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MONKEYPOX: A NEGLECTED VIRAL ZOONOTIC DISEASE

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ABSTRACT

During period of the ongoing COVID-19 pandemic, the unexpected outbreak and worldwide spread of monkeypox has gained global attention. Monkeypox is a viral zoonotic disease caused by MPXV, which is an enveloped, linear, double-stranded DNA virus belonging to the Orthopoxvirus genus, of the Chordopoxvirinaesubfamily, within the Poxviridaefamily. Monkeypox virus (MPXV) is transmitted from human-to-human through direct contact with infectious skin or mucosal skin lesions, respiratory droplets, or indirect contact with contaminated objects or materials, as well as mother-to-child vertical transmission. It is also possibly sexually transmitted through semen/vaginal fluid, and the possibility of community transmission cannot be ruled out. The typical presentation of monkeypox includes prodromal symptoms, followed by a rash that usually begins within13 days of symptom onset, and the skin lesions can last for 24 weeks and then gradually resolve. A definite diagnosis of monkeypox virus infection requires nucleic acid amplification testing via the polymerase chain reaction method. Supportive care is essential along with treatment of complications affecting multiple organs of the body.
Keywords: Monkeypox, Orthopoxvirus, Lab Diagnosis, Transmission, Treatment

INTRODUCTION

Various emerging infectious virus disease outbreaks with zoonotic origin have occurred in recent years such as SARS-CoV-2, MERS-CoV, H7N9 (highly pathogenic avian influenza), Ebola virus, Chikungunya virus, Dengue Virus, and Japanese encephalitis virus, which are

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highly pathogenic in nature[1-3].It was observed that these viruses are spread by international travellers from time to time. One most recently re-emerging zoonotic diseases is monkeypox[4].

Monkeypox is a zoonotic viral disease caused by a double-strand enveloped DNA virus, a member of the Poxviridae family under the umbrella of the Orthopoxvirus genus, including smallpox. Monkeypox is transmitted mainly by direct animal contact via bodily fluids, blood, aerosol, or infected lesions. Furthermore, it can be through human-to-human close contact or respiratory secretions, similar to smallpox in terms of the clinical features and formation of serologically cross-reactive immunity. Interestingly, WHO reported its primary transmission through male-to-male close physical contact, causing the most recent surge, however this is not yet a confirmed route of transmission and is under study.

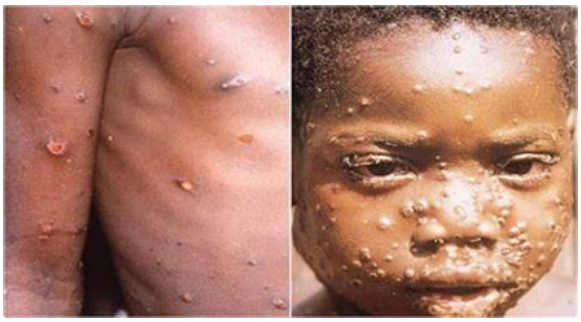

Fig. 1: **monkey pox diserase**

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CLINICAL MANIFESTATIONS

After exposure, it may be several days to a few weeks before you develop symptoms. Early signs of monkeypox include flu-like symptoms, including:

- Chills
- Headache
- Muscle aches
- Fatigue
- Swollen lymph nodes
- After a few days, a rash often develops.
- The rash starts as flat, red bumps, which can be painful.
- Those bumps turn into blisters, which fill with pus.
- Eventually, the blisters crust over and fall off — the whole process can last two weeks to four weeks.
- Sores in mouth, vagina or anus.
- Not everyone with monkeypox develops all the symptoms. In fact, in the current (2022) outbreak, many cases aren't following the usual pattern of symptoms. This atypical presentation includes only a few lesions, no swollen lymph nodes, less fever and other signs of illness. You can have it and not know it. Even if you don't show

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many signs of infection, you can spread still spread it to others through prolonged close contact. [5,6,7,8]

