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Review Article

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Review on Recent Updates of Monkey Pox: Role of Diabetes Mellitus ?

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1. Overview

In May 2022, the World Health Organization (WHO) reported an outbreak of human monkeypox affecting multiple countries [1]. As of September 21, 2022, there have been a total of 64,290 confirmed monkeypox cases reported across 106 countries worldwide, with 20 deaths attributed to the disease since the outbreak began [2]. The rapid spread of the outbreak has increased public anxiety about the possibility of another viral pandemic and a significant public health threat [3].

Monkeypox (MPX) is a newly emerging zoonotic disease caused by the monkeypox virus (MPXV), which belongs to the Orthopoxvirus genus within the Poxviridae family. MPXV is one of four Orthopoxvirus species that can infect humans. The others are the variola virus, which causes smallpox and has been eradicated; cowpox virus; and vaccinia virus. Smallpox, characterized by a 30% case fatality rate (CFR) and high virulence, is regarded as one of the most dreaded diseases in human history.

Monkeypox virus (MPXV) is highly pathogenic and produces clinical symptoms similar to those of smallpox [4,5]. Smallpox vaccination is known to offer cross-immunity, providing up to 85% protection against infection or lessening the severity of the disease [6-11]. Monkeypox can affect a diverse array of mammalian species, but the natural host of the virus remains unidentified [12]. Monkeypox presents with clinical features similar to smallpox, but a key difference is the early onset of lymph node enlargement, which often occurs at the start of the fever [13]. Patients may experience various complications, such as secondary bacterial infections, respiratory issues, bronchopneumonia, gastrointestinal problems, dehydration, sepsis, encephalitis, and corneal infections that can lead to vision loss [14].

2. History & Discovery

MPXV was initially identified during an outbreak in monkeys at a Danish laboratory in 1958 [15]. However, it wasn't identified as a human disease until 1970, when a nine-month-old child contracted it in the Democratic Republic of Congo (formerly Zaire) [15]. Monkeypox is commonly found in the tropical rainforests of the Congo Basin and West Africa with the Democratic Republic of Congo reporting the majority of cases annually predominantly affecting children under 10 years old [16-19]. Nigeria is among the West African countries that have previously reported monkeypox, with two human cases documented in 1971 and another in 1978 [21,22]. Other African countries where the disease has been reported include Côte d'Ivoire, Liberia, Sierra Leone, Gabon, Cameroon, the Republic of Congo, the Central African Republic, and South Sudan [20].

In 2003, the United States reported the first instance of monkeypox outside Africa, with 47 cases connected to wild animals imported into the country as part of the pet trade [21]. There is no specific treatment or vaccine for human monkeypox infections; however, prior smallpox vaccination has been found to provide a high level of cross-protection against monkeypox [23,24].

In 1971, two cases of monkeypox were reported, one involving a four-year-old child who had not been previously vaccinated against smallpox, followed by a third case in 1978. Following this, no additional cases were reported until September 2017, when Nigeria experienced a resurgence of monkeypox [25]. By December 2018, Nigeria had reported 132 confirmed and probable monkeypox cases, resulting in seven deaths and a case fatality rate of 5.3%. In September 2018, the United Kingdom confirmed two imported monkeypox cases. Following this, Israel reported one case in October 2018 and Singapore identified another case in May 2019, with all cases having travel connections to Nigeria. An additional case of monkeypox, which was transmitted within a healthcare setting, was recorded in the UK and was linked to the management of one of the cases imported from Nigeria [26].

3. Virology

3.1. Causative Agents

The monkeypox virus (MPXV), which is part of the **Orthopoxvirus**

genus within the **Poxviridae** family, is the organism responsible for causing monkeypox. The virus is mainly present in animals such as rodents and non-human primates, although it can also infect humans [26]. Monkeypox shares similarities with smallpox, though it is usually less severe.

The monkeypox virus exists in two primary clades:

3.1.1. The Congo Basin (Central African) Clade

This variant typically causes more severe illness and has a higher mortality rate.

3.1.2. The West African Clade

This variant is generally less severe and associated with a lower fatality rate [27].

MPXV can spread between humans through direct contact with lesions, bodily fluids, respiratory droplets, or contaminated items like bedding [28].

4. Transmission

The three primary routes of Mpox transmission are human-to-human, animal-to-human, and animal-to-animal [30]. The most frequent way for the virus to move from animals to humans is through direct contact with fluids and secretions from infected animals. Consequently, the rate of Mpox infection in humans is affected by the frequency of animal contacts. The presence of various sources of animal exposure makes it challenging to pinpoint the specific source of infection for an individual patient. Additionally, human-to-human transmission can occur through shared contaminated objects or living in close proximity to Mpox patients. Other methods of transmission include large respiratory droplets and direct contact [31]. During the 2022 outbreak, while monkeypox virus DNA is almost consistently present in skin samples, it is less frequently detected in other body parts and usually at lower viral loads. For instance, monkeypox virus DNA is found in only 60–70% of samples from the anus and throat, 50% of semen samples, and 20% of blood and urine samples. Investigations have also identified the Mpox virus in semen samples. Indeed, genital fluids, such as vaginal and seminal fluids, from infected individuals consistently contain the Mpox virus [32,33]. In some patients, Mpox virus DNA was found in seminal fluid even long after the onset of clinical symptoms [34]. Additionally, viable Mpox virus can be cultured from urethral and anal swabs taken from infected individuals [35].

Vertical transmission to the fetus can occur, potentially resulting in congenital monkeypox, though the risk associated with various stages of pregnancy remains undetermined [36]. Between 2007 and 2011, there were four pregnant women with monkeypox in the Democratic Republic of the Congo. One gave birth to a healthy infant, two experienced miscarriages, and one had a fetal death characterized by widespread maculopapular skin lesions, indicating potential vertical transmission [37]. During the 2022 outbreak, at least 12 pregnant women were infected, but vertical transmission was not observed in any of these cases. This difference may be partly due to the greater invasiveness of clade 1 compared to clade 2 [38].

Environmental contamination with monkeypox virus DNA has been reported in both the households and patient-care settings of individuals with monkeypox, including the detection of replication-competent virus samples [39-41]. Investigations in respiratory isolation rooms at a hospital detected viral DNA in various areas, including rooms, bathrooms, anterooms, health care workers' personal protective equipment, and non-touch surfaces (e.g., over 1.5 meters from the bed) [42]. It is uncertain whether indirect contact with fomites is a common transmission route; however, the extensive surface contamination in patient-care environments emphasizes the need for a systematic approach to surface cleaning and the proper use of personal protective equipment by health care workers.

Transmission risks can differ across various environments, including households, congregate settings, health care facilities, and the wider community. Prior to the 2022 outbreak, transmission primarily took place within households, and sustained human-to-human spread was uncommon. In contrast, household transmission has been infrequent during the 2022 outbreak, representing only 0.6–3.0% of cases which includes several pediatric cases and one neonatal infant who lived with an infected adult [43,46]. In 2022, most infections have been linked to community transmission, with an estimated reproductive number between 1.40 and 1.80, suggesting the potential for sustained local transmission [47]. Before May 2022, health care-associated transmission of monkeypox had been reported in a dozen cases in Africa and in one case outside endemic areas [48,49]. During the 2022 outbreak, the risk of transmission has been low, with only a few transmission events reported following exposure to fomites or needlestick injuries. Subclinical or asymptomatic monkeypox infections are considered rare. However, seroepidemiological studies in Africa and retrospective PCR detection among male attendees at sexual health clinics in France and Belgium indicate that some individuals may have asymptomatic infections. Additionally, modeling studies suggest that during the 2022 outbreak, roughly half of the transmissions occurred in the pre-symptomatic phase [50,51].

