. 2023).

v. Wound Care: Proper wound care and hygiene are crucial to prevent secondary bacterial infections. Lesions should be kept clean, and topical antibiotics may be used if there is evidence of infection. (Patel, Bilinska et al. 2022)

vi. Respiratory Support: In severe cases with respiratory involvement, such as pneumonia, oxygen therapy and mechanical ventilation may be required.

vii. Psychological Support: Individuals infected with Monkeypox may experience psychological distress due to the nature of the disease and its potential for complications. Providing emotional support and mental health resources is important(Dubey, Chakole et al. 2023).

It's important to emphasize that there is no specific, universally approved treatment for Monkeypox, and management largely focuses on supportive care to alleviate symptoms and prevent complications. Early detection, isolation, and appropriate infection control measures play a critical role in managing Monkeypox outbreaks and reducing its impact on affected individuals and communities.

11. Prevention and Control

Vaccination Strategies:

Historically, the smallpox vaccine (vaccinia virus vaccine) has shown cross-protective immunity against Monkeypox. Individuals previously vaccinated against smallpox may have some level of protection against Monkeypox. However, routine smallpox vaccination was discontinued after the eradication of smallpox, and the vaccine is no longer widely available(Poland, Kennedy et al. 2022). Several Monkeypox vaccine candidates have been developed and tested in recent years. These include live attenuated vaccines and subunit vaccines. These vaccines aim to provide specific protection against Monkeypox and are under evaluation for their safety and efficacy(Saadh, Ghadimkhani et al. 2023). Some are intended for use in outbreak settings or for individuals at high risk of exposure, such as healthcare workers.

Public Health Measures:

1. Surveillance: Early detection of Monkeypox cases is crucial for outbreak control. Surveillance systems should be in place to monitor for suspected cases, conduct laboratory testing, and investigate contacts of infected individuals(Martínez, Montalbán et al. 2022).
2. Isolation and Quarantine: Infected individuals should be isolated to prevent further transmission. Close contacts may be quarantined and monitored for signs of illness.
3. Contact Tracing: Identifying and monitoring individuals who have had close contact with confirmed cases is essential. Contact tracing helps identify potential secondary cases and limit the spread of the virus(Organization 2022).
4. Infection Control: Healthcare facilities should implement strict infection control measures, including isolation of suspected cases, appropriate personal protective equipment (PPE) for healthcare workers, and proper disposal of contaminated materials.
5. Public Education: Public health authorities should provide education and awareness campaigns to inform the public about Monkeypox, its transmission, and preventive measures such as hand hygiene and avoiding contact with wildlife(Jairoun, Al-Hemyari et al. 2022).
6. Travel Advisories: During outbreaks, travel advisories may be issued for affected regions to reduce the risk of disease spread to other areas.

Global Efforts to Control Outbreaks:

i. International Collaboration: Global health organizations like the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) work with affected countries to provide technical assistance, resources, and expertise in outbreak response(Tappero, Cassell et al. 2017).

ii. Vaccine Stockpiles: Some countries maintain stockpiles of smallpox vaccine for emergency use. These vaccines can be deployed in the event of Monkeypox outbreaks, as they may provide partial immunity(Grosenbach, Jordan et al. 2011).

iii. Research and Development: Ongoing research efforts focus on developing more effective Monkeypox vaccines, antiviral therapies, and diagnostic tools. International collaboration supports these efforts(Torreele, Boum et al. 2023).

iv. Capacity Building: Building local healthcare capacity in affected regions is crucial for rapid response to outbreaks. This includes training healthcare workers, improving laboratory facilities, and enhancing surveillance systems(Ibrahim 2020).

v. One Health Approach: Given the zoonotic nature of Monkeypox, a One Health approach is important, involving collaboration between human health, animal health, and environmental experts to identify and mitigate the risk of transmission from animals to humans(Reynolds, Doty et al. 2019).

vi. Preventing and controlling Monkeypox outbreaks require a multifaceted approach involving vaccination, public health measures, and global collaboration. Timely detection, isolation, and contact tracing, along with ongoing research and preparedness, are key to reducing the impact of this infectious disease(Huggett, French et al. 2022).

12. Epidemiology

Monkeypox is considered a rare disease, with sporadic outbreaks occurring primarily in Central and West Africa. The exact incidence varies from year to year and region to region, but it is generally low. Human cases have also been reported outside of Africa, including in the United States and the United Kingdom, often linked to travelers returning from affected regions. Monkeypox is not endemic worldwide(Bunge, Hoet et al. 2022). Its prevalence is mainly confined to specific regions within Central and West Africa, where it is considered an endemic disease. The first recognized human case of Monkeypox occurred in the Democratic Republic of the Congo (DRC) in 1970. Subsequent outbreaks in the 1970s and 1980s in various African countries highlighted the virus's presence and impact in the region(Rahimi, Afaghi et al. 2022). In 2003, the United States experienced its largest Monkeypox outbreak. It was linked to the importation of infected rodents from Africa, leading to cases in several states. Fortunately, there were no deaths, but the outbreak raised concerns about the potential for Monkeypox to spread beyond Africa. Nigeria has experienced multiple Monkeypox outbreaks. The 2017 outbreak involved several states, and over 100 suspected cases were reported. While no deaths were reported, the outbreak underscored the need for surveillance and control measures in endemic areas(Reed, Melski et al. 2004).