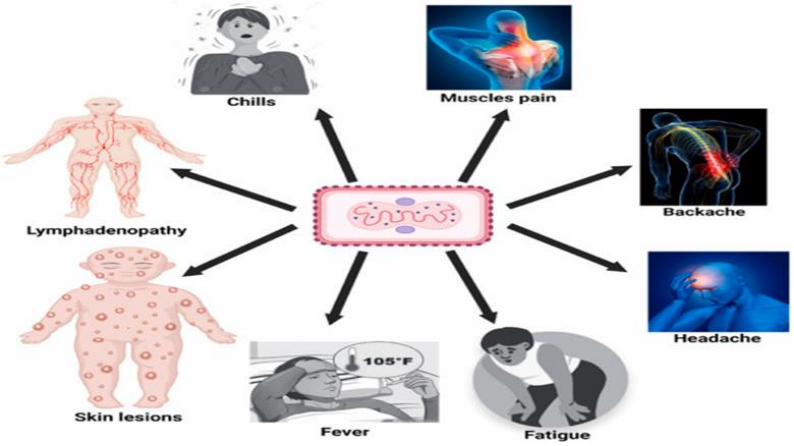

Fig. 2: **Clinical menifestation of monkey pox virus**

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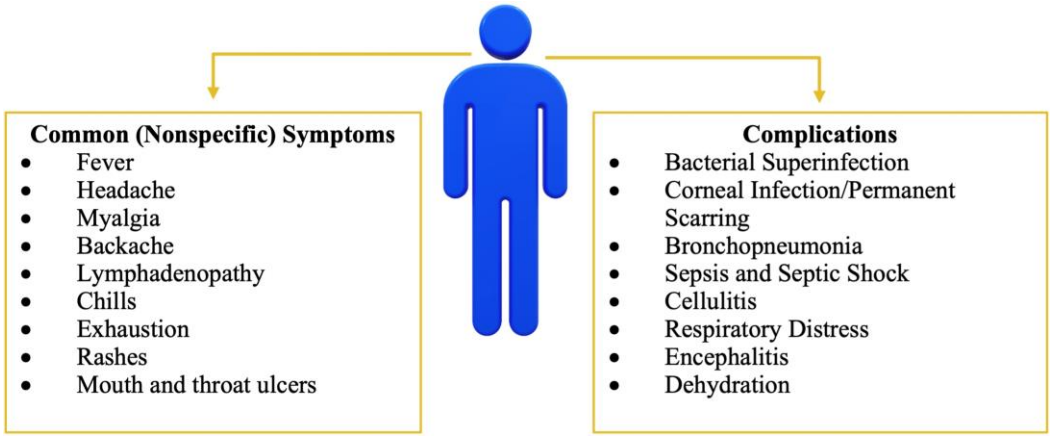

Fig. 3 : **clinical manifestation of monkey pox virus**

source:https://tse1.mm.bing.net/th?id=OIP.Wy4lHijnQd0i0gscVTt_VAHaDE&pid=Api&P=0

How it is transmitted to humans ?

- The MPV transmission occurs through contact with skin lesions of the infected animals, body fluids or respiratory droplets.
- The virus enters the body through the respiratory tract, broken skin, or mucous membranes (eyes, nose, or mouth). Transmission from animal to human may occur through scratch, bite, bush meat preparation, or direct or indirect contact with body fluids or lesion material [primary host to secondary host].
- Human-to-human transmission occurs through large respiratory droplets, sneezing, coughing, etc. Respiratory droplets do not travel more than a few feet; therefore, prolonged face-to-face contact is necessary for transmission to occur. Other transmission methods from human to human are direct contact with the viral lesion

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and body fluids and indirect contact with infected materials through clothing or infected linens.

- Mother-to-child transmission (MTCT) may also occur via the placenta (congenital Monkeypox), via close contact during and after birth. Although close physical is needed for the transmission of Monkeypox, it is not clear whether the monkeypox virus can be transmitted through sexual routes[9,10-18].

