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AN APPRAISAL OUTLINE ON MONKEYPOX VIRUS

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ABSTRACT

Following two reports of monkeypox virus infection in individuals who returned from Nigeria to the USA, one who returned to Texas in july 2021 and other to Washington, DC area in november 2021, the number of monkeypox infection have dramatically increased. This sounded an alarm of potential for spreading of the virus throughout the USA. During 2022, there was a report of monkeypox virus infection in may 2022 in a British national following a visit to Nigeria who developed readily recognizable signs and symptoms of monkeypox virus infection. More than 57,995 confirmed cases had been reported as of September 13, 2022, according to the US Centers for Disease Control and Prevention (CDC). While the prevalence of the monkeypox virus is well known in central and western Africa, its presence in the developed world has raised disturbing signs for worldwide spread. While infection was reported during the past half-century, starting in the Democratic Republic of Congo in 1970, in the United States, only sporadic monkeypox cases have been reported. All cases have been linked to international travel or through African animal imports. The monkeypox virus is transmitted through contact with infected skin, body fluids, or respiratory droplets. Monkeypox disease begins with constitutional symptoms that include fever, chills, headache, muscle aches, backache, and fatigue. Phylogenetically the virus has two clades. One clade emerged from West Africa and the other in the Congo Basin of Central Africa. During the most recent outbreak, the identity of the reservoir host or the primary carriage remains unknown. African rodents are the suspected intermediate hosts. At the same time, the Centers for Disease Control (CDC) affirmed that there are no specific treatments for the 2022 monkeypox virus infection; existing antivirals shown to be effective against smallpox may slow monkeypox spread. A smallpox vaccine JYNNEOS (Imvamune or Imvanex) may also be used to prevent infection.

INTRODUCTION

The monkeypox virus was discovered in late 1958 in Copenhagen during two outbreaks of a smallpox-like disease in a cynomolgus monkey colony. Before the eruptive phase of the disease, which was characterised by a maculopapular rash, no clinical signs were observed. The virus was named monkeypox virus because it resembled other known poxviruses.

Several other outbreaks of monkeypox were reported in captive monkey colonies in the United States and the Netherlands between 1960 and 1968. Despite the deaths of many affected animals, no cases of monkeypox were detected in humans during these outbreaks, indicating that humans were not susceptible to monkeypox.[1, 2]

In 1970, as part of the national smallpox monitoring and eradication effort that was in place at the time in Africa, the first incidence of monkeypox in a person was documented. In one instance, a 9-month-old kid got fever, which was followed two days later by a centrifugal rash (i.e., a rash with the majority of lesions on the arms and legs). He was hospitalised to a hospital in Basankusu, Democratic Republic of the Congo, on September 1st, 1970. (DRC). The patient had severe cervical lymph nodes, mastoiditis, and otitis, and the monkeypox virus was found in his skin lesions. Monkeypox was treated and he was discharged, but measles struck and he passed away. Six further cases of monkeypox were found in humans in West African nations between September 1970 and March 1971. None of these patients had had a smallpox vaccination, and the majorities were young children.[3,4]

Monkeypox in humans remained an exclusively African disease, with sporadic cases diagnosed in forested areas of Central or West Africa and small outbreaks mainly in the DRC, until 2003, when the first cases outside Africa were reported. These incidents took place in the US and were connected to the Texas importation of Gambian pouched rats from Ghana. The rodents transmitted the virus to prairie dogs housed in the same exotic-animal facility, and the prairie dogs then infected humans, mostly young adults and children.[5, 6, 7]

Five infected patients were found in 2018: three in Singapore, one in Israel, and three in the United Kingdom. These imported cases were connected to people from Nigeria, the country that experienced a significant outbreak in 2017-2018.[6, 8, 9, 10, 11] With only very infrequent isolated instances in the United Kingdom and the United States, the disease has continued to be widespread in Africa. A number of cases of monkeypox were discovered in May 2022 in the UK, Portugal, and Italy, with the majority of those affected being guys who have intercourse with other men (MSM). Health authorities quickly determined that this outbreak was just getting started with this series.[12-15]

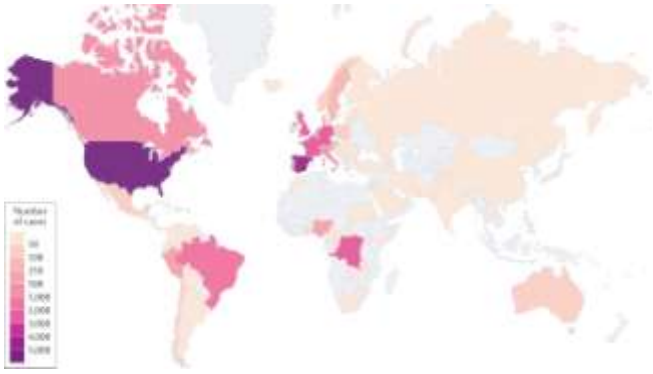

Figure 1: Geographical distribution of confirmed and suspected monkeypox cases during the outbreak between May and August 2022.[18]

