

# Monkeypox: A Systemic Review and Meta-Analysis after the Declaration of Global Emergency

Mohd Kaif\*<sup>1</sup>, Mohd Amaan<sup>2</sup>, Vaibhav Singh<sup>3</sup>

<sup>1,2,3</sup>Student, Department of Pharmaceutical Sciences, Seiko College of Pharmacy, Lucknow, Uttar Pradesh, India

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## ABSTRACT

A zoonotic orthopoxvirus called human monkeypox has symptoms that resemble smallpox. It is challenging to clinically distinguish the condition from varicella and smallpox. New tests are required for a more accurate and quick diagnosis because laboratory diagnostics are key to illness identification and surveillance. The majority of human infections occur in Central Africa, where surveillance in underdeveloped rural areas can be challenging but is achievable with the use of evidence-based technologies and training materials for public health professionals. Throughout western and central Africa, monkeypox is endemic. Previous outbreaks in the United States have been attributed to visitors returning from Africa or to animal imports from endemic regions. The present outbreak appears unusual, has intriguing epidemiology, and is usually associated with men having sex with other men. Cases are also happening in non-endemic nations without any relevant travel. Fever, rash, and lymphadenopathy are the three main signs of monkeypox. A 5 to 21-day incubation period is average. Prodromal symptoms of infection are immediately followed by an enanthem. One to three days later, the vesiculopustularexanthem appears, starting on the face and spreading centrifugally. It may also affect the genitalia and palmoplantar surfaces. Lesions are painful rather than irritating and can number from a few to thousands. Until all lesions are crusted over with complete re-epithelization, patients are regarded as contagious. Dermatologists may notice an increase in visits for fever with rash-suspect monkeypox. In addition to contact with lesions, bodily fluids, and contaminated items like bedding and towels, monkeypox can also spread by respiratory aerosols. Monkeypox appears to have a much lower basic reproduction rate than COVID-

19, so transmission should proceed more slowly than what has been seen in COVID-19 outbreaks.

**KEYWORDS:-** Monkeypox, zoonotic orthopoxvirus, smallpox, endemic

## I. INTRODUCTION

Monkeypox cases have been reported to WHO from 107 Member States in all 6 WHO regions since January 1, 2022. A total of 71,237 laboratory-confirmed cases and 1,097 suspected cases, including 26 fatalities, had been reported to WHO as of October 6 at 17h CEST. A significant majority of these cases since May 13th, 2022, have come from nations where there has never before been evidence of monkeypox transmission. The occurrence of cases and maintained chains of transmission in nations with no immediate or direct epidemiological ties to regions of West or Central Africa is a first [1]. The monkeypox virus (MPXV), a member of the genus Orthopoxvirus, is responsible for the zoonotic disease known as human monkeypox (family Poxviridae, subfamily Chordopoxvirinae). This group also includes the variola virus, which causes smallpox, and the vaccinia virus, which is utilized in smallpox vaccines. Members like the camelpox and cowpox viruses are less well-known. Since the worldwide eradication of smallpox in 1977, significant emphasis has been focused on monkeypox as a smallpox-like disease and potential agent of bioterrorism since it is clinically almost identical to common smallpox. When this virus first appeared in the Western Hemisphere in the spring of 2003 and caused a large number of cases in the US Midwest, it attracted further attention. Reviewing the present body of knowledge regarding human monkeypox, this article will focus on epidemiologic traits, clinical traits, diagnosis, therapy, and prevention [2].

## II. KEY FIGURES:



Fig -1: The global statistics of Monkey pox virus [1].

In week 39 (26 Sep - 02 Oct), there were 16.8% fewer weekly reported new cases worldwide than in week 38 (19 Sep - 25 Sep) (n = 3,662 cases). The Region of the Americas (86.3%) and the European Region (12.1%) received the majority of the cases recorded in the previous four weeks. United States of America (n = 26,723), Brazil (n = 8,147), Spain (n = 7,209), France (n = 4,043), United Kingdom (n = 3,654), Germany (n = 3,640), Peru (n = 2,587), Colombia (n = 2,453), Mexico (n = 1,968), and Canada (n = 1,400) are the 10 most impacted nations in the world. Together, these nations are responsible for 86.8% of all recorded cases worldwide<sup>1</sup>. 26 nations have noted an increase in the weekly number of cases during the last 7 days, with Nigeria reporting the largest increase. In the previous 21 days, 39 countries have reported no new cases. One country reported its first case in the past seven days. The following nation have reported their first case in the previous seven days: Viet Nam (03 October). Global data are information gathered from open sources. These statistics mostly comprise cases that have been recorded from public and authorized national sources. The epidemic curve below displays the total number of cases broken down by week and case reporting date [1].