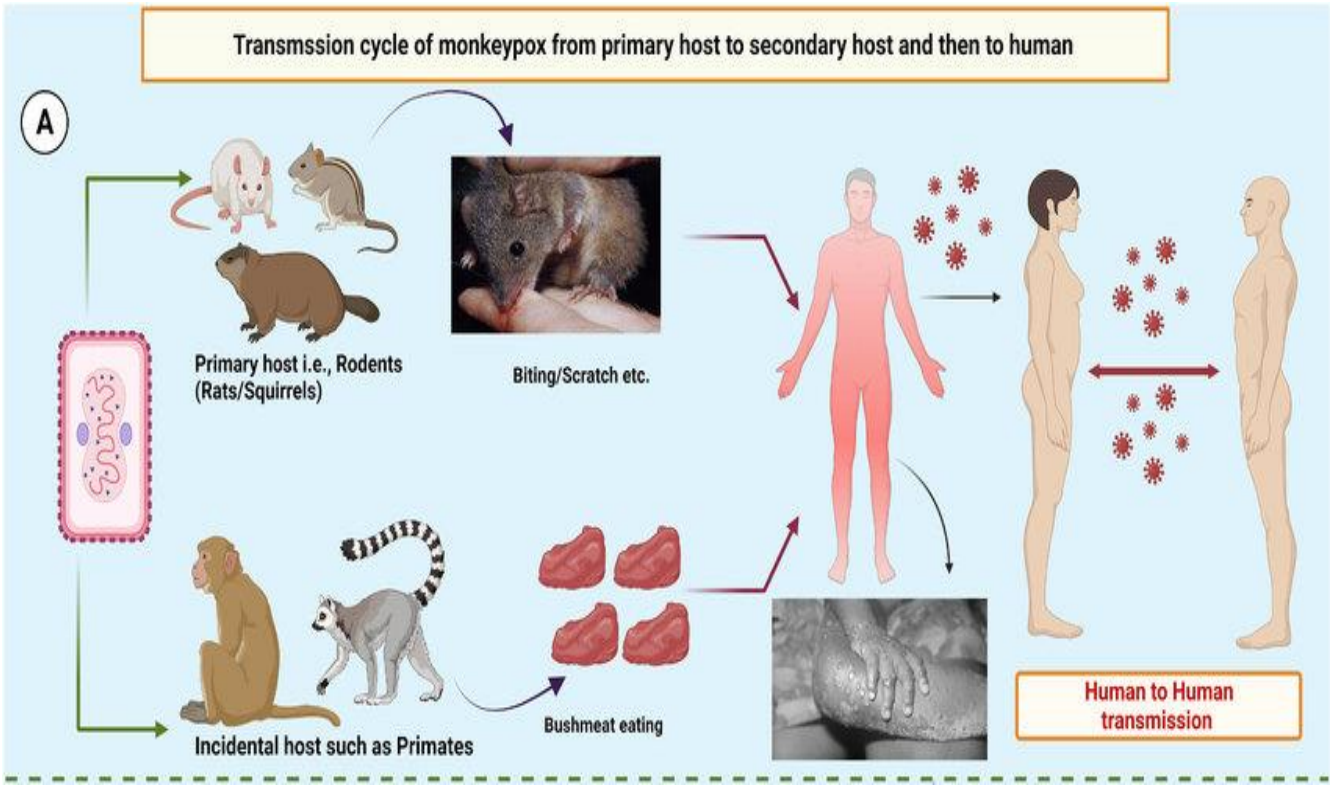

Fig. 4: **Transmission cycle of MPV**

Source
https://www.researchgate.net/publication/361421301/figure/fig1/AS:1171185337401344@1656243752309/

DIAGNOSIS and DETECTION

To diagnose cases of monkeypox, epidemiological and clinical characteristics are required. WHO has developed surveillance case definitions for the current monkeypox outbreak in non-endemic countries. [19]

Table 1 :**The definitions of cases of MPXV infection**.

Type of case	Definitions
Suspected	A person of any age presenting in a monkeypox non-endemic country with an unexplained acute rash.

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AND

1. Acute onset of fever (>38.5°C), Headache, Lymphadenopathy, Myalgia, Back pain, Asthenia.
2. The common causes of acute rash do not explain the clinical picture, such as: varicella zoster, herpes zoster,

Measles, Zika, dengue, chikungunya, herpes simplex, bacterial skin infections, and so on.