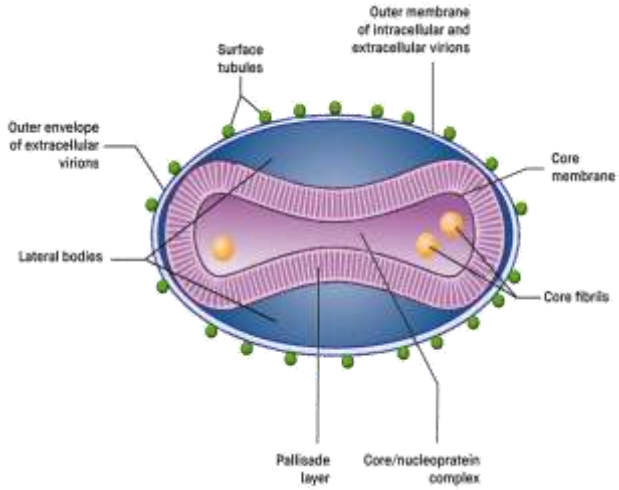

Figure 2: Structure of Monkeypox Virus

The cytoplasm of the infected cell is where poxviruses produce their DNA and RNA. The Poxviridae viral family, which is separated into two categories, contains numerous vital viruses. There are 16 families and 16 genera. Entomopoxvirinae, which infects insects, and Chordopoxvirinae, which infects vertebrates, are separated by their host range. Monkeypox, cowpox, and tanapox are only a few examples of the second group of viruses that cause illness in people. The Monkeypox virus, which causes a pox-like illness in monkeys, was identified in 1958 and given its name in 1971. Later, it was assigned to the Poxviridae family and Orthopoxvirus genus. MPXV is a brick-shaped virus with a 190 kb double-stranded DNA genome that is encapsulated and a dumbbell-shaped pleomorphic core that is between 140 and 260 nm in size.

The genome's ends are tightly packed. Unlike many DNA viruses, they are capable of producing the proteins required for transcription and subsequent replication. Viral ligands interact with cellular receptors like chondroitin sulphate or heparan sulphate to adhere to cell surfaces, which is the first step in viral entrance that depends on the cell type and viral clades. Viral fusion with cell membrane or endosomal uptake by a mechanism similar to macropinocytosis involving actin promotes posterior passage through cell membrane. [1, 19-23]

REPLICATION: The monkeypox virus replicates at the inoculation site after viral entrance; in human-to-human transmission, the inoculation site is the respiratory and oropharyngeal mucosa. In primary viremia, the viral load multiplies and then spreads to the neighbourhood lymph nodes.[24]

SIGNS AND SYMPTOMS: Monkeypox causes a rash on or near the genitals (penis, testicles, labia, and vagina) or anus (butthole), as well as other areas such as the hands, feet, chest, face, or mouth. Before healing, the rash will go through several stages, including scabs. The rash may appear as pimples or blisters at first and may be painful or itchy.

Other symptoms of monkeypox can include:

- Chills
- Fever
- Swollen lymph nodes
- Fatigue
- Headache
- Muscle aches and backache
- Respiratory symptoms (e.g. sore throat, nasal congestion, or cough)

You may experience all or just a few of the symptoms.

- Sometimes, people have flu-like symptoms before the rash.
- Some people get a rash first, then other symptoms, while others only get a rash.[25]

COMPLICATIONS:

- Bacterial superinfection of skin
- Permanent skin scarring
- Hyperpigmentation or hypopigmentation
- Permanent corneal scarring (vision loss)
- Pneumonia
- Dehydration (vomiting, diarrhea, decreased oral intake due to painful oral lesions, and insensible fluid loss from widespread skin disruption)
- Sepsis
- Encephalitis
- Death.[26]

INCUBATION PERIOD: The incubation period is 3-17 days. During this time, a person does not have symptoms and may feel fine. The illness typically lasts 2-4 weeks.[27]

