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MONKEY POX: AN UPCOMING THREAT IN WORLD; A SYSTEMATIC REVIEW

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ABSTRACT

Monkeypox is the most common orthopoxvirus infection in humans since the abolition of smallpox in the 1970s. Human monkeypox is a unique viral zoonosis native to central and western Africa that has lately erupted in the United States, North America, Spain, the United Kingdom, and Europe by May 2022. Because the virus can produce disease that is usually asymptomatic from other pox-like disorders, notably smallpox and chickenpox, laboratory identification is critical. People who were immunised for smallpox are probably to be immune to monkeypox infection. New medicines and vaccines give promise for the treatment and prevention of monkeypox; however, additional study is needed before they may be used in an endemic situation. Human monkeypox cases have grown in frequency and geographical distribution in recent years, but we still have a lot to learn about the disease's origin, epidemiology, and ecology. The monkeypox virus is a rising illness that poses a significant public-health danger. WHO urges all Member States, medical regulators at all levels, clinicians, healthcare and social service partners, as well as academic, research, and commercial partners, to take immediate action to curb local spread and, by extension, the number of co monkeypox crisis. As a result, there is an immediate need to focus on developing surveillance capacities that will give vital information for creating effective preventative, readiness, and response operations. This page discusses the symptoms, transmission, epidemiology, diagnosis, available vaccinations, and FDA-recommended treatments for monkey pox virus.

Keywords*: Monkey pox virus, Small pox, Vaccines, WHO*

1. INTRODUCTION

Virus that causes monkeypox is zoonotic, that is it can transfer from animals to people. It is a double-stranded DNA virus with an envelope that can also travel between people. [1,2] Monkeypox is from the family: *Poxviridae*, subfamily: chordopoxvirinae, genus: orthopoxvirus, and species: Monkeypox virus.[1] The research suggests that African rodents are the natural reservoir, despite the fact that the disease was initially discovered in captive monkeys (thus the name). [1]

Monkeypox can spread to people when they come into physical contact with an infected animal or those who are sick or dead. It is transmitted from one person to another by close contact with lesions, body fluids, respiratory droplets and contaminated materials such as bedding.[3] Transmission can also occur via the placenta from mother to foetus (which can lead to congenital monkeypox) or during close contact during and after birth[3]

Monkeypox is usually a self-limited disease with the symptoms lasting from 2 to 4 weeks, evidence of monkeypox virus infection has been found in many animals including rope squirrels, tree squirrels, Gambian poached rats, dormice, different species of monkeys and others [3]

Symptoms of monkeypox typically occurs in two period: 1) invasion period (lasts between 0–5 days) include a fever, intense headache, muscle aches, back pain, low energy, lymphadenopathy (swelling of the lymph nodes), back pain, myalgia (muscle aches) and intense asthenia (lack of energy).2) skin eruption: usually begins within 1–3 days of appearance of fever. It affects not only face palms of the hands and soles of the feet, oral mucous membranes, genitalia, and conjunctivae, as well as the cornea.[3]

New-borns, children and people with underlying immune deficiencies may be at risk of more serious symptoms and death from monkeypox. Complications from severe cases of monkeypox include skin infections, pneumonia, confusion and eye infections which can lead to loss of vision. Mortality rates of monkey pox virus are 1%–10% [4]