5. Epidemiology

5.1. Geographical Distribution of Monkeypox

Monkeypox is a viral zoonotic disease caused by the monkeypox virus, a member of the Orthopoxvirus genus. Initially identified in 1970, the disease has primarily been endemic to Central and West Africa. However, in recent years, monkeypox has emerged in non-endemic regions, raising global health concerns. Understanding the geographical distribution of monkeypox is essential for effective public health responses [52].

6. Endemic Regions

6.1. Central Africa

• Democratic Republic of the Congo (DRC): The DRC is the

epicenter of monkeypox, reporting the highest incidence of cases. Outbreaks often occur in rural areas where human contact with wildlife is more common. A study by Kaltcheva et al. (2021) highlighted that the DRC accounts for the majority of cases reported since the virus was first identified, particularly in provinces like Équateur and Tshuapa.

• Republic of the Congo: This region has also reported endemic cases. A significant outbreak was documented in 2017, with links to animal reservoirs being a key factor in transmission.

6.2. West Africa

• Nigeria: Since 2017, Nigeria has seen several outbreaks, marking a shift in monkeypox's geographical reach. The 2022 outbreak was particularly significant, with over 200 confirmed cases reported. Studies like those by Adesola et al. (2022) have analyzed transmission dynamics and public health responses in this region.

• Ghana and Cameroon: Both countries have reported sporadic cases linked to wildlife interactions. In 2021, Ghana reported its first confirmed cases in a decade, underscoring the ongoing risk in West Africa.

7. Historical Context

Monkeypox was initially recognized in humans in the DRC in 1970, with the first recorded case outside Africa occurring in the U.S. in 2003, linked to imported animals. Until recently, cases outside Africa were rare, primarily involving travelers to endemic areas or contact with infected animals [53].

8. Recent Global Outbreaks

In 2022 and 2023, monkeypox cases surged in non-endemic countries, leading to significant public health interventions.

9. North America

• United States: The first U.S. case in 2022 was reported in Massachusetts. Subsequent cases spread rapidly across the country, often among networks of men who have sex with men, prompting a re-evaluation of risk factors and prevention strategies (CDC, 2022).

• Canada: Canada reported cases in conjunction with the U.S. outbreak. Public health authorities implemented vaccination programs targeting high-risk populations [54].

10. Europe

United Kingdom: The UK reported its first cluster of cases in May 2022. Health authorities noted a connection to sexual networks, which highlighted the need for targeted communication strategies regarding transmission (UKHSA, 2022).

Spain and Portugal: Both countries experienced significant outbreaks, with health agencies monitoring transmission patterns and implementing vaccination campaigns [55].

11. Asia and Australia

• Australia: A limited number of cases were reported in 2022, primarily associated with travel. Public health measures were enhanced to monitor and contain potential outbreaks.

• Other Asian Countries: Cases have been rare but reported sporadically, prompting health officials to strengthen surveillance and preparedness.

12. Transmission Dynamics

12.1. Monkeypox Primarily Spreads Through

• Direct Contact: Close physical contact with infected individuals, including skin lesions and respiratory droplets.

• Animal Reservoirs: The virus is zoonotic, and animal reservoirs include rodents and primates. The WHO (2022) notes that human infections can result from contact with infected animals or their bodily fluids.

• Contaminated Materials: The virus can survive on surfaces, increasing transmission risk in communal settings.

13. Public Health Responses

13.1. In Response to the Increased Incidence of Monkeypox

• Surveillance and Reporting: Enhanced surveillance systems have been established globally to quickly identify and report cases, including contact tracing.

• Vaccination: The use of smallpox vaccines, such as ACAM2000 and JYNNEOS, has been recommended for high-risk populations to curb outbreaks. The CDC and WHO have advocated for vaccination strategies focusing on close contacts of confirmed cases.

• Public Awareness Campaigns: Health authorities are actively disseminating information regarding symptoms, transmission, and preventive measures to mitigate the spread [56].

• Outbreaks and Cases of Monkeypox

14. Notable Outbreaks

13.1. 2003 U.S. Outbreak

• Location: Midwestern United States (Illinois, Indiana, Wisconsin).

• Cases: 47 confirmed cases were reported, linked to exposure to pet prairie dogs that had been infected by imported rodents.

• Response: The outbreak prompted health officials to educate the public about transmission risks and safe handling of animals [57].

13.2. 2017 Nigeria Outbreak

• Location: Multiple states in Nigeria, including Akwa Ibom and Cross River.

• Cases: Over 200 suspected cases were reported, with 63 confirmed cases. This outbreak marked the first resurgence of monkeypox in Nigeria in nearly 40 years.

• Research: Studies conducted by Adesina et al. (2018) documented the epidemiological trends and highlighted the need for improved surveillance [58].

13.3. 2022 Global Outbreak

• Initial Cases: In May 2022, cases began appearing in non-endemic countries, particularly in Europe, North America, and Australia.

• Location: Significant clusters were reported in the UK, Spain, Portugal, Canada, and the United States.

• Cases: By mid-August 2022, over 35,000 confirmed cases had been reported globally across more than 70 countries. The WHO

declared monkeypox a Public Health Emergency of International Concern (PHEIC) on July 23, 2022.

• Transmission Dynamics: Many cases were identified among networks of men who have sex with men, raising awareness of specific transmission routes. Health authorities emphasized the importance of vaccination and awareness in at-risk populations [55].

13.4. Recent Developments In 2023

• Continued Surveillance: The outbreak continued into 2023, with cases reported in several countries. Although the number of cases declined compared to the peak in 2022, sporadic outbreaks and isolated cases were noted in various regions.

• Public Health Measures: Vaccination campaigns were implemented, particularly targeting high-risk groups. The JYNNEOS vaccine was prioritized in many countries, including the U.S. and UK.

• Case Reports: As of September 2023, cumulative global case counts exceeded 80,000 since the beginning of the 2022 outbreak, with significant cases reported in the U.S., Brazil, and several European nations [55].

13.5. Geographic Distribution of Cases

• Africa: Historically the epicenter, with the DRC and Nigeria reporting the highest numbers.

• Europe: Countries such as the UK, Spain, and Portugal saw significant outbreaks in 2022.

• North America: The U.S. and Canada reported multiple cases linked to international travel.

• Other Regions: Cases were also reported in Australia and several Asian countries, albeit in smaller numbers [56].

14. At-Risk Populations

14.1. Individuals in Endemic Regions

• Geographical Context: People living in Central and West Africa, particularly in rural areas, are at higher risk due to closer interactions with wildlife that may harbor the virus (e.g., rodents, monkeys).

• Cultural Practices: Hunting, handling, and consuming bushmeat are common practices that increase exposure risk. A study by Parker et al. (2007) indicated that cultural factors significantly influence monkeypox transmission in these communities.

15. Men Who Have Sex with Men (MSM)

• Recent Outbreaks: The 2022 global outbreak revealed that a significant proportion of cases were among MSM, particularly in urban settings. Studies from the UK Health Security Agency (UKHSA) noted that many infections were linked to close contact during sexual activities.

• Transmission Dynamics: The virus can spread through skin-to-skin contact, making intimate relationships a risk factor. Health authorities emphasize the importance of awareness and preventive measures within this community.

16. Healthcare Workers

• Exposure Risk: Healthcare workers in endemic regions face increased risk when treating infected patients without proper personal protective equipment (PPE). The World Health Organization (WHO) has documented instances where healthcare workers contracted monkeypox during outbreaks due to inadequate precautions.

• Training and Preparedness: Ensuring that healthcare personnel are trained and equipped to handle monkeypox cases is essential for minimizing transmission within healthcare settings.