RISK: The most susceptible group of people are those who live with or have intimate relationships (including sexual ones) with someone who has monkeypox. A person should take precautions to lessen their chance of contracting the disease if they live with someone who has monkeypox. A health care professional should evaluate a person who has monkeypox to see if they are healthy enough to be cared for at home and if isolation can be properly maintained there. When caring for patients who have monkeypox, healthcare professionals should adhere to infection prevention and control procedures to keep themselves safe. The chance of developing more severe symptoms and, in rare instances, dying from monkeypox may be increased in newborns, young children, and persons with underlying immune weaknesses. A woman's risk of unfavourable outcomes, such as miscarriage or stillbirth, might increase during pregnancy. Those who had the smallpox vaccine may be somewhat protected from monkeypox. However, it is doubtful that younger people received the smallpox vaccination because it was no longer administered in the majority of settings globally after the illness was declared eradicated in 1980. Those who have received the smallpox vaccine should continue to take preventative measures to safeguard both themselves and others.[28]

TRANSMISSION: As shown in Figure 3, the monkeypox virus is thought to have a variety of modes of transmission, all of which are linked to close contact with infected humans or animals. Human infections have been linked to animal contact, but it can be challenging to identify the exact animal

contact that led to a case in regions where bushmeat from a variety of species is frequently hunted or prepared, as well as where rodent infestations in homes are common. Investigations are still ongoing to determine the precise means of monkeypox transmission. Direct contact or exposure to infected animals can result in animal to human transmission. This is most frequently caused by bodily fluids like saliva, respiratory excretions, or exudate from cutaneous or mucosal lesions. Another exposure source may be the shedding of viruses through faeces. In endemic areas of Africa with limited resources and infrastructure, where people frequently sleep outside, on the ground, or near or travel to the forest where infected animals are much more common, exposure to the faeces of infected animals can be a significant risk factor. Households are forced to hunt and cook small mammals in areas with a shortage of resources, such as food, raising their risk of exposure to monkeypox. Despite being less frequent than animal-to-human transmission, human-to-human transmission typically involves respiratory droplets during prolonged face-to-face contact or contact with an infected person's lesions. Living in the same home or using the same dishes that have been used by an infected person are examples of contaminated objects or surfaces that are thought to increase the risk of viral transmission among members of the same household. In the midst of the ongoing monkeypox epidemic, it has also been noted that males who have sex with other males are more likely to contract the illness. Monkeypox can be transmitted through close contact, but the World Health Organization (WHO) does not yet know whether it is sexually transmitted or not. Whether the virus is transmitted from human to human or from animal to human, the pathogenesis and pathophysiology of monkeypox start with this transmission. Respiratory droplets are the most frequent source of human-to-human transmission, despite the stigma attached to it. Direct contact with infected people's mucocutaneous lesions as well as contact with contaminated objects or surfaces is listed in Figure 4. Similar to smallpox, the infectious process for monkeypox virus starts with exposure of the host's oropharyngeal or respiratory mucosa. The monkeypox virus replicates at the inoculation site after viral entry; in human-to-human transmission, the inoculation site is the respiratory and oropharyngeal mucosa. In primary viremia, the viral load multiplies and then spreads to the neighbourhood lymph nodes. In secondary viremia, the viral load travels through circulation to distant lymph nodes and organs. The entire procedure represents the incubation period, which can last up to 21 days and typically lasts seven to fourteen days. Monkeypox does not exhibit clinical manifestation during the incubation stage, so this period is not contagious. The prodromal stage can be related to monkeypox symptoms and clinical manifestation. Secondary viremia spreads from the lymphoid organs to the skin and tertiary organs like the lungs, eyes, gastrointestinal tract, etc. during the prodromal stage. An individual is thought to be the most contagious during the prodromal stage. This is largely because symptoms like lymphadenopathy and mucocutaneous lesions, among other various symptoms, are present. [24, 29, 30, 31]