Probable

A person meeting the case definition for a suspected case

AND

1. Has an epidemiological link; direct physical contact with skin or skin lesions in the 21 days before symptom onset.
2. Reported travel history to a monkeypox endemic country1 in the 21 days before symptom onset.
3. Had multiple or anonymous sexual partners in the 21 days before symptom onset.
4. Has a positive result of an orthopoxvirus serological assay, in the absence of smallpox vaccination or other known exposure to orthopoxviruses.

Confirmed

A case meeting the definition of either a suspected or probable case and is laboratory confirmed for monkeypox virusby detection of unique sequences of viral DNA either by real-time polymerase chain reaction (PCR) and/or sequencing.

Discarded

A suspected or probable case for which laboratory testing by PCR and/or sequencing is negative for monkeypox virus.

Detection

The early and accurate laboratory testing of samples from cases is an essential part of the diagnosis and surveillance of this emerging infection. Confirmation of monkeypox depends on the type and quality of the specimen and the type of laboratory test. The recommended clinical specimen type for laboratory confirmation of MPXV includes specimens from skin lesion material, such as swabs of the lesion surface, exudate, or roof from more than one lesion, or lesion crust. Nasopharyngeal swabs and saliva are also important specimens for detection, while blood specimens are not usually used for diagnostic purposes [19, 20].

- **Nucleic acid amplification testing**

Identification of MPXV infection is based on nucleic acid amplification testing, using real-time or conventional polymerase chain reaction as the primary detection method for the detection of unique sequences of MPXV viral DNA [21]. The WHO suggested that if a specific MPXV test is unavailable, a positive polymerase chain reaction result for *Orthopoxvirus* is considered confirmation in non- endemic countries [22].

- **Antibody detection**

Antibodies of plasma or serum should not be used alone for diagnosis. Acute and convalescent sera can be used for MPXV-specific immunoglobulin M detection and immunoglobulin G detection. However, there is 130 antigenic cross-reactivity between MPXV and other orthopoxviruses[19].

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- **Electron microscopy**

Electron microscopy can be used to visualize potential poxvirus in a sample, but cannot distinguish MPXV from poxvirus. Furthermore, this method is highly technical and complex, requires expensive equipment and facilities, and only offers low detection sensitivity.

- **Virus isolation**

To date, the standard diagnostic method of infection is the isolation of MPXV from clinical samples. How- ever, MPXV should only be performed in laboratories with appropriate experience and containment facilities. Hence, this method is not optimal as a routine diagnostic procedure[19,20]. Virus isolation should be carried out in P2-level biosafety laboratories but technicians should take personal protective measures according to the stan- dards of P3-level laboratories

PREVENTION

- Monkeypox virus can be transmitted by close contact with the lesion or fluid secretions, the most important preventive measure is to avoid close contact with infected individuals and isolate them.
- Personal hygiene and avoiding contact are not the only methods of prevention. However, they are highly effective, there is a vaccine accepted for the prevention of monkeypox virus despite its non-specific nature, but cross-immunity with the pox virus may provide some protection against it.
- Currently, there are two live attenuated vaccines available in the U.S. (JYNNEOS, the non-replicating live vaccine approved by the US Food and Drug Administration (FDA) for both smallpox and monkeypox).
- FDA-approved vaccine Jynneos (Bavarian Nordic) protects against monkeypox. According to Adalja and Inglesby, an older-generation vaccine (ACAM2000, Sanofi Pasteur Biologics Co.) may be used off-label for monkeypox. Early detection and management of cases are important preventive measures in preventing the further spread of the disease.

❖ **TREATMENT**

- Many individuals infected with MPXV have a mild self-limiting disease course without specific treatment.
- However, the prognosis of monkeypox depends on many factors, such as initial health status, concurrent diseases, complications, and previous vaccination status.
- People who should be considered for treatment may include:
    1. Those suffering from serious diseases (such as haemorrhagic diseases, confluent lesions, sepsis, encephalitis, or other diseases requiring hospitalization).
    2. The immunocompromised population (for example, those with human immunodeficiency virus/acquired immunodeficiency syndrome infection, tumors, transplantation, and those receiving radiotherapy or high-dose corticosteroids).
    3. The paediatricpopulation, especially those under 8 years old.
    4. Pregnant or breastfeeding women.

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5. Those with a history of allergic dermatitis or allergic dermatitis, and those