17. Travelers to Endemic Regions

• Travel-Related Risk: Individuals traveling to areas where monkeypox is endemic are at increased risk of exposure. This includes tourists, business travellers, and expatriates.

• Public Health Recommendations: The CDC and WHO recommend that travellers receive information on monkeypox, including symptoms and preventive measures before traveling to endemic areas.

18. Household Contacts of Infected Individuals

• Close Contact Transmission: Individuals living with someone infected with monkeypox are at risk due to close physical interactions. This includes family members and caregivers who may have direct contact with lesions or bodily fluids.

• Infection Control: Proper isolation and hygiene measures are vital to reduce the risk of secondary transmission within households.

19. Immunocompromised Individuals

• Vulnerability: People with weakened immune systems (due to conditions such as HIV/AIDS, cancer treatments, or organ transplants) may be more susceptible to severe disease if infected.

• Preventive Strategies: This population should be prioritized in vaccination campaigns and public health messaging to enhance awareness and prevention [60].

20. Geographic and Demographic Factors

• Urban vs. Rural: Urban areas may see higher transmission rates due to higher population density and social networks, especially among MSM. In contrast, rural areas often face risks associated with wildlife interactions and limited healthcare access.

• Age & Gender: While monkeypox can affect individuals of any age and gender, data suggest that certain outbreaks have seen higher incidence rates among young adults and males, particularly in the context of the 2022 outbreak [57].

21. Public Health Implications

• Surveillance & Monitoring: Continuous monitoring of at-risk populations is essential for early detection and response to outbreaks.

• Targeted Vaccination: Vaccination campaigns should prioritize high-risk groups, particularly MSM and healthcare workers, to prevent further spread.

• Education and Awareness: Public health campaigns must focus on educating at-risk populations about transmission, symptoms,

and prevention strategies [55].

22. Symptoms & Clinical Presentation

Monkeypox is a zoonotic viral disease that resembles smallpox but is generally milder. Here is a summary of the symptoms and clinical presentation:

22.1. Incubation Period

- The incubation period typically ranges from 5 to 21 days, with symptoms most commonly appearing between 7 and 14 days after exposure.

22.2. Initial Symptoms (Prodromal Phase)

Fever: One of the earliest symptoms, usually accompanied by chills.
Headache: Moderate to severe headaches often occur.
Muscle Aches (Myalgia): Patients report generalized muscle pain.
Backache: Back pain is common during this phase.
Swollen Lymph Nodes (Lymphadenopathy): Swelling of lymph nodes in the neck, armpits, or groin is a characteristic feature of monkeypox, which helps differentiate it from smallpox.

Fatigue: Patients often experience a general feeling of tiredness and malaise [62].

22.3. Rash Development

rash typically begins 1 to 4 days after the onset of fever.
It usually starts on the face and then spreads to other parts of the body, including the palms of the hands and soles of the feet.
The rash progresses through several stages:
Macules: Flat, discolored spots on the skin.
Papules: Raised, firm bumps.
Vesicles: Small fluid-filled blisters.
Pustules: Pus-filled lesions.

Pustules: Pus-filled lesions.
Scabs: Lesions that crust over and fall off in the final stages.

23. Vaccination

Vaccines developed for smallpox provide some protection against monkeypox. Additionally, a more specific monkeypox vaccine has been developed and is used in certain high-risk groups [54].

24. Diagnosis

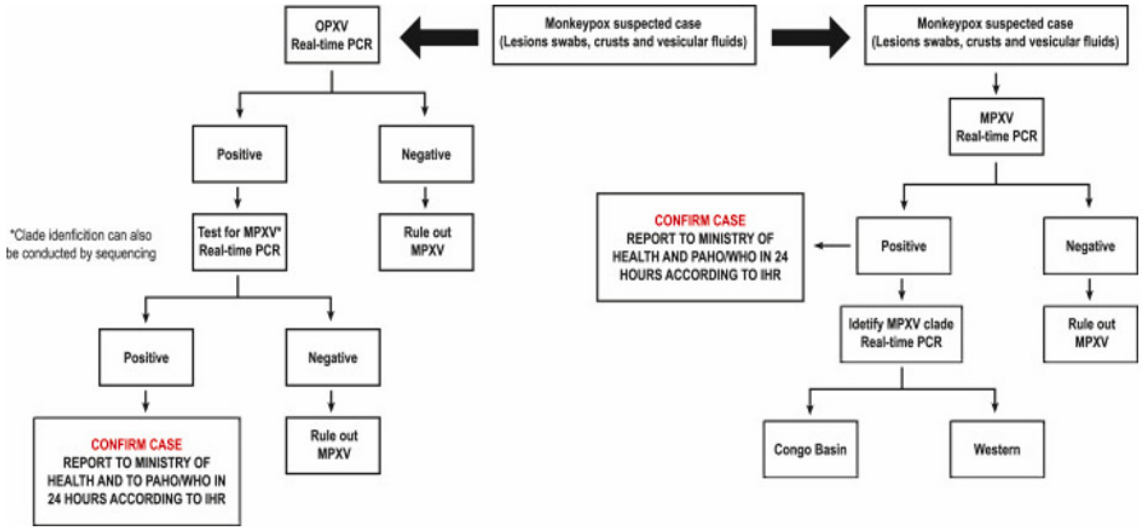

Figure 1: Algorithms for OPXV Initial PCR or for MPXV Specific Initial PC

Enzyme-linked immunosorbent assay (ELISA) can identify specific IgM and IgG antibodies in the serum of individuals infected with monkeypox, with IgM detectable after 5 days and IgG detectable after 8 days of infection for serological analysis. A four-fold rise in serum antibodies can be used to diagnose monkeypox virus infection during both the acute and recovery phases. The specificity is inadequate because of antigenic cross-reactions between MPXV and other poxviruses. As a result, this method is not effective at detecting monkeypox virions and is commonly used instead in epidemiological studies. Similarly, identification using an electron microscope is not completely reliable because virions cannot be differentiated based on their morphology [63].

Real-time polymerase chain reaction (RT-PCR) is a genetic technique used to detect monkeypox. The conserved regions of the extracellular envelope protein gene (B6R), DNA polymerase gene (E9L), DNA-dependent RNA polymerase subunit 18 (RPO18) gene, and the complement binding protein genes C3L, F3L, and N3R are commonly chosen as targets for PCR amplification. Additionally, recombinase polymerase amplification (RPA), loop-mediated isothermal amplification (LAMP), and restriction fragment length polymorphism (RFLP) have also been developed for the detection of MPXV DNA [64].

Sample Type	Collection Material	Storage Temperature	Collection Purpose
Skin lesion material, including: - Swabs of lesion exudate - Lesion roofs - Lesion crusts	Should be collected with a dry swab or VTM **(Dacron or polyester flocked swabs should be used)**	Store in a refrigerator (2–8°C) after collection until sent to the laboratory, and maintain the cold chain.	Recommended for diagnosis.
Oropharyngeal swab	Should be collected with a dry swab or VTM **(Dacron or polyester flocked swabs should be used)**	Store in a refrigerator (2–8°C) after collection until sent to the laboratory, and maintain the cold chain.	Recommended for diagnosis, if feasible, in addition to skin lesion material.
Serum	Serum separator tubes	Store in a refrigerator (2–8°C) after collection until sent to the laboratory, and maintain the cold chain.	Considered for serology for differential diagnosis and to support research efforts.