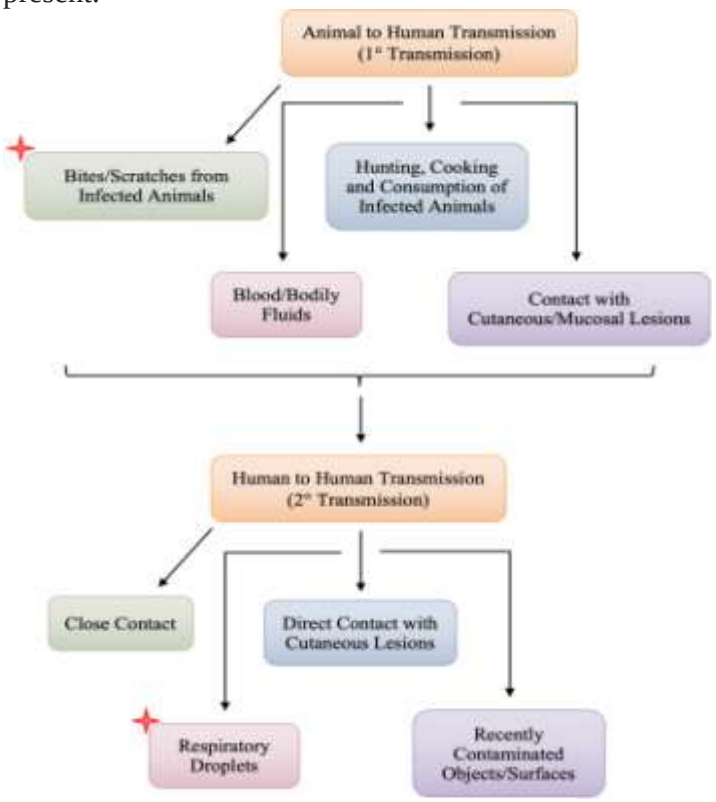

Figure 3: Suspected Modes of Transmission of Monkeypox to Humans[24]

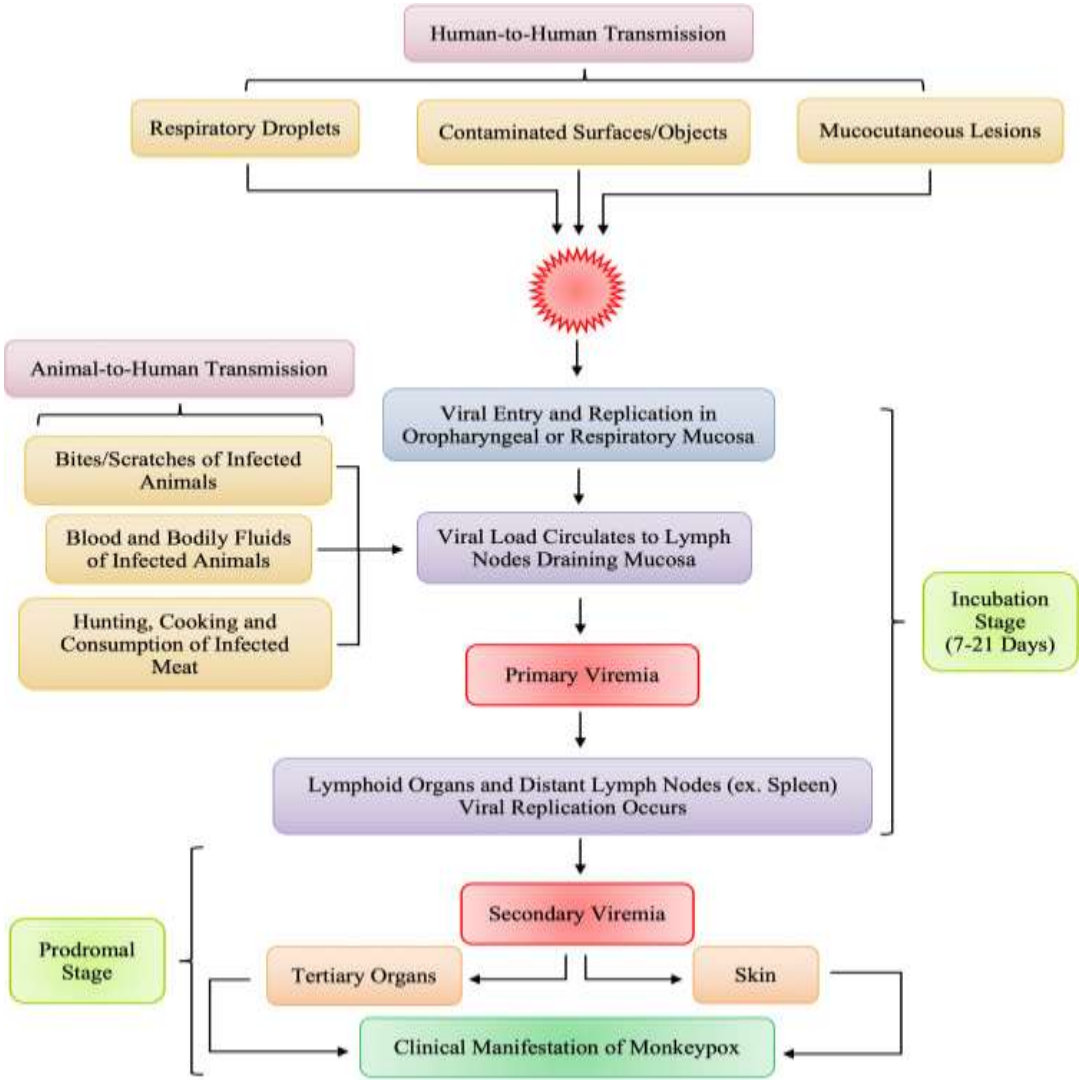

Figure 4: Human to human transmission[24]

PREVENTION: Prevention depends decreasing human contact with infected animal and limiting person-to-person spread.