## III. HISTORY

In 1970, two years after the last occurrence of smallpox in the region, the first case of monkeypox was identified in a male in the Basankusu district of Equateur Region, Zaire. Clinically, it is similar to smallpox, although there are significant epidemiological differences [3]. The Democratic Republic of the Congo has been declared to be home to this illness. According to studies, the Congo basin and West Africa's rural rainforest areas have been the main targets of virus epidemics from the Central and West African clades. In the West African clade, there are fewer cases of the illness, fewer fatalities, and less

human-to-human transmission. In West Africa, just 10 cases have been documented since 1970; in the United States, 81 cases (41% laboratory confirmed) were reported in 2003[4].

## IV. CAUSATIVE AGENT

As an orthopoxvirus, MPV is genetically distinct from other variola, vaccinia, ectromelia, camelpox, and cowpox viruses as well as other members of the Poxviridae family. At the State Serum Institute in Copenhagen, it was originally determined to be the root of a pox-like sickness in captivity monkeys in 1958. Since the eradication of smallpox, monkeypox is recognized as the most significant orthopoxvirus infection in humans. The vast range of hosts that MPV possesses, in contrast to the variola virus, has allowed it to maintain a reservoir in wild animals while sporadically infecting humans and has prevented its universal eradication by human immunization[5]. The scope of published information on the physical and chemical characteristics of MPV is constrained. The morphological characteristics of other poxviruses are present in MPV. It has a brick-like form and measures roughly 200 by 250 nm[6]. The virus is relatively resistant to desiccation in both heat and cold and is resistant to ether. According to heat stability studies, heating for 20 minutes at 40 C did not significantly reduce the infectivity of the sample, whereas heating for 20 minutes at 50 or 56 C resulted in either a nearly total (92.3%) or complete loss of infectivity<sup>7</sup>. The amount of infectious virus lost after up to 12 cycles of freezing and thawing was just 0.2 to 0.6 log<sub>10</sub>. Over 15 months, the stability of viral stocks kept at various temperatures was investigated. The infectivity titer of stocks kept at 4 C remained constant after 6 months, however at -20 C and -70 C, there was a loss of infectious virus of 2.2 log<sub>10</sub> and 1.5 log<sub>10</sub>, respectively. The loss was 2.5 log<sub>10</sub> at 4 C, 3 log<sub>10</sub> at -70 C, and more than 4 log<sub>10</sub> at -20 C after 15 months of storage[7]. MPV is also

rendered inactive by several substances, including formaldehyde, sodium dodecyl sulfate (SDS), chloroform, methanol, and phenol[7,8]. No specific sexual orientation is associated with the monkeypox virus, which can infect anyone. There are a number of causes for this increase, including the lack of social distance, which is known to increase the risk of viral infections, and the observation of certain cases from attendees of festivals, saunas, and parties[9].

### V. EPIDEMIOLOGIC CHARACTERISTICS

Sub-Saharan Africa has likely had monkeypox for thousands of years since humans first contracted the virus through close contact with diseased animals. MPXV's reservoir is still a mystery. The reservoir, however, is likely to be one or many species of rodents or squirrels that live in the secondary forest of central Africa, as evidence suggests that monkeys are inadvertent hosts, just like humans are[10]. In the first epidemiological studies conducted between 1970 and 1979, 47 cases of human monkeypox were found close to rain forests in sub-Saharan Africa, of which 38 cases occurred in the DRC and the remaining cases in Cameroon, the Central African Republic, Gabon, Cote d'Ivoire, Liberia, Nigeria, and Sierra Leone[11,12]. The bulk of human monkeypox cases each year are still reported from the DRC. Infections have also recently been reported in the Central African Republic, the ROC, and Sudan[13,14,15], though it is unclear whether these infections were brought about by travel across the DRC border or by the prevalence of local disease in those countries. The distribution of cases will be better understood with the use of improved phylogeography and georeferencing of human