Table 1: Sample, Collection Material and Storage Temperature for MPXV Diagnostic and Differential Purpose

Two papers were found that assessed case definitions, with one being a conference abstract [65,66]. Surveillance case definitions were primarily non-specific and very sensitive to guarantee the detection of all potential monkeypox cases, which is essential for initiating an outbreak investigation and estimating the overall annual burden of monkeypox cases. This results in a significant number of false positive cases. Outbreak case definitions were more focused on the specific symptoms of monkeypox and were designed to differentiate monkeypox from other rash-like illnesses, particularly Varicella Zoster Virus (VZV). McCollum and colleagues assessed a suspected case definition for surveillance employed by the DRC Ministry of Health (MOH) in endemic regions: "an individual with 'febrile prodrome and either the presence of a) vesicular or pustular rash or scars on face, palms, and soles, or b) the presence of 5 or more variola-like scar" When applied to clinical symptoms for six suspected cases with available laboratory data, the sensitivity was 100% and the specificity was 80% [65]. The six cases were part of a total sample of 33 suspected cases from various unspecified African countries that were sent to the CDC in Atlanta.

In a larger study, Osadebe et al. examined the previously mentioned definition along with a second Ministry of Health definition used at the outbreak level [66]. "Individuals who have a vesicular or pustular eruption with deep-seated, firm pustules and at least one of the following a) febrile prodrome, b) lymphadenopathy (inguinal, axillary, or cervical), and/or c) pustules of crusts on the palms of the hands or soles of the feet". Both definitions were applied to a cohort of 645 individuals from 2009 to 2014 who met the surveillance criteria for monkeypox and had laboratory results available. Both the 'detection' and 'discriminatory' definitions exhibited high sensitivities of 93% and 98%, respectively, but had low specificities of 9% and 26%.

25. Treatment

25.1. Antiviral Medications

Electronic searches were conducted in PubMed, Scopus, and Google Scholar using key terms such as monkeypox, mpox, monkeypox treatments, tecovirimat, TPOXX, ST-246, CMX001, TEMBEXA, cidofovir, brincidofovir, as well as drug–drug interactions related to tecovirimat, cidofovir, and brincidofovir.

26. Experimental Therapies

26.1. Tecovirimat

Tecovirimat (TPOXX, ST-246), a low-molecular-weight antiviral drug, is the first FDA-approved treatment for smallpox treatment in adults and pediatrics weighing ≥13 kg. Tecovirimat has been licensed for the treatment of mpox in the European Union and the US [67-69]. It inhibits orthopoxvirus replication by inhibiting the p37 envelope protein.[70,71] The details of the molecular mechanism of action of tecovirimat are shown in Figure 2. Animal studies showed that tecovirimat could inhibit a range of other viruses including vaccinia, ectromelia, cowpox, variola, and rabbitpox. Sbrana et al. investigated the prophylactic effect of tecovirimat in a subcutaneous mpox model [72-76]. In this study, tecovirimat 100 mg/kg was given within 0–4 days after infection for 14 days and demonstrated 100% protection against MPOX.

Tecovirimat with doses of 3–300 mg/kg demonstrated 100% protection if administered up to 5 days postinfection. In a study with a duration of 14 days; 3 mg/kg was the effective dose, but the dose of 10 mg/kg also decreased viremia and lesion count. Administration of tecovirimat with food may significantly increase its absorption with the maximum plasma concentration (Cmax) and area under the curve (AUC) 0–24 increasing about 45% at a steady state [77,80]. The most common adverse effects experienced with tecovirimat are headache and nausea [81]. Based on the pivotal study, the rate of drug adverse events leading to discontinuation of tecovirimat was very low (1.7%). Also, the clinical safety study showed that tecovirimat at a dose of 600 mg orally twice daily for 14 days is safe [81]. Thus, tecovirimat may be a good option for the treatment of patients with mpox infection due to the favorable clinical efficacy, safety, and side effect profile. Tecovirimat is a weak cytochrome P450 (CYP) 3A4 inducer and a weak inhibitor of CYP2C19 and CYP2C8 [81].

It may increase the serum levels of repaglinide in diabetic patients via CYP2C8 inhibition which can result in hypoglycemia, thus

monitoring of blood glucose and hypoglycemia symptoms is necessary. It also may decrease the serum concentration of midazolam and may require dose adjustment or alternative sedatives. Coadministration of tecovirimat with QT-prolongation agents (such as class I or class II antiarrhythmics) may increase the risk of long QT syndrome and should be avoided [83]. Tecovirimat may decrease the serum level of tacrolimus and sirolimus via induction of CYP3A4. Thus, close monitoring of therapeutic levels of these immunosuppressive drugs is recommended in solid organ transplant recipients receiving tacrolimus or sirolimus with tecovirimat. It also may reduce the serum level of hormonal contraceptives by induction of CYP3A4 but there was no report on drug-related pregnancies in clinical trials [81]. However, the patient should use an alternative method of contraception during the co-administration of tecovirimat with hormonal contraceptives and for 28 days after tecovirimat discontinuation. Due to the decreasing efficacy of tecovirimat in obese and immunocompromised patients, it should be used with close monitoring in these populations. Animal studies have not shown that tecovirimat has embryotoxic and teratogenic effects [82]. Tecovirimat has not been evaluated in breastfeeding and data are not available in this population therefore it was not recommended for use during the breastfeeding period [83].

26.2. Brincidofovir

Brincidofovir (CMX001, TEMBEXA), an analog of cidofovir, is converted to cidofovir and inhibits orthopoxvirus DNA polymerase mediated viral DNA synthesis (Figure 2)[84]. It was granted fast-track designation and Orphan Drug Status for the treatment of smallpox in June 2018 [85]. It has activity against other DNA viruses such as adenovirus, BK virus, and cytomegalovirus (CMV). Based on limited studies in animal models, oral administration of brincidofovir is effective in the treatment of mpox animal infection model but the use of brincidofovir (200 mg once weekly orally) in three human patients with mpox has resulted in no clinical benefit to patients [86,87]. Diarrhea is the most frequent dose-limiting adverse effect associated with brincidofovir (reported in approximately 70% of patients) and may be often serious (in 33% of patients) [88,89]. Thus, monitoring of diarrhea and dehydration symptoms in patients under treatment with brincidofovir is recommended. Also, the dose of brincidofovir should be limited to 200 mg/week or less for the prevention of diarrhea [88-89]. Nausea, vomiting, and abdominal pain are additional gastrointestinal reported adverse effects of brincidofovir [88]. Oral brincidofovir should be administered on an empty stomach as food decreases its Cmax and AUC but it can be taken with a low-fat meal to decrease gastrointestinal adverse effects. Elevated alanine aminotransferase (ALT) is a common finding seen during treatment with brincidofovir. Thus, liver function tests should be obtained before initiating and during treatment with brincidofovir, and discontinuation of brincidofovir should be considered if ALT levels are persistently greater than 10 times the upper limit of normal[90].

Brincidofovir has less kidney toxicity than cidofovir because it is not a substrate of the human organic anion transporters (OATPs) and hence, it does not accumulate in renal tubules [88]. It is recommended that brincidofovir should not be administered with intravenous cidofovir because brincidofovir is converted to cidofovir and increases the risk of nephrotoxicity [90]. The reproductive study showed that brincidofovir is embryotoxic in rabbits and therefore contraindicated in pregnancy [88]. It has not been assessed in breastfeeding and data are not available in this population. However, breastfeeding is not recommended in patients with mpox, due to the potential risk of virus transmission through direct contact between the mother and breastfed infant [90]. It is also considered a probable human carcinogen and mutagen and may decrease male fertility via the reduction in sperm motility and effect on mitotic spermatogenesis.[90] Brincidofovir is a substrate of OATP1B1/1B3 transporters and inhibits the multi-drug resistance protein 2 (MRP2). It may increase the plasma concentration of cabozantinib by MRP2 inhibition [91]. Brincidofovir may decrease the therapeutic effect of cladribine via intracellular phosphorylation and the combination of these drugs should be avoided. Immunosuppressants such as cyclosporine may reduce the effect of brincidofovir. Corticosteroids and methotrexate may reduce the therapeutic effect of brincidofovir [92]. OATP1B1/1B3 inhibitors, such as rifampin, cyclosporine, clarithromycin, erythromycin, and gemfibrozil may elevate brincidofovir levels and increase brincidofovir adverse effects. Therefore, the clinician should consider alternatives to OATP1B/1B3 inhibitors for the treatment of patients treated with brincidofovir or these drugs should be taken at least 3 h apart [92]. Brincidofovir may decrease the protective effect of live smallpox and mpox vaccines via the reduction of the immune response to the vaccine.