- Avoid contact with infected animal (especially sick or dead animal).
- Avoid contact with bedding and other material contaminated with virus. Thoroughly cook all foods that contain animal meat or parts.
- Wash your hands frequently soap and water.
- Avoid contact with people who may infect with virus.
- Practice safe sex, including the use of condoms and dental dams.
- Wear mask that covers your mouth and nose when around others.
- Clean and disinfect frequently touched surfaces. Use personal protective equipment (PPE) caring for people infected with virus.[32]

DIAGNOSIS: Viral isolation, immunohistochemistry in tissues, molecular diagnosis, electron microscopy, and serology are some of the available laboratory techniques for diagnosis. Recombinase polymerase amplification (RPA), loop-mediated isothermal amplification (LAMP), restriction-fragment-length polymorphism (RFLP), and other molecular tests are among them. Monkeypox can be accurately diagnosed using a real-time PCR (RT-PCR) test on samples taken from skin lesions, the

throat, blood, and urine. These tests aren't offered commercially and are pricey. After 5 and 8 days of infection, specific IgG and IgM against MPX may be found using an ELISA (enzyme-linked immunosorbent assay). The distinct pox viruses are not distinguished by these, which are genus-specific. IgG can also be positive as a result of past exposure or vaccination against smallpox. IgG is less focused than IgM. A point-of-care diagnostic test called the Orthopox BioThreat Alert® (Tetracore, Rockville, MD) may quickly identify pox virus antigens in samples taken from skin lesions. As a result, it is helpful in field situations, although it is less sensitive than PCR and unable to differentiate between monkeypox and other pox viruses. The Indian Government has released guidelines for diagnosis of patients with monkeypox. Samples including skin scrapings, EDTA blood, serum urine, and nasopharyngeal/ oropharyngeal swab will be processed for orthopox genus-specific PCR. If positive, then the samples will be processed for monkeypox-specific PCR.[33, 34, 35]

TREATMENT: Monkeypox infection is usually self-limiting, and supportive care is advised. Individuals who are not at risk of experiencing severe symptoms can remain at home. Healthcare personnel should assess whether the infection prevention and control conditions in the home environment are met on a case-by-case basis.

Management of Mild or Uncomplicated Monkeypox: Symptomatic relievers, such as antipyretics, analgesics, or antiemetic medication, can be prescribed based on the patient's condition. Particularly in paediatric patients, adequate hydration, vaccination review, and nutritional assessment should be performed. Vitamin A supplementation, which has been shown to play an important role in wound healing, may benefit deficient patients. Mild skin rashes can be treated with supportive care to reduce irritation and promote healing. If a secondary bacterial infection is suspected, antimicrobial agents to eradicate Streptococcus pyogenes or Staphylococcus aureus are advised. Cellulitis, necrotizing soft tissue infection, and abscess should be monitored and treated as needed. Patients with monkeypox should also have their mental health checked. Long-term isolation can lead to anxiety and depression, which can be alleviated with psychological support.

High-Risk Patients and Severe or Complicated Monkeypox Management: The prognosis for monkeypox is determined by several factors, including age, previous vaccine history, current health status, and comorbidities. Children (especially those under the age of eight, who have the highest mortality rate), pregnant women, the immunocompromised, and individuals with poor skin integrity (e.g., atopic dermatitis or exfoliative skin conditions) should be hospitalised for monitoring and considered for antiviral treatment. According to smallpox research, confluent rashes or skin lesions numbering more than a hundred indicate severe disease. Monkeypox infection with progressive illness or complications, as well as high-risk patients, should be treated.Antiviral Agents: There is no specific treatment for monkeypox at this time. Several antiviral drugs that were previously used to treat smallpox or other orthopoxviruses have been repurposed to treat monkeypox infection.

1) Tecovirimat: Tecovirimat (ST-246 or TPOXX®) inhibits the spread of orthopoxviruses in vitro by blocking the p37 envelope protein, which is essential for virus wrapping. Tecovirimat, in particular, inhibits the formation of cell-associated enveloped virion (CEV) and extracellular enveloped virion (EEV), two virion forms responsible for virus egress and dissemination (Figure 5).