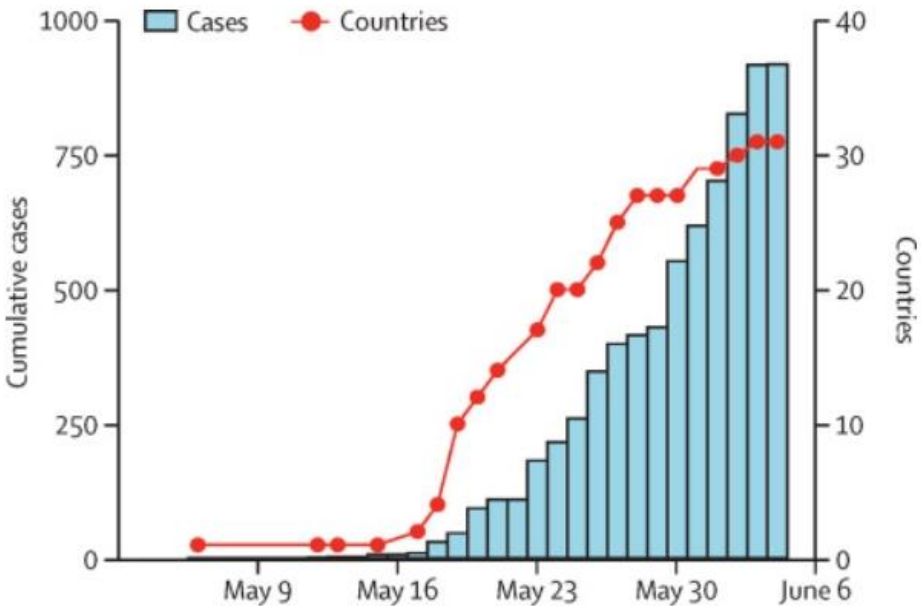
2. EPIDEMIOLOGY

Monkey pox is frequently found in central and west Africa, although infrequently, after travel from areas where monkey pox is widespread, cases of monkeypox are discovered in other nations outside of central and west Africa. An infant boy in Zaire who was 9 months old when the first human case was discovered in 1970 (now the Democratic Republic of the Congo, DRC). The Democratic Republic of the Congo has received the majority of reports of cases (DRC). Since then, monkeypox has spread to other African nations, primarily in Central and West Africa, and has become endemic in the DRC. The first cases of monkeypox outside of Africa were identified in 2003. [5]

Monkeypox has been regarded as the most significant orthopoxvirus infection in people since smallpox was eradicated worldwide in 1977. (First reported on 1970) and in 2006, a number of cases were initially recorded in Sudan. [4] Monkeypox instances were recorded in the UK, Spain, North America, and Europe in early May 2022. [6]

Cumulative number of confirmed cases (by confirmation date) since the first reported case in the 2022 outbreak, and cumulative number of countries reporting confirmed cases is shown in figure 1.

Figure 1: Showing Rapid expansion of the 2022 monkeypox outbreak [6]



3. DIAGNOSIS

The primary diagnostic tools for the monkey pox virus are symptoms and past travel experiences. In terms of biotechnology, transmission electron microscopy, PCR, tissue culture, and ELISA are used to identify viruses in pustule swabs. The spread of monkeypox in West Africa demands that public health authorities everywhere up their game. [7]

4. VACCINES

Smallpox vaccination was discontinued globally in 1980, when smallpox became the first human illness to be wiped. People who were immunised for smallpox are considered to be immune to monkeypox infection. A newer vaccine (MVA-BN, also abbreviated as Imvamune, Imvanex, or Jynneos) designed for smallpox was licenced in 2019 for use in eradicating monkeypox but is not yet generally available3. Smallpox immunizations are no longer accessible to the general population, and anyone under the age of 40-50 are uncommon to have been immunised.

There are three vaccination options for eliminating the monkey pox virus. Post-Exposure Prophylaxis (PEP) for Monkeypox Vaccine: This approach is currently considered "standard PEP" for monkeypox. Following monkeypox exposure, people can be immunised to help prevent sickness from the monkeypox virus. If administered within 4 and 14 days from the date of infection, immunisation may minimise symptoms but not prevent disease, but if given within 4 days of exposure, it can prevent disease formation. PEP is crucial to reducing outbreaks and stopping the spread of monkeypox.

Post-Exposure Prophylaxis (PEP) for Outbreak Response Monkeypox Vaccine: This enlarged method can be deemed "individual-directed PEP" for monkeypox in the present outbreak; public health professionals refer to it as "expanded PEP," "PEP plus-plus," or "PEP. Even if they have not had recorded contact to somebody with confirmed monkeypox, the PEP++ method tries to reach these persons for post-exposure prophylaxis. When used in conjunction with self-isolation as well as other preventive measures when signs first appear, PEP++ may help reduce the development of the disease in locations with a high number of monkeypox cases, implying a greater degree of monkeypox viral transmission.