cases, and these results can be utilized to create more precise ecological models of monkeypox transmission[16,17]. In-country outbreaks of monkeypox among people and captive prairie dogs occurred in the United States in 2003, and traceback investigations indicated a shipment of wild rodents from Ghana as the most likely source[18,19]. Since the beginning of May 2022, cases of monkeypox have been recorded in non-endemic countries, and they have continued to be reported in many endemic countries. Most confirmed patients with travel histories cited trips to Europe and North America, as opposed to West or Central Africa, where the monkeypox virus is common. For the first time, a large number of monkeypox cases and clusters have been noted concurrently in endemic and non-endemic countries across a variety of geographical regions<sup>20</sup>. The majority of documented instances to date have mostly, but not exclusively, involved males who have sex with men and have been discovered through sexual health or other health services in primary or secondary health-care facilities. To stop the disease from spreading further, WHO is working with the relevant health authorities? To educate communities at risk and the wider public about monkeypox and how to stay safe, WHO is providing countries with information on surveillance, laboratory work, clinical care, infection prevention, and control, as well as risk communication and community involvement? To support efforts to strengthen laboratory diagnosis, disease surveillance, readiness, and response activities to prevent new infections, WHO is also closely collaborating with nations in Africa, regional institutions, and technical and financial partners[20].

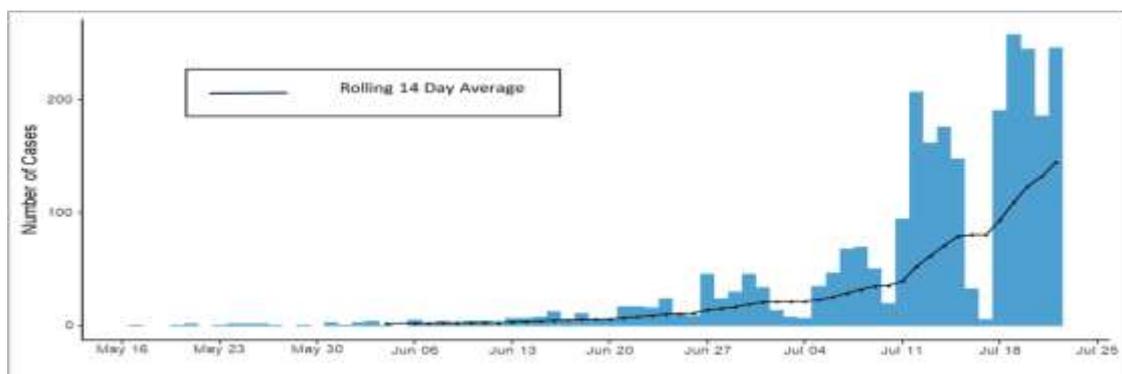


Fig -2: FIA monkeypox epidemiological curve is shown above (for 2,657 cases with available reporting dates) to July 22, 2022[21].

## VI. CLINICAL CHARACTERISTICS OF HUMAN MONKEYPOX VIRUS

Human monkeypox has several clinical traits with the discrete or semi confluent forms of ordinary or modified smallpox. The incidence and severity of certain clinical characteristics did not change by sex, age, or vaccination status, but they did[22]. By July 27, the CDC had received case report forms for 1,195 (41%) cases. Ninety-four percent of the instances, or 99% of those for whom information was available, involved men and occurred within the three weeks before the onset of symptoms. Out of the 88% of instances for which data were available, 41% involved non-Hispanic

White (White) individuals, 28% involved non-Hispanic Hispanic or Latino (Hispanic) individuals, and 26% involved non-Hispanic Black or African American (Black) individuals. Among those with monkeypox for whom data were available, 42% did not report the normal prodrome as their initial symptom, 46% had one or more genital lesions while unwell, and 41% were HIV-positive. According to data, racial and ethnic minorities as well as gay, bisexual, and other males who have sex with men have been disproportionately infected by broad community transmission of monkeypox[23].