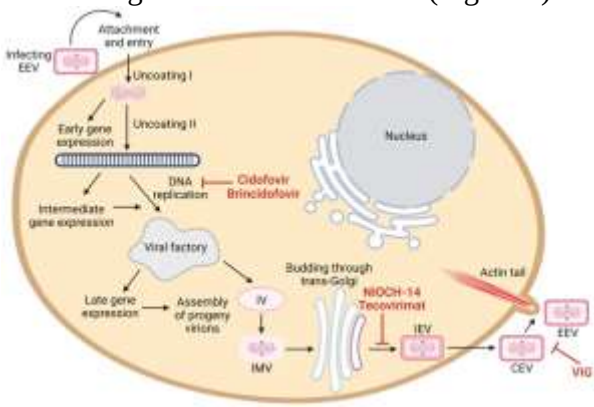

Figure 5: A diagram depicting the life cycle of the monkeypox virus and the mechanism of action of anti-poxvirus drugs.

Monkeypox virus, like all poxviruses, replicates in the cytoplasm of infected cells. Cidofovir and brincidofovir inhibit viral DNA polymerase; tecovirimat and NIOCH-14 prevent the formation of CEV and EEV; and VIG prevents virion infection of new cells. Biorender was used to create the figure. In vitro and in animal models, the antiviral potency of tecovirimat against monkeypox virus was evaluated. In cell culture assays, a submicromolar concentration of tecovirimat inhibited plaque formation of broad-spectrum orthopoxviruses, including monkeypox virus. The efficacy of tecovirimat against monkeypox virus was demonstrated in a variety of animal models, including ground squirrels, prairie dogs, and nonhuman primates. In nonhuman primates infected with a lethal dose of monkeypox, a dose of 10 mg/kg administered on day 4 or 5 post-infection for at least 7 consecutive days provided the highest survival rate and a decrease in viral load. Because smallpox had been eradicated, the FDA Animal Rule 21 CFR 314 Subpart I was used to develop and approve tecovirimat. Thus, tecovirimat effective doses in nonhuman primates that protect the animals from a lethal dose of orthopoxvirus infections were extrapolated and used in clinical trials. The safety and pharmacokinetics of an oral regimen of 600 mg twice daily for 14 days to a significant number of human volunteers were further validated in a phase III clinical trial (NCT02474589). To treat human smallpox diseases, tecovirimat is available as an oral (approved by the FDA on July 13, 2018) and intravenous (approved on May 18, 2022) formulation. The European Medicines Agency (EMA) and the Food and Drug Administration (FDA) have both given their approval for the oral formulation of tecovirimat (200 mg capsule) for the treatment of smallpox, monkeypox, cowpox, and complications from vaccinia in adults and children weighing 13 kg and above. A smallpox injection formulation was also approved for use in people weighing at least 3 kg. Prior to FDA clearance, tecovirimat was used to treat severe eczema vaccinatum and progressive vaccinia in conjunction with VIG and brincidofovir (CMX001) under an Emergency Investigational New Drug (EIND) application. An immunosuppressed patient with widespread cowpox virus infection and a patient with laboratory-acquired vaccinia virus infection both received treatment with tecovirimat in conjunction with VIG. In the US and the UK, tecovirimat has recently been used to treat monkeypox virus infection. There were no side effects noted over the course of treatment, and it is noteworthy that the patients in the UK experienced symptoms and viral shedding for a shorter period of time than the other patients who did not get tecovirimat.

2) Brincidofovir and Cidofovir: In the event of a smallpox outbreak, cidofovir (CDV) may be used as an emergency investigational treatment. Since 1996, the drug Cidofovir in intravenous form (marketed as Vistide) has been approved for the treatment of cytomegalovirus rhinitis in AIDS patients. A cytidine nucleotide analogue called cidofovir can prevent the synthesis of viral DNA (Figure 4). The use of cidofovir for treating poxvirus, however, may be hindered by cidofovir's shortcomings. Nephrotoxicity, a lack of oral bioavailability, and a diminished effect of cidofovir when given along with the smallpox vaccine are a few of the safety issues raised. The lipid-conjugated nucleotide analogue of cidofovir, brincidofovir (BCV, CMX001, HDP-CDV, TEMBEXA®), has better cellular uptake and conversion to the active form than cidofovir (Figure 5). The lipid moiety makes it easier for cells to absorb brincidofovir. Cidofovir is released from cells by intracellular phospholipase enzymes, and kinases then change it into cidofovir diphosphate. Due to its availability as an oral regimen and lack of nephrotoxicity, brincidofovir overcomes two of the main drawbacks of cidofovir. Under the FDA Animal Rule, brincidofovir's effectiveness and safety as a treatment for orthopoxviruses are assessed. The effectiveness of brincidofovir has been examined in mice infected with ectromelia virus, rabbits infected with rabbitpox virus, and prairie dogs infected with monkeypox virus since the non-human primate model is not ideal for studying the efficacy of brincidofovir due to the rapid metabolism of brincidofovir into its inactive