26.3. Cidofovir

Cidofovir, a cytidine nucleotide analog of cytosine, is converted to an active metabolite (cidofovir diphosphate) by the host-cell enzymes and inhibits the viral DNA polymerase (Figure 2). It has potent

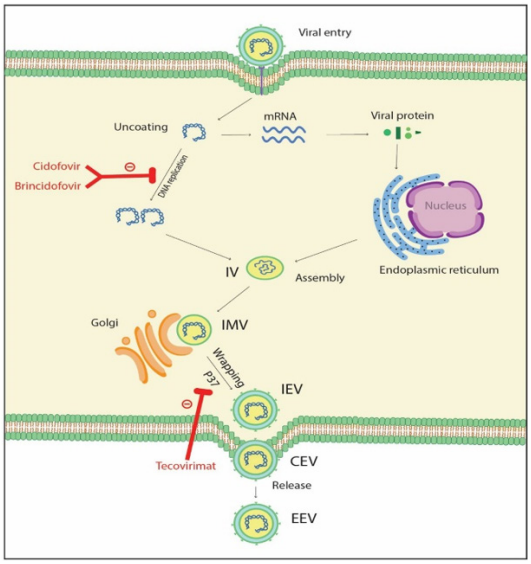

Figure 2: Molecular Mechanism of Action of Tecovirimat, Cidofovir & Brincidofovir in MPOX CEV, Cell-Associated Enveloped Virus; EEV, Extracellular Enveloped Virus; IEV, Intracellular Enveloped Virus; IMV, Intracellular Mature Virus; IV, Immature Virus

activity against CMV, herpes simplex virus, varicella-zoster virus, and Epstein–Barr virus [93-95]. The effectiveness of cidofovir in the treatment of lethal mpox infection in animal models has been demonstrated, but the evidence for cidofovir efficacy against human mpox infection is lacking [96,97]. Cidofovir was dosed for mpox as 5 mg/kg intravenously once weekly for 2 weeks, followed by 5 mg/kg IV once every other week [98]. Animal studies showed that cidofovir is carcinogenic. Based on the National Institute for Occupational Safety and Health (NIOSH) recommendation, double gloving, a protective gown, and ventilated engineering controls are required during the administration of cidofovir. The most common adverse effects of cidofovir include proteinuria, nephrotoxicity, neutropenia, hypotony of the eye, uveitis, and infection [96]. Nephrotoxicity is the main dose-limiting toxicity of cidofovir. Therefore, consideration must be given toward the appropriate hydration and the use of probenecid 2 g 3 hours prior to the cidofovir dose, then 1 g 2 h and 8 h after completion of the cidofovir infusion [99].

To reduce the risk of nephrotoxicity associated with cidofovir, serum creatinine and urine protein should be closely monitored 48 hours prior to each dose of cidofovir, and dose adjustment or discontinuation of therapy may be required depending on the degree of renal impairment [100]. Also, nephrotoxic medications, such as amphotericin B, pentamidine, cyclosporine, contrast media, tacrolimus, nonsteroidal anti-inflammatory drugs, and aminoglycosides, should be avoided during and at least 7 days before the initiation of cidofovir [101]. The neutrophil count should be checked at baseline and during cidofovir therapy because neutropenia has been reported in approximately 20% of patients in clinical trials [100]. A monthly ophthalmologic exam of the retina is necessary because hypotony and uveitis have also been reported following cidofovir therapy [100]. Other adverse effects include nausea, vomiting, dyspnea, and Fanconi syndrome. Contraindications for the use of cidofovir include serum creatinine >1.5 mg/dL, calculated creatinine clearance ≤55 mL/min, proteinuria ≥2+, co-administration with nephrotoxic medications, and hypersensitivity to cidofovir [100]. Cidofovir is embryotoxic and teratogenic, and should not be used in pregnant women.

It may consider only in critically ill pregnant patients who failed to respond to tecovirimat [82,102]. Due to the potential risk of cidofovir for serious adverse effects in breastfeeding infants, breastfeeding is not recommended [99]. Cidofovir inhibits MRP2 and may increase the plasma concentration of cabozantinib [91]. Cidofovir may diminish the effect of cladribine via intracellular phosphorylation; thus, the coadministration of these drugs should be avoided [98]. Zidovudine plasma levels may increase when coadministered with probenecid, therefore, it is recommended that zidovudine should be discontinued or administered with 50% dose on the day of cidofovir infusion [100]. Tenofovir may increase the plasma levels of cidofovir and enhance its nephrotoxicity.

26.4. Supportive Care

Most patients with monkeypox infection recover without medical treatment. Those with gastrointestinal symptoms (e.g., vomiting, diarrhea) will require oral/intravenous rehydration to minimize gastrointestinal fuid losses [103].

27. Prevention

Vaccine	Pros	Cons	Stage of development or Use
ACAM2000: Live vaccinia virus	Single-dose administration. A successful take is noted by observation of a lesion at the vaccination site. Lyophilized preparation for long-term storage.	Live viral vaccine that replicates in mammalian cells; autoinoculation and contact transmission are risks. In lowdisease-risk situations, should not be used for individuals with immunocompromising conditions, history of eczema or atopic dermatitis, or pregnant females. Cardiac events postvaccination have been noted to occur.	Licensed vaccination in the United States. Currently available to specific populations from the Strategic National Stockpile.
Modified vaccinia Ankara; IMVAMUNE (US); IMVANEX (Europe): Attenuated vaccinia virus	The virus has limited replication in mammalian cells. No lesion produced at the vaccination site.	Two-dose administration by injection.	European Commission has authorized marketing for immunization of the general adult population, including those who are immunocompromised. Maintained in the United States' Strategic National Stockpile.
LC16m8: Attenuated vaccinia virus	Single-dose administration. Exhibits a safer profile and less adverse events than ACAM2000 in human and animal vaccinations.	Attenuated virus that can still replicate in mammalian cells.	Licensed for use in Japan.

Table 2: Vaccination

28. Public Health Measures

Monkeypox meets all International Health Regulations (IHR) criteria for a PHEIC. Current clusters represent "an extraordinary event" as nontravel-associated cases have never been reported outside endemic areas of central and west Africa.[104] Given the spread of MPXV to more than 70 countries in 6 WHO regions, this outbreak clearly constitutes "a public health risk to other States through the international spread of disease." Given the pace with which cases are being detected and the global scope, the risk that MPXV will become entrenched globally is increasing and "a coordinated international response" is essential. Coordinating global outbreak alerts and response networks include intensifying surveillance and public measures. Preventive and public health measures represent an important arm of infection containment.

While quarantine and isolation are essential for disease management, present global guidelines do not recommend mobility restrictions for preventing disease transmission. With changes in guidelines with increasing knowledge of the outbreak, standard risk reduction protocols will hold ground for safeguarding public health. Proactive environmental infection control should be integrated with the initiatives, including standard cleaning and infection procedures, especially in healthcare settings. Source control will also include the prioritisation of transport and movement of patients as well as standard waste management practices. Elaborating and increasing the awareness and elaboration of physical distancing measures, personal protection and hygiene, as in handwashing and personal protective equipment holds great value for public acceptance.