Geographical Distribution and Risk Factors:

i. Endemic Regions: Monkeypox is endemic in certain forested regions of Central and West Africa, including Nigeria, Cameroon, the Central African Republic, and the Democratic Republic of the Congo. Within these countries, specific regions with dense forest cover are more prone to Monkeypox transmission(Reynolds, Doty et al. 2019).

ii. Zoonotic Transmission: The virus is believed to circulate among animal populations, particularly rodents, which serve as reservoirs. Activities such as hunting and consumption of bush meat are considered risk factors for zoonotic transmission(Guagliardo, Monroe et al. 2020).

iii. Human-to-Human Transmission: Close contact with infected individuals, especially during caregiving, is a significant risk factor for human-to-human transmission. Crowded living conditions and limited access to healthcare facilities can facilitate the spread of the virus within communities.

iv. Vaccination Status: Prior smallpox vaccination may offer some cross-protection against Monkeypox, but this protection wanes over time. Unvaccinated or immuno-compromised individuals are at higher risk of severe disease(Weese and Fulford 2011).

v. International Travel: Travellers to endemic regions are at risk of acquiring Monkeypox, especially if they have close contact with animals or individuals with the disease. Importation of the virus to non-endemic regions has occurred, leading to localized outbreaks. Understanding the epidemiology of Monkeypox is essential for implementing effective prevention, surveillance, and control measures. Efforts to reduce zoonotic transmission, improve healthcare infrastructure, and enhance public awareness are critical in regions where Monkeypox is endemic. Additionally, global vigilance is necessary to detect and respond to cases in non-endemic areas to prevent further spread(Uwishema, Adekunbi et al. 2022).

13. Challenges and Future Directions

On-going Research and Gaps in Knowledge:

1. Genomic Studies: Ongoing research aims to understand the genetic diversity and evolution of Monkeypox virus strains. This includes studying how the virus adapts to different hosts and environments(Zhan, Zha et al. 2023).

2. Host Susceptibility: Gaps exist in our understanding of why some individuals develop severe Monkeypox while others experience milder cases. Research is needed to investigate host factors influencing susceptibility and immune response(Lum, Torres-Ruesta et al. 2022).
3. Vaccine Development: Although progress has been made in Monkeypox vaccine development, further research is required to refine vaccine candidates, assess their safety and efficacy, and determine the most suitable vaccination strategies(Saadh, Ghadimkhani et al. 2023).
4. Treatment Options: Research into antiviral therapies for Monkeypox continues, with a focus on identifying effective drugs and improving treatment protocols. Developing therapies that can be administered orally or topically would be valuable(Russo, Grosenbach et al. 2021).
5. Transmission Dynamics: A better understanding of how Monkeypox virus spreads within communities, including human-to-human transmission patterns, can inform control measures and outbreak response strategies(Beer and Rao 2019).

Emerging Trends in Monkeypox Virus Research:

Research increasingly emphasizes the importance of a One Health approach, recognizing the interconnectedness of human, animal, and environmental health. This approach is essential for understanding zoonotic diseases like Monkeypox. Genomic sequencing of Monkeypox virus strains is becoming more accessible and affordable, enabling researchers to track genetic changes and their implications for transmission and virulence(Giovanetti, Cella et al. 2023). Studies are focusing on the intricate interactions between Monkeypox virus and host cells, shedding light on the mechanisms of infection, immune evasion, and pathogenesis. Research on the animal reservoirs of Monkeypox is critical to identify potential spill over risks and develop targeted prevention strategies(Chadha, Khullar et al. 2022).

Potential Threats and Preparedness:

The potential for Monkeypox to spread globally is a concern, particularly given international travel and trade. Preparedness plans must be in place to rapidly detect and respond to cases in non-endemic regions. Ensuring equitable access to Monkeypox vaccines, once they are available and proven effective, is essential to protect vulnerable populations in endemic regions and prevent global transmission(Nuzzo, Borio et al. 2022). Strengthening surveillance systems, enhancing reporting mechanisms, and training healthcare workers to recognize Monkeypox are vital for early case detection and outbreak response. Building local healthcare capacity in endemic regions is crucial for effective case management, infection control, and community engagement during outbreaks(Durski, McCollum et al. 2018). International collaboration and information sharing are key in Monkeypox research and preparedness efforts. This includes sharing data on outbreaks, genetic sequences, and research findings. Monkeypox remains a complex and evolving public health challenge. Ongoing research, international cooperation, and proactive preparedness measures are essential for effectively addressing the potential threats posed by Monkeypox virus and protecting global health(Giovanetti, Cella et al. 2023).

14. Conclusion

Monkeypox virus is an emerging infectious disease primarily found in Central and West Africa. Monkeypox is an Orthopoxvirus that can infect both animals and humans. It is transmitted through zoonotic and human-to-human routes. Monkeypox leads to a range of symptoms, from fever and rash to more severe cases with complications like pneumonia and eye involvement. Diagnosis involves laboratory methods such as PCR and serology, with a focus on differential diagnosis from similar diseases. There is no specific antiviral treatment, so management centers on supportive care and symptom relief. Strategies include vaccination, public health measures, and international collaboration to manage outbreaks and prevent global spread. Monkeypox incidence is low but concentrated in endemic regions, with potential for global transmission, necessitating surveillance and preparedness. On-going research aims to address gaps in knowledge, understand virus-host interactions, and develop effective vaccines and treatments. Preparedness efforts are vital to address potential threats. In conclusion, the study of Monkeypox virus underscores the importance of continued research, global cooperation, and vigilance to protect public health and respond effectively to emerging infectious diseases in an interconnected world.

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