Pre-Exposure Prophylaxis (PrEP) for Monkeypox Vaccination: This method involves delivering vaccine to someone who is at higher danger for monkeypox (for example, laboratory workers who handle specimens that might contain monkeypox virus). Two vaccines licensed by the U.S. Food and Drug Administration (FDA) are available for preventing monkeypox infection – ACAM2000 and JYNNEOS (also referred as Imvamune or Imvanex). People are considered completely immunised around 2 weeks after having their second JYNNEOS dose and 4 weeks after getting ACAM2000.

JYNNEOS:

- JYNNEOS includes a live virus that does not reproduce well in human cells.
- It is provided in two subcutaneous injections four weeks interval.
- The immunological response takes two weeks to fully emerge after the second dosage.
- FDA-approved for use in the prophylaxis of smallpox or monkeypox in persons aged 18 and up. Animal studies back up JYNNEOS's efficacy against monkeypox.
- There is no existing data on the effectiveness of JYNNEOS for PEP or PrEP. Concerns have been expressed by public health professionals regarding the paucity of effectiveness evidence for JYNNEOS, particularly because it takes two doses 28 days apart.
- Adverse reactions include injection site reactions such as pain, swelling, and redness.
- People with a severe allergy to any component of the vaccine (gentamicin, ciprofloxacin, egg protein) should not receive this vaccine.
- Safe for administration to people with HIV and atopic dermatitis.
- While there is no research in pregnant or nursing women, animal data shows no indication of reproductive damage.

ACAM 2000:

- ACAM2000 is a live *Vaccinia virus* vaccine that is replication competent.
- Administered as one percutaneous dose via multiple puncture technique with a bifurcated needle.
- The immune response takes 4 weeks for maximum development.
- A lesion will form at the location of the vaccine after a successful inoculation; the lesion will take four to six weeks or longer to heal.
- FDA-approved for treatment against smallpox; permitted for use by monkeypox through an Expansive Access IND, which involves informed permission and the completion of extra paperwork.
- The effectiveness of ACAM2000 is supported by human clinical trials and animal studies.
- There are no data on the efficacy of ACAM2000 for PEP or PrEP from the current outbreak.
- Adverse reactions include injection site pain, swelling, and redness; fever; rash; lymph node swelling; and complications from inadvertent inoculation.
- Individuals who have a serious allergy to any element of the vaccination should not get it. Furthermore, persons with significantly compromised immune systems should not take this vaccination.

ACAM2000 should not be given to people with the following conditions:

- Cardiac disease
- Eye disease treated with topical steroids
- Congenital or acquired immune deficiency disorders, including those taking immunosuppressive medications and people living with HIV
- Atopic dermatitis/eczema and persons with a history of atopic dermatitis/eczema or other acute or exfoliative skin conditions
- Infants less than 12 months of age
- Pregnancy

5. TREATMENT

There is currently no authorised therapy for monkeypox virus infections.

Tecovirimat (also known as TPOXX, ST-246), Vaccinia Immune Globulin Intravenous (VIGIV), Cidofovir (also known as Vistide), Brincidofovir (also known as CMX001 or Tembexa) are the medications currently approved by US-FDA for the treatment of monkeypox.

TECOVIRIMAT :

Adult and paediatric antiviral medicine for the therapy of monkeypox. Tecovirimat has been proven in animal studies to be beneficial in treating illness caused by orthopoxviruses. Clinical studies in individuals indicated the medication was effective and had just mild negative effects. [9]

The most common adverse reactions are: headache, nausea, abdominal pain, and vomiting with capsules and administration site reactions and headache with injections. TPOXX Injection is contraindicated in patients with severe renal impairment.