29. Personal Protective Measure

Self-monitoring daily for the occurrence of signs/symptoms associated with MPX for a period of 21 days after the last contact with a patient or their contaminated materials during the infectious period. During the surveillance period, MPX infection contacts should avoid encounters with immunocompromised persons, pregnant women, and children under 12 years of age, and should not donate blood, cells, tissues, organs, breast milk, or semen [105].

30. Public Health Response

Robust surveillance for monkeypox (MPX) cases is important to detect and prevent further transmission. It involves case detection, investigation and contact follow-up. MPX is epidemic prone and should be reported immediately. Suspected monkeypox cases may be detected using standard case definitions. Cases of suspected monkeypox should be reported immediately to the LGA Disease Surveillance and Notification Officers (DSNOs) or State Epidemiologist or NCDC. Reporting of suspected cases should follow the IDSR reporting flow.

31. Surveillance and Reporting

31.1. Case Investigation

Case investigation Once a suspected case is detected, states are to intensify surveillance and actively engage in case detection. All rumours should be investigated and documented. A Case Investigation Form (CIF) should be completed for all suspected cases who should also be entered into a line-list. The following should be carried out for every suspected case:

1. Clinical examination
2. Questioning about possible sources of infection and the presence of apparent disease in the person's community
3. Completion of a case investigation form for everyone who meets the case definition
4. Collection and transportation of samples as detailed in sample

collection protocol.
5. Ensure referral to the nearest designated isolation facility or a secondary health facility for management
6. Include all contacts in a line-list.

31.2. Contact Tracing

1. Identification of contacts – all contacts of every suspected case should be identified during case investigation
2. Contact listing – all contacts of every suspected case should be included in a line-list and also the contact listing section of the MPX CIF. All listed contacts should also be classified according to the type of contact had with the case as discussed in the introduction session Surveillance Strategies The aims of the proposed surveillance strategy are to rapidly identify cases and clusters of infections and the sources of infections as soon as possible in order to:
a) isolate cases to prevent further transmission
b) provide optimal clinical care
c) identify and manage contacts
d) protect frontline health workers
e) effective control and preventive measures based on the identified routes of transmission.

Surveillance outline:
a) Use Standard Case Definitions by all District Surveillance Units (DSUs) under Integrated Disease Surveillance Programme (IDSP) and at Points of Entry (PoEs).
b) Even one case of monkeypox is to be considered as an outbreak. A detailed investigation by the Rapid Response Teams needs to be initiated through IDSP.
c) Report any suspected case immediately to the DSU/State Surveillance Units (SSUs) and CSU (Central Surveillance Unit), which shall report the same to Dte. GHS MoHFW.
d) Send the samples as per the guidelines to the designated laboratories.

The salient features include:
a) Targeted surveillance for probable case or clusters.
b) Initiate contact tracing and testing of the symptomatic after the detection of the probable/confirmed case.

Core Surveillance Strategy
a) Hospital based Surveillance: - Health facility-based surveillance & testing – in Dermatology clinics, STD clinics, medicine, paediatrics OPDs etc.
b) Targeted Surveillance: This can be achieved by: i) Measles surveillance by Immunization division ii) Targeted intervention sites identified by NACO for MSM, FSW population [106].

32. Containment and Control Measures

Raising awareness of risk factors and educating people about the measures they can take to reduce exposure to the virus is the main prevention strategy for monkeypox. There are number of measures that can be taken to prevent infection with monkeypox virus:

· Avoid contact with any materials, such as bedding, that has been in contact with a sick person.
· Isolate infected patients from others.
· Practice good hand hygiene after contact with infected animals or humans. For example, washing your hands with soap and water or using an alcohol-based hand sanitizer.
· Use appropriate personal protective equipment (PPE) when caring for patients.

The prevention of MPXV infection remains a challenge due to remaining questions regarding the virus' mode of transmission as well as a lack of clarity regarding which animal acts as the reservoir for the virus in Nigeria. Control involves the prevention of primary transmission from animals by avoiding contact with rodents and primates as well as limiting direct exposure to their blood and other body fluid and inadequately cooked meat (e.g. bush meat preparation and or consumption). Control of rodents is an important measure to prevent the spread of diseases. This can be ensured through good hygiene among household members or inmates/residents of closed settings, regular removal of refuse and breeding grounds, screens on windows and doors as well as fumigation. Infection control measures are vital to the prevention of human-to-human transmission in the community and in health care settings with standard precautions as the standard of care for all patients. Improved use of PPE (e.g. gloves, protective clothing, surgical masks), isolation practices and proper waste management through continuous education as well as adequate facilities and staffing are also essential for prevention of human-tohuman transmission. Robust health education campaigns are needed to increase general awareness of the public of the dangers posed by the monkeypox virus and to advise on proper handling of potential animal reservoir species as well as avoiding close contact with infected persons.

Standard precautions Health Care Workers (HCWs) working in facilities where suspected cases are handled should ensure they

a. Use contact precautions when in direct contact with patients and to help prevent indirect contact with blood or other bodily fluids and contaminated environment
b. Wear gloves to prevent contact with blood, infectious materials or other potentially contaminated surfaces and items
c. Always wear face protection (face mask/or N95, googles or face shield) against droplets
d. Observe hand hygiene following the five moments for hand hygiene and wash hands thoroughly under running water before and after a procedure.
e. Do not recap needles and handle all sharps with caution
f. Safely dispose of all sharps in labelled, puncture-proof boxes
g. Report to a supervisor immediately should there be a puncture wound or exposure to infectious substances in the facility
h. Correctly contain and dispose of contaminated waste (e.g. dressings) in appropriate color-coded bags. All waste from patients with suspected/confirmed monkeypox infection is classified as highly infectious waste. This includes PPE worn in the isolation

wards and should be disposed of in red bags.
i. Take appropriate care when handling soiled laundry and other equipment (e.g. bedding, towels, personal clothing) to avoid contact with lesion material, as some orthopox viruses are known to persist in the environment
j. Do not shake or handle soiled laundry materials or linen in a manner that may disperse infectious particles
k. Clean and decontaminate all used equipment appropriately (e.g. As much as possible, single use devices should be used in care of monkeypox patients.

l. Critical and semi critical equipment should be sterilised and disinfected as appropriate.
m. Other non-critical patient care equipment should be cleaned with detergent, warm water and disinfected with 1.0% chlorine solution prior to disposal or re-use [107].