form. Additionally, the randomised phase 2 and phase 3 clinical trials of brincidofovir against different DNA virus infections were used to gather safety data. Bowel reactions, hepatotoxicity, elevations of the liver enzymes ALT and AST, and elevations of total bilirubin are among the notable mild side effects of brincidofovir. To achieve the required safety profile for treating smallpox, the recommended oral brincidofovir dosage is two doses of 200 mg once a week (two 100 mg tablets or 20 mL of suspension). Brincidofovir received FDA approval on June 4th, 2021 for the treatment of smallpox in adults, children, and neonates. Brincidovofir (CMX001) was used to treat severe eczema vaccinatum and progressive vaccinia in conjunction with VIG and tecovirimat. Three out of seven patients who had been given brincidofovir during the UK monkeypox virus outbreak experienced elevated liver enzymes (ALT and AST), and the medication was ineffective. Brincidofovir would complement tecovirimat in order to ensure a robust availability of therapeutics, particularly in the presence of the tecovirimat-resistant virus or in case of an emergency involving smallpox due to its synergistic effect with tecovirimat and approval for use in treating paediatric patients.

3) NIOCH-14: The State Research Center of Virology and Biotechnology, Russia, have recently created the tecovirimat analogue NIOCH-14. This orally accessible substance showed in vitro results that were equivalent to those of tecovirimat investigations, offering a promising possibility for the next wave of anti-orthopoxvirus medications.

4) Vaccinia Immunoglobulin (VIG):

The anti-vaccinia antibodies in VIG are produced from pooled plasma taken from healthy donors who received the vaccine and had high anti-vaccinia antibody titers. The poxvirus virion can be bound by the antibodies, which stops the virus from infecting new cells (Figure 5). The FDA has authorised two passive-immunization VIG intravenous (VIGIV) formulations for the management of vaccinia vaccination-related side effects (VIGIV Cangene and VIGIV Dynport; VIGIV product insert). In 1960, the first VIG therapy for severe vaccinia infections was made available. A total of 142 healthy male and female volunteers participated in three clinical trials to assess VIGIV's pharmacokinetic, pharmacodynamic, and safety profiles. VIG is made from pooled plasma obtained from healthy donors who received the vaccine against vaccinia and had high anti-vaccinia antibody titers. The antibodies can attach to the poxvirus virion and stop it from infecting fresh cells (Figure 5). The FDA has authorised the use of two passive-immunization VIG intravenous (VIGIV) formulations to treat side effects from vaccinia vaccination (VIGIV Cangene and VIGIV Dynport; VIGIV product insert). It was first introduced in 1960 to employ VIG to treat severe vaccinia infections. The pharmacokinetic, pharmacodynamic, and safety profiles of VIGIV were assessed in three clinical trials including a total of 142 healthy male and female volunteers. Although not yet formally recommended, prophylaxis may be given to an exposed person who cannot receive the smallpox vaccine.

Table: 1 Showing Symptoms/Complications And Alternative Treatment of Monkeypox

S. No.	Symptom/Complication	Alternative Treatment
1	Respiratory distress/Bronchopneumonia	Prophylactic antibiotics, nebulizer treatments, and non-invasive ventilation (ex. CPAP)
2	Sepsis	Antibiotics, supplemental oxygen, corticosteroids, and insulin
3	Gastrointestinal/mouth and throat ulcers	Oral/intravenous rehydration, oral/intravenous antiemetic and antidiarrheal medicines
4	Fever	Medicines to reduce fever, external cooling
5	Superinfection skin	Antibiotics administered orally or intravenously, incision and drainage, and sophisticated wound care (such as negative pressure wound therapy)
6	Inflammation/Lymphadenopathy	Oral/intravenous painkillers and anti-inflammatory drugs
7	Corneal infection	Corticosteroids, ophthalmic antibiotics, and antivirals
8	Skin scarring/Cellulitis/Skin lesions	To encourage re-epithelization, moist occlusive dressings are applied.