**Table -1:** Individuals with monkeypox in the United States from May 17 to July 22, 2022[23].

Characteristics	No. (%)
<b>Total</b>	<b>1,195(100)</b>
<b>Gender identity (1,195)</b>	
Man	1,178(98.7)
Transgender man	3(0.3)
Woman	5(0.4)
Transgender woman	5(0.4)
Prefer not to answer	4(0.3)
Missing	0(-)
<b>Race and ethnicity (1,054)</b>	
Asian, non-Hispanic	48(4.6)
Black, non-Hispanic	276(26.2)
White, non-Hispanic	428(40.6)
Hispanic	296(28.1)
Multiple races, non-Hispanic	6(0.6)
Missing	141

A person of any age who has a localized or generalized rash (at any stage, macular, papular, vesicular, or pustular phase), as well as anogenital complaints (such as ulcers), with sudden onset of symptoms since March 15, 2022, is considered to be a suspected case after ruling out other differential diagnoses (including other sexually transmitted infections [STIs]). Additionally, this individual exhibits one or more of the following signs or symptoms: (i) abrupt onset fever (38.0°C), (ii) asthenia, (iii) myalgia, (iv) backache, (v) headache, and (vi) lymphadenopathy. In addition to meeting the above criteria, a subject is considered to be a probable case if they also exhibit one or more of the signs or symptoms listed below: (i) contact with a suspected, probable, or confirmed case of monkeypox within 21 days before the onset of symptoms; (ii) multiple or anonymous sexual encounters within 21 days before the onset of symptoms; (iii) hospitalization due to a clinical condition consistent with a suspected case; and (iv)

before the onset of symptoms, travel history to nations where monkeypox is common. An individual with a monkeypox infection that has been demonstrated in a laboratory setting (in a clinical sample utilizing dependable and validated procedures, such as real-time polymerase chain reaction [PCR] and/or nucleotide sequencing) is referred to as a verified case. In other nations, comparable working definitions have been suggested[24].

## VII. PREVENTION

According to data, smallpox vaccination may reduce clinical signs of infection and may have a protective effect against the monkeypox virus. The Aventis Pasteur Smallpox Vaccine (APSV) could be used for smallpox under an investigational new drug (IND) protocol. Currently, there are three smallpox vaccines in the US Strategic National Stockpile (SNS): JYNNEOSTM<sup>®</sup> (also known as IMVAMUNE,

IMVANEX, MVA-BN) and ACAM2000<sup>®</sup> are licensed for smallpox<sup>25</sup>. JYNNEOSTM<sup>®</sup> is an attenuated, non-replicating orthopoxvirus that is created from the modified vaccinia Ankara-Bavarian Nordic (MVA-BN strain). It is now approved by the US Food and Drug Administration (FDA) and advised for persons 18 years of age and older who are at high risk for contracting smallpox or monkeypox disease. According to historical statistics, vaccinating against monkeypox with smallpox was about 85% successful<sup>[25]</sup>. ACAM2000<sup>®</sup>, (Smallpox [Vaccinia] Vaccine, Live), a replication-competent vaccine, has been granted approval by the U.S. Food and Drug Administration (FDA) for use in those who have been identified as having a high risk of contracting smallpox. Since the vaccination lacks the variola virus, it cannot spread smallpox. It contains the vaccinia virus, a member of the Orthopoxvirus genus and the poxvirus family. Rash, fever, and body and headaches can all be symptoms of the vaccine virus. The vaccinia virus can cause serious difficulties in a certain category

of people, especially those who have impaired immune systems. ACAM2000<sup>®</sup> is injected intravenously in a single dose by the multiple puncture method<sup>[26]</sup>.

Because the monkeypox virus is spread through close body contact and contact with an infected person's bodily fluids, it can be prevented by avoiding close contact with an infected person's rash and by not sharing bedding, clothing, or eating utensils. After coming into touch with suspected instances, it's crucial to wash hands with soap or alcohol-based hand sanitizers. Using personal protective equipment (PPE) when providing care for those who are afflicted with the virus is also highly advantageous. To avoid the spread of zoonotic diseases, animal management and contacts with non-vaccinated animals, like rodents and primates, are crucial. Avoid touching sick or dead animals, and promptly discard any objects they come into contact with. Depending on how severe their symptoms are, infected people must be kept at home alone<sup>[27]</sup>.