33. Guidelines for Healthcare Workers

33.1. This is in continuation of this Ministry's earlier communication vide DO No. 2.2801510612022; dated 31st May 2022 wherein a comprehensive 'Guidelines for Management of Monkeypox Disease' issued by this Ministry was shared with all States/UTs.
33.2. As reported by World Health Organization (WHO), Since 1 January 2022 and as of 22 June2022, a total of 3413 laboratory confirmed cases of Monkeypox and one death have been reported to WHO from 50 countries/territories. Majority of these cases have been reported from the European Region (86%) and the Americas (11%). This points to a slow but sustained increase in spread of cases globally. Considering this is the first time that cases and clusters are being reported concurrently in five WHO Regions, WHO has assessed the overall risk of spread of cases as "Moderate" at global level.
33.3. Continued expansion of spread of Monkeypox disease globally calls for proactive strengthening and operationalization of requisite public health actions for preparedness and response against the disease in lndia also.
33.4. I would, therefore, Iike to reiterate some of the key actions that are required to be taken by all States/UTs in line with MoHFW's guidance issued on the subject:
33.5. As COVID-19 pandemic continues to pose challenges, it is vital we remain aware and alert about other public health threats and proactively prepare ourselves to tackle them.
33.6. States/UTs shall make all efforts to ensure effective preparedness and take required action as per the guidelines. Union Ministry of Health shall continue to monitor the situation closely and will extend all requisite support in this regard [108].
a) Orientation and regular re-orientation of all key stakeholders including health screening teams at Points of Entries (PoEs), disease surveillance teams, doctors working in hospitals about common signs and symptoms, differential diagnosis, case definitions for suspect and probable/confirmed cases and contacts, contact tracing and other surveillance activities that need to be undertaken following detection of a case, testing, IPC protocols, clinical management etc.
b) Screening and testing of all suspect cases at points of entries, and in the community (either through hospital-based surveillance and targeted surveillance under measles surveillance or intervention sites identified by NACO for MSM, FSW population)
c) Patient isolation (until all lesions have resolved and scabs have completely fallen off), protection of ulcers, symptomatic and supportive therapies, continued monitoring and timely treatment of complications remain the key measures to prevent mortality.
d) intensive risk communication directed at healthcare workers, identified sites in health facilities (such as skin, paediatric OPDs, immunization clinics, intervention sites identified by NACO etc.) as well as general public about simple preventive strategies and need for prompt reporting of cases needs to be undertaken.
e) Hospitals must be identified and adequate human resource and logistic support should be ensured at identified hospitals equipped to manage suspect and confirmed cases of Monkeypox.

34. Research and Future Directions

34.1. Research Directions

34.1.1. Understanding the Virus

• Genomic Studies: Researchers are sequencing the monkeypox virus to understand its genetic variability and evolution, which can help in tracking outbreaks and developing targeted treatments.
• Pathogenesis: Understanding how the virus causes disease at a molecular and cellular level can lead to better treatment strategies.

34.1.2. Vaccine Development

• Efficacy Studies: Ongoing studies are assessing the effectiveness of existing smallpox vaccines against monkeypox and exploring new vaccines.
• New Vaccine Platforms: Development of new vaccine platforms specifically targeting monkeypox, such as recombinant vaccines or nanoparticle-based vaccines, is underway.

34.1.3. Antiviral Research

• Drug Development: Researchers are investigating antiviral drugs that could target the monkeypox virus more effectively. This includes screening existing antiviral agents for activity against monkeypox.

34.1.4. Transmission Dynamics

• Modelling and Surveillance: Improved models for understanding transmission dynamics can help predict and manage outbreaks. Enhanced surveillance systems are also crucial for early detection and response.

34.1.5. Zoonotic Transmission

• Animal Reservoirs: Identifying the animal reservoirs and understanding their role in virus transmission can help in controlling outbreaks and preventing cross-species transmission [109].

35. Future Directions

35.1. Global Health Strategies

• Strengthened Surveillance: Increasing global and regional surveillance efforts to monitor and respond to monkeypox

outbreaks quickly.
• Public Health Preparedness: Developing frameworks and response plans to manage potential outbreaks, including stockpiling vaccines and antivirals.

35.2. International Collaboration:
Global Coordination: Enhancing international collaboration for research, information sharing, and response strategies to tackle monkeypox on a global scale.

35.3. Education and Awareness:
Community Outreach: Increasing awareness and education about monkeypox in affected regions to promote early detection and reduce stigma.

35.4. Environmental and Ecological Studies:
• Ecosystem Impact: Researching the environmental factors and ecological changes that may influence the emergence and spread of monkeypox.
• In summary, while monkeypox remains a significant public health concern, ongoing research and collaborative efforts are key to improving our understanding of the virus, developing effective treatments and vaccines, and managing future outbreaks [110].

36. Current Research Initiatives
As of 2024, several research initiatives are actively addressing various aspects of monkeypox. These initiatives span epidemiology, virology, vaccine development, treatment options, and public health strategies. Here's a detailed look at current research efforts:

36.1. Vaccine Development and Evaluation
• New Vaccines: Researchers are exploring novel vaccine candidates specifically tailored to monkeypox. This includes recombinant vaccines and other innovative platforms designed to enhance efficacy and safety.
• Vaccine Efficacy Studies: Clinical trials are ongoing to evaluate the effectiveness of existing smallpox vaccines against monkeypox, including their duration of protection and any need for booster doses.
• Combination Vaccines: Efforts are underway to develop combination vaccines that can protect against both smallpox and monkeypox, which may offer broader protection and streamline immunization strategies.

36.2. Antiviral Drug Research
• Drug Repurposing: Scientists are testing existing antiviral medications, such as those used for other viral infections, to determine their effectiveness against monkeypox.
• Novel Antivirals: Research is also focused on developing new antiviral drugs that specifically target the monkeypox virus, aiming for greater efficacy and reduced side effects.
• Drug Mechanism Studies: Understanding the mechanisms by which antiviral drugs inhibit monkeypox replication is critical for designing more effective treatments.

36.3. Virology and Pathogenesis
• Virus Genomics: Sequencing the genomes of monkeypox virus strains helps researchers understand genetic variations, track outbreaks, and identify potential targets for treatments and vaccines.
• Host-Pathogen Interactions: Studies are investigating how the monkeypox virus interacts with human cells and the immune system, which can provide insights into its pathogenesis and help identify potential therapeutic targets.
• Animal Models: Development and use of animal models to study monkeypox infection and disease progression are essential for testing new treatments and vaccines.

36.4. Epidemiology and Transmission Dynamics
• Outbreak Tracking: Enhanced surveillance systems are being developed to monitor and track monkeypox outbreaks globally. This includes using advanced data analytics and modeling to predict and manage outbreaks.
• Transmission Studies: Research is focusing on understanding how monkeypox spreads between humans and animals, including the role of asymptomatic carriers and environmental factors.
• Public Health Impact: Assessing the socio-economic impact of monkeypox outbreaks helps in developing strategies for better preparedness and response.

36.5. Diagnostics
• Improving Diagnostic Tests: Researchers are working on more rapid, accurate, and accessible diagnostic tests for monkeypox, including point-of-care tests and improved PCR assays.
• Diagnostic Platforms: Development of multiplex diagnostic platforms that can detect multiple pathogens, including monkeypox, in a single test is being explored.

36.6. Public Health and Community Engagement
• Education Campaigns: Initiatives to increase awareness about monkeypox symptoms, prevention, and treatment options, particularly in regions at high risk, are underway.
• Stigma Reduction: Addressing the stigma associated with monkeypox through public health messaging and community engagement efforts is a key focus.

36.7. Environmental and Zoonotic Research
• Animal Reservoirs: Identifying and monitoring animal reservoirs of monkeypox to understand their role in the virus's lifecycle and transmission to humans.
• Ecological Factors: Investigating environmental changes and ecological factors that might influence the emergence and spread of monkeypox.

36.8. Global Collaboration and Response
• International Partnerships: Collaborations between global health organizations, governments, and research institutions aim to coordinate responses, share data, and improve global preparedness for future outbreaks.
• Policy Development: Research is informing policy development

related to vaccination strategies, outbreak response, and public health measures to manage monkeypox effectively.

These research initiatives are critical for advancing our understanding of monkeypox and improving our ability to prevent, diagnose, and treat the disease. Continued investment in these areas will be crucial for managing current and future outbreaks effectively [111].

37. Challenges In Eradication

Eradicating monkeypox presents several challenges, which stem from the disease's biological characteristics, transmission dynamics, and socio-environmental factors. Here's a comprehensive look at these challenges:

37.1. Biological and Environmental Factors

• Wildlife Reservoirs: Monkeypox is zoonotic, meaning it can be transmitted from animals to humans. Identifying and controlling the wildlife reservoirs and intermediaries of the virus is challenging. The virus is believed to be maintained in various wild animals, and controlling these animal populations is complex.