Table 1: Recommended Paediatric and Adult Dosage and Preparation Instructions TPOXX Injection for IV Infusion:

BODY WEIGHT	DOSAGE UP TO 14 DAYS	VOLUME OF TPOXX INJECTION
3 kg to less than 35 kg	6 mg/kg every 12 hours by intravenous infusion over 6 hours	0.6 ml/kg
35 kg to 120 kg	200 mg every 12 hours by intravenous infusion over 6 hours	20 ml
120 kg and above	300 mg every 12 hours by intravenous infusion over 6 hours	60 ml

VACCINIA IMMUNE GLOBULIN INTRAVENOUS (VIGIV):

VIGIV is used for the treatment of complications due to vaccinia vaccination.[9] CDC holds an expanded access protocol that allows the use of VIGIV for the treatment of orthopoxviruses (including monkeypox) in an outbreak. VIG can be considered for prophylactic use in an exposed person with severe immunodeficiency in T-cell function for which smallpox vaccination following exposure to monkeypox virus is contraindicated.[9]

VIGIV at a dosage of 6,000 U/kg should be given as soon as symptoms develop and are determined to be caused by a serious vaccinia-related consequence.

The most common adverse drug reactions are headache, nausea, rigors and dizziness.

VIGIV is contraindicated in isolated vaccinia keratitis, individuals with a history of anaphylaxis or prior severe systemic reaction associated with the parenteral administration of this or other human immune globulin preparations, IgA-deficient patients with antibodies against IgA and a history of IgA hypersensitivity, as it contains trace amounts of IgA (40 mcg/mL).

CIDOFOVIR:

It is an antiviral medicine licenced by the Food and Drug Administration for the treatment of cytomegalovirus (CMV) retinitis in individuals with acquired immunodeficiency syndrome (AIDS). 9 The CDC has an enhanced access procedure in place that authorises the use of stored Cidofovir for the treatment of orthopoxviruses (including monkeypox) during an outbreak. It is uncertain whether or whether a person with a serious monkeypox infection will recover from Cidofovir therapy, however it may be explored.

Dosage in monkey pox is 5mg/kg once weekly for two weeks followed by 5 mg/kg intravenously once every other week.

Adverse Reactions are nephrotoxicity, neutropenia, metabolic acidosis, decreased intraocular pressure, uveitis

Contraindicated in renal impairment, hypersensitivity reactions, direct intraocular injection of cidofovir is contraindicated.

BRINCIDOFOVIR:

Brincidofovir is an antiviral medication for the treatment of human smallpox disease in adult and pediatric patients, including neonates. CDC is currently developing an EA-IND to help facilitate use of Brincidofovir as a treatment for monkeypox.[9]

Common adverse reactions (occurring in at least 2% of TEMBEXA-treated subjects) were diarrhoea, nausea, vomiting, and abdominal pain and there are no contraindications.

Dosage form and strength: Tablets: 100 mg &Oral Suspension: 10 mg/mL

6. DISCUSSION

Until recently, monkeypox has not produced significant epidemics outside of Africa. Scientists have discovered no significant genetic alterations in the virus, and a senior WHO consultant stated last month that the recent increase in infections in Europe was most likely caused by sexual activity among homosexual and bisexual males at two raves in Spain and Belgium.

Too far, the Centers for Disease Control and Prevention in the United States has confirmed more than 3,300 cases of monkeypox in 42 nations where the virus is uncommon. And over 80% of occurrences occur in Europe. However, Africa has now seen almost 1,400 instances this year, with 62 deaths.

WHO has also advocated establishing a vaccine-sharing system to assist afflicted nations, which may result in doses being sent to wealthier countries such as Britain, which has the largest monkeypox outbreak outside of Africa — and has lately expanded its use of vaccines. WHO and others should do more to combat monkeypox in Africa and everywhere else, but a worldwide emergency declaration is unlikely to help. Surveillance, isolation of patients, and public education are all important factors in containing the outbreak. [10]

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