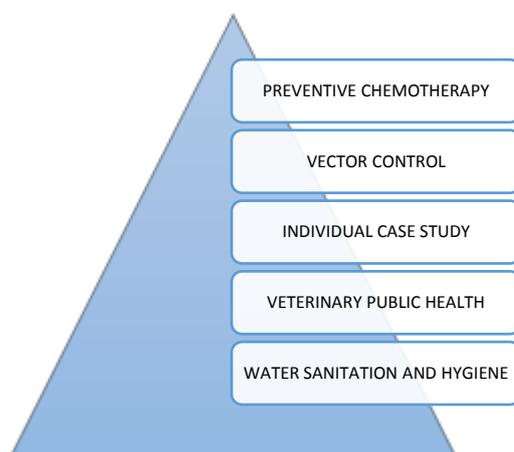


Fig -3:Prevention of monkeypox

### VIII. DIAGNOSIS

For public health and healthcare workers (HCWs), monkeypox poses difficulties in terms of surveillance and laboratory capabilities. Monkeypox is typically endemic, although it has recently been reported to have spread to non-endemic countries, with instances rising in Europe,

North America, and Australia. This might be a result of more infected people traveling, a lack of surveillance procedures, and laxer COVID-19 regulations. Additionally, since 1982, no one has received the smallpox vaccine, which offers about 85% protection against monkeypox infection<sup>[28]</sup>.

Table -1: Criteria for diagnosing patients with cases of chickenpox, smallpox, and monkey pox<sup>[6]</sup>.

Variable	Monkeypox	Smallpox	Chickenpox
Incubation period, days	7-17	1-7	12-14
Prodrome period, days	1-4	0-2	0-2
<b>Symptoms</b>			
Fever, severity	Moderate	Severe	Mild or none

Malaise, severity	Moderate	Moderate	Mild
Headache, severity	Moderate	Severe	Mild
Lymphadenopathy, severity	Moderate	None	None
<b>Lesions</b>			
Depth (diameter in mm)	Superficial to deep (4-6)	Deep(4-6)	Superficial(2-4)
Distribution	Centrifugal (mainly)	Centrifugal	Centripetal
Evaluation	Homogenous rash	Homogenous rash	Heterogeneous rash
Time to desquamation, days	14-21	14-21	6-14
Frequency of lesions on palms or soles of feet	Common	Common	Rare

Laboratory confirmation is necessary for a conclusive diagnosis, even though clinical characteristics can help differentiate poxvirus infections from other causes of vesiculopustular rashes. Monkeypox can be diagnosed in the lab using some assays, including virus isolation, electron microscopy, PCR, IgM and IgG, ELISA, immunofluorescent antibody assay, and histopathologic evaluation. Unfortunately, a lot of

these techniques lack specificity and cannot distinguish between MPXV infection and infection with other poxviruses. For instance, histopathologically, the lesions of monkeypox are comparable to those of other viral exanthems (such as those caused by variola, cowpox, varicellazoster, and herpes simplex viruses) and include spongiosis, cutaneous edema, and acute inflammation[2].