• Virus Variability: The monkeypox virus exhibits genetic variability, which can complicate vaccine and treatment development. Different strains or variants may have different characteristics, affecting how well existing vaccines and treatments work.

• Limited Knowledge of Transmission Dynamics: Understanding all the factors that influence monkeypox transmission, including asymptomatic cases and the role of various animal species, is still incomplete. This makes it difficult to implement effective control measures.

37.2. Public Health and Medical Challenges

• Surveillance and Diagnosis: Effective eradication requires robust surveillance and accurate diagnosis. In some regions, especially in remote or under-resourced areas, diagnostic tools and surveillance systems may be inadequate.

• Vaccine Coverage: While smallpox vaccines can offer some protection against monkeypox, global vaccination coverage is limited. Ensuring high vaccine coverage in both endemic and at-risk populations is a significant challenge, particularly in areas with logistical and infrastructure issues.

• Treatment Limitations: There are no specific antiviral treatments for monkeypox; management primarily involves supportive care. Developing effective treatments is a critical step but remains a challenge due to the complex nature of the virus and its effects on the body.

37.3. Socio-Economic and Cultural Factors

• Health System Capacity: In many affected regions, healthcare systems may be under-resourced, with limited access to medical facilities, trained personnel, and essential supplies. Strengthening these systems is crucial but can be difficult due to financial and logistical constraints.

• Public Awareness and Education: Raising awareness about monkeypox and educating communities about prevention and control measures is essential. In some areas, there may be a lack of awareness or misinformation about the disease, which can hinder efforts to control it.

• Stigma and Cultural Beliefs: Stigma associated with monkeypox can deter individuals from seeking medical care or participating in vaccination programs. Cultural beliefs and practices may also influence the effectiveness of public health interventions.

37.4. Global and Regional Coordination

• International Cooperation: Effective eradication requires coordinated international efforts. Political, logistical, and financial challenges can complicate global cooperation and response efforts.

• Funding and Resources: Adequate funding and resources are necessary for research, vaccination programs, and outbreak management. Securing and maintaining this support can be challenging, especially in the face of competing health priorities.

37.5. Emergence of New Cases

• Epidemic Resurgence: Even with significant progress in control efforts, the emergence of new cases or outbreaks in previously controlled areas can undermine eradication efforts. This is especially challenging in regions with continuous zoonotic transmission or where public health infrastructure is weak.

• Global Travel and Trade: Increased global travel and trade can facilitate the spread of monkeypox to new regions, complicating eradication efforts and requiring international vigilance.

37.6. Environmental Changes

• Climate Change: Changes in climate and land use can alter the habitats of wildlife reservoirs and vectors, potentially increasing the risk of monkeypox transmission to humans.

Addressing these challenges requires a multi-faceted approach, including:

• Strengthening Surveillance and Diagnostic Capabilities: Improving monitoring systems and diagnostic tools to quickly identify and respond to cases.

• Enhancing Vaccination Programs: Ensuring widespread access to vaccines and addressing logistical challenges in vaccine distribution.

• Developing Effective Treatments: Investing in research to develop and test new antiviral drugs and therapeutic interventions.

• Public Education and Engagement: Increasing awareness and education efforts to promote prevention and reduce stigma.

• International Collaboration: Fostering global cooperation and resource-sharing to coordinate efforts and manage outbreaks effectively.

Eradicating monkeypox is a complex and challenging task, but with sustained efforts and global collaboration, progress can be made toward controlling and eventually eliminating the disease [112].

38. Future Prospects

The future prospects of monkeypox disease involve both potential advancements and ongoing challenges. Here's a look at what could shape the future trajectory of monkeypox:

38.1. Advancements in Vaccination and Treatment

• Development of New Vaccines: Continued research may lead to the development of more effective and specific vaccines against monkeypox. This includes vaccines tailored to different strains of the virus and those that provide longer-lasting immunity.

• Enhanced Vaccination Strategies: Innovations in vaccine delivery methods and improved logistics could make vaccination campaigns more efficient and widespread, especially in high-risk areas.

• Antiviral Drug Development: Ongoing research into new antiviral drugs could provide effective treatments for monkeypox. These could offer better outcomes for patients and reduce the severity of outbreaks.

• Combination Vaccines: There is potential for developing combination vaccines that protect against both smallpox and monkeypox, simplifying immunization schedules and enhancing overall protection.

38.2. Improved Diagnostics

• Rapid and Accurate Testing: Advances in diagnostic technology could lead to the development of more rapid, accurate, and accessible tests for monkeypox, including point-of-care tests that can be used in remote areas.

• Integrated Diagnostic Platforms: Development of multiplex diagnostic platforms that can simultaneously test for multiple pathogens, including monkeypox, could streamline disease management.

38.3. Enhanced Surveillance and Global Coordination

• Global Surveillance Systems: Strengthening global surveillance systems to monitor outbreaks and track virus mutations will be crucial for early detection and response.

• International Collaboration: Increased international cooperation and data sharing will help manage and mitigate outbreaks more effectively, improving global preparedness and response.

38.4. Public Health Strategies

• Education and Awareness: Ongoing public health campaigns and education will be important for increasing awareness about monkeypox, promoting vaccination, and reducing stigma.

• Strengthening Health Systems: Investing in and strengthening healthcare infrastructure in endemic regions will improve the ability to manage outbreaks and provide care.

38.5. Zoonotic and Environmental Research

• Understanding Reservoirs: Continued research into animal reservoirs and the ecology of monkeypox will be essential for controlling the disease and preventing new outbreaks.

• Impact of Climate Change: Studying the effects of climate change on monkeypox transmission will help in predicting and managing future risks, particularly as environmental factors influence the spread of zoonotic diseases.

38.6. Challenges to Address

• Emergence of New Variants: The potential for new variants of the monkeypox virus could affect vaccine and treatment efficacy. Ongoing genomic surveillance and adaptability in response to new variants will be necessary.

• Global Health Disparities: Addressing disparities in healthcare access and resources between different regions will be critical to ensure equitable disease management and prevention efforts.

• Mitigating Stigma: Reducing stigma associated with monkeypox through effective communication and community engagement will be important for encouraging timely medical care and public health participation [113].

38.7. Research and Innovation

• Basic and Applied Research: Continued investment in both basic researches to understand the virus and applied research to develop interventions will be crucial for managing monkeypox.

• Technological Innovations: Leveraging advancements in technology, such as genomic editing, artificial intelligence, and novel drug delivery systems, may offer new tools for tackling the disease.

In summary, while there are significant challenges to eradicating or controlling monkeypox, ongoing research, advancements in medical science, and improved global coordination offer promising prospects. With sustained efforts and collaboration, the future of monkeypox management looks hopeful, aiming towards better prevention, treatment, and ultimately, disease control [114].

39. Conclusion

It is a viral zoonotic disease caused by the monkeypox virus, which is related to the variola virus that causes smallpox. It primarily occurs in Central and West Africa but has recently been reported in non-endemic countries. The disease is characterized by fever, rash, and swollen lymph nodes, and it can lead to more severe health issues, especially in immunocompromised individuals.

The transmission of monkeypox can occur through direct contact with infected animals, humans, or contaminated materials. While the risk of widespread transmission is lower than that of other diseases like smallpox, outbreaks can still occur, and public health measures are crucial in controlling its spread.

In conclusion, monkeypox is an important public health concern that requires ongoing surveillance, research, and education to prevent outbreaks and ensure effective responses. Vaccination against smallpox has been shown to be effective in preventing monkeypox, and public health authorities are working to enhance awareness and readiness in both endemic and non-endemic regions.

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