Vaccines and Vaccination: One of the major contributions of modern medicine was the successful vaccination programme that led to the eradication of smallpox. After carefully weighing the risks and benefits, vaccination of the general population was discontinued after smallpox was eradicated in 1980. The majority of people are vulnerable to the current monkeypox virus threat because almost all children and the majority of the world's population have little to no defence against orthopoxviruses. The Advisory Committee on Immunization Practices (ACIP) advised pre-exposure prophylaxis for medical professionals, laboratory workers, clinical laboratory staff, and other people who might be at risk of contracting the monkeypox virus in light of the rising number of monkeypox virus infection cases around the world. Here, we examine the effectiveness and security of ACAM2000 and JYNNEOS, two vaccines against monkeypox virus infections that are advised by ACIP. More than 100 million doses of ACAM2000 and more than 1000 doses of the JYNNEOS vaccine are currently present in the U.S. SNS. Approximately 2.4 million doses of the smallpox vaccine are currently held by the WHO in Switzerland, and more than 30 million doses have been pledged by various donor nations in case of a global emergency.

1) ACAM2000: The replication-competent vaccinia virus vaccine known as ACAM2000 was used to develop the Dryvax vaccine, one of the initial generations of vaccines used to eradicate smallpox. As of August 2007, ACAM2000 was the only orthopoxvirus vaccine FDA-approved for preventing smallpox. For those at a high risk of exposure, such as those in the armed services and those working in research facilities, ACAM2000 has been used as prophylaxis. Following a successful vaccination, an infectious lesion will develop where the ACAM2000 injection was given (15 jabs with a bifurcated needle are used to provide the single dosage of ACAM2000 over the deltoid muscle). Six clinical trials including 2893 patients who received ACAM2000 evaluated the drug's safety. The ACAM2000 vaccination can result in both minor and serious side effects, such as generalised and progressive vaccinia, eczema vaccinatum, accidental inoculation, encephalitis, myocarditis, and pericarditis. The frequency and severity of major adverse events could be decreased with improved pre-vaccination screening for contraindications, such as people with immunocompromised conditions, atopic dermatitis, HIV infection, and vaccine allergies. A vaccine with a stronger safety profile, such as an attenuated vaccinia virus vaccine, can alternatively be provided to people with contraindications.

2) JYNNEOS: JYNNEOS, also known as Imvamune or Imvanex, is a live attenuated vaccine made from a replication-deficient modified vaccinia virus Ankara (MVA). It was given FDA approval in September 2019 for the treatment of adults over the age of 18 who want to avoid contracting smallpox and monkeypox. JYNNEOS is given subcutaneously in two doses of 0.5 mL each, four weeks apart. Vaccine protection is not given until two weeks after the second dosage is finished. Since JYNNEOS is a live attenuated virus that cannot multiply, there is no risk of dissemination to other areas of the body or to other persons since there is no obvious cutaneous reaction following vaccination. As a result, it can be administered to people who are ineligible to receive live, replication-competent vaccines like ACAM2000. In studies using animal models, the effectiveness of JYNNEOS against monkeypox has been evaluated. To determine its effectiveness and safety against monkeypox in adult healthcare workers in the Republic of the Congo, a phase III clinical trial is now being conducted (NCT02977715). The efficacy and safety of the JYNNEOS vaccine were assessed in phase II and phase III clinical trials encompassing 22 studies and more than 7000 persons (healthy volunteers, HIV-positive participants, and people with atopic dermatitis or a history of atopic dermatitis). Since there have been no myocarditis or pericarditis reports, JYNNEOS is thought to have a better cardiac safety profile. The JYNNEOS vaccine has been suggested by ACIP as an alternative to ACAM2000 due to its overall enhanced safety profiles and efficacy. For persons who work with severe orthopoxviruses (smallpox and monkeypox) and less virulent

orthopoxviruses (cowpox viruses), the JYNNEOS booster is advised by ACIP every two years and every ten years, respectively. Furthermore, for people who received ACAM2000 as their primary immunisation, ACIP advises JYNNEOS boosters as an alternative to ACAM2000. There are currently no data available on the JYNNEOS's safety and effectiveness in treating certain demographics (e.g., children, pregnant women, and breastfeeding women). Special populations may be prescribed JYNNEOS in cases of high-risk exposure after carefully considering the risks and benefits in conjunction with their healthcare provider.[36-55]

CONCLUSION: Monkeypox outbreaks in non-endemic regions serve as a reminder that viruses and infectious illnesses do not respect national boundaries. Although no cases of the monkeypox virus or disease have been identified in India during the current outbreak, better preparation is still required. The key to responding is strict surveillance at the point of entrance, early detection, isolation, and case management. The main techniques are disease surveillance, contact tracing, and ring vaccination with smallpox vaccinations that are available and approved for monkeypox off-label use. India and other nations should take advantage of the outbreak in non-endemic nations to improve public health surveillance and health system capacity for outbreak and epidemic planning and response.

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