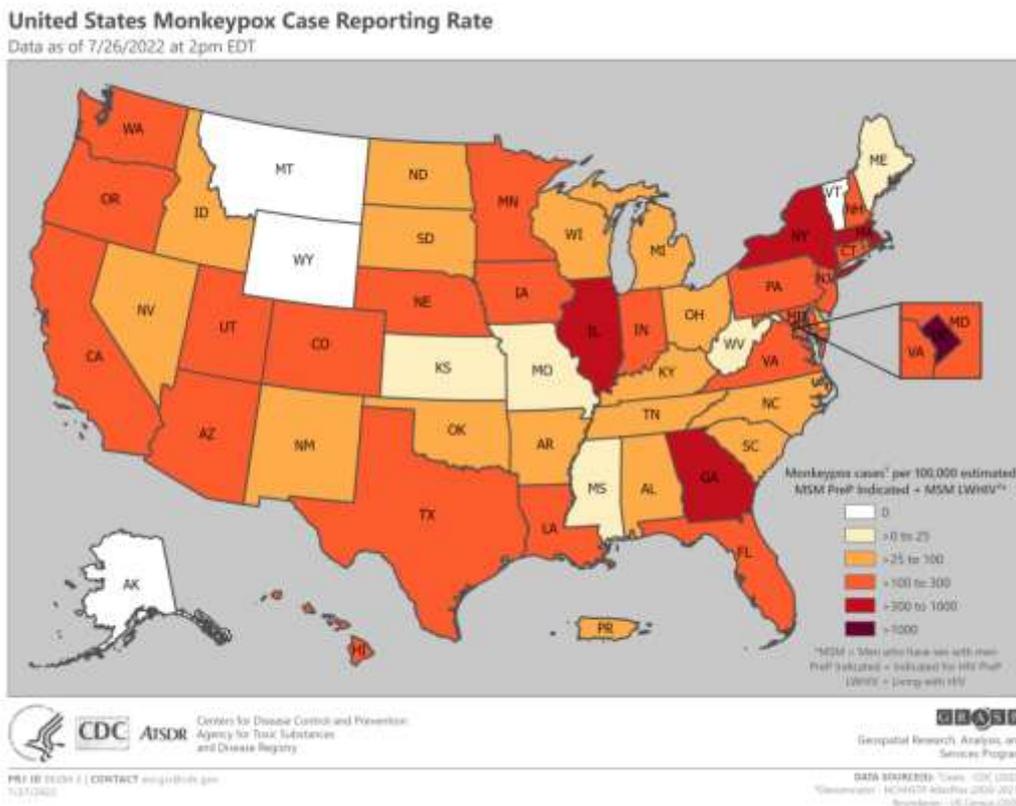


Fig -4:Case frequency and diagnostic rate for monkey pox[21].

## IX. TREATMENT

### 1.1. Enhancing Supportive Care

The majority of monkeypox patients heal without any medical assistance. To reduce gastrointestinal fluid losses, those with gastrointestinal symptoms (such as vomiting or diarrhea) will need oral or intravenous rehydration[29].

### 1.2. Antivirals

Monkeypox cannot be treated with commercially available antiviral medications, although there are (at least) two oral experimental medicines that have shown promise in treating orthopoxvirus infections (ST-246<sup>®</sup>, SIGA Technologies, Inc., New York, USA; and CMX-001<sup>®</sup>, Chimeix, Inc., Durham, NC, USA). Both medications can be administered orally and have successfully passed phase 2 safety and efficacy trials in people[29]. Antivirals should be taken into account in cases of severe illness, immunosuppressed individuals, children, pregnant and lactating women, complicated lesions, and when lesions develop close to the mouth, eyes, or genitalia[30]. In adults and children weighing at least 13 kg, TPOXX<sup>®</sup> is prescribed to treat human smallpox sickness brought on by the variola virus. Because adequate and well-controlled field trials have not been possible and because it is unethical to intentionally produce smallpox in humans to assess the efficacy of a medicine, the effectiveness of TPOXX<sup>®</sup> for treating smallpox sickness has not been established in humans[31].

### 1.3. Vaccine

The World Health Organization (WHO) ultimately declared smallpox eradicated from the world in 1980 as a result of an extensive vaccination campaign against the disease that had been started in 1967. In the USA, routine smallpox immunization of the populace was stopped in 1972. Although routine vaccination against smallpox was subsequently terminated in the early 1980s in the UK and 1990 in the USA, the British and American armed forces continued smallpox immunization for many years. Although there was knowledge of a potential bioterror threat before September 11, 2001, taking precautions wasn't seen as vital. However, the anthrax attacks through the US mail placed the bioterrorism threat into sharp attention after September 11, 2001. The smallpox virus (variola virus) is a bioterrorist agent of particular concern and, for many reasons, makes a perfect terrorism weapon of mass destruction<sup>32</sup>. Vaccinia immune globulin (VIG) is frequently used to treat major side effects that are caused by the smallpox vaccine itself. Although it is not currently approved in these circumstances, VIG may be required as prophylaxis in patients for whom pre-exposure smallpox vaccination is contraindicated (such as those with eczema or pregnant women). For the treatment of patients with progressive vaccinia, eczema vaccinatum, severe generalized vaccinia, extensive body surface involvement, or periocular implantation following accidental inoculation, the FDA has granted licenses to two intravenous formulations of VIG (VIGIV Cangene and VIGIV Dynport)[32].

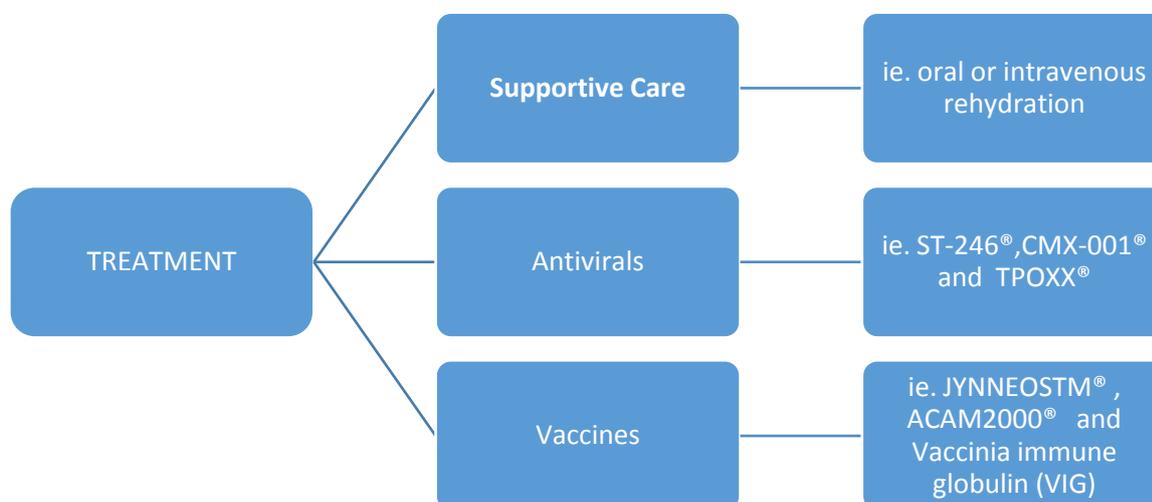


Chart -1: Treatment of Monkeypox virus

## X. FUTURE RECOMMENDATIONS

Monkeypox is endemic in Central and West Africa, unlike COVID-19, and is considerably less contagious than the coronavirus. Since the COVID-19 pandemic, additional infectious diseases have been overlooked, as shown by the rising number of outbreaks. Worldwide travel and simple access to remote, likely monkeypox-endemic places are other factors contributing to a rise in global awareness. The ultimate eradication of monkeypox in Africa depends on concentrating on vaccination and disease surveillance activities and carefully observing the effects of such programs[27]. Proper environmental management to stop the spread of viruses from wild species to humans will be needed to stop any upcoming pandemics.

To find possible infections and how wild animals respond to them, more research on wildlife immunology and virology needs to be done[33]. By providing research money to organizations specializing in the creation of drugs and vaccines that would result in the complete eradication of disease, the government must design strategies to prioritize funding for research on previously known zoonotic viruses like monkeypox. The identification of hosts for these viruses in various regions of Africa, for example, will help with a better understanding and eventual eradication of the virus, as well as data coverage of certain traits. Improved descriptions of epidemic trends in terms of magnitude and duration, better characterization of the range of diseases and clinical conditions, including asymptomatic carriage and acquisition risk factors, and measurement of the risk of transmission are all linked to various types of interactions with clinical cases[34-37].

## XI. CONCLUSION

Most cases of monkeypox are found in the forests of central and western Africa. In contrast to smallpox, the illness is a typical zoonosis, meaning that most cases are brought on by close contact with an infected animal. Accurate and speedy laboratory diagnoses are crucial for managing an outbreak because the illness, symptoms in people can be extremely similar to those of smallpox, chickenpox, or other forms of vesiculopustular rash. As the world is still recovering from the COVID-19 pandemic's repercussions, this viral outbreak poses a significant threat to global public health. To better understand the variety of elements involved in disease transmission and distribution, the recorded increase in the frequency of human

disease requires deeper investigation and analysis. Advances in our knowledge of this essential zoonosis will assist in better direct prevention tactics and lessen human disease. There are still numerous mysteries concerning human disease, animal reservoirs, and the virus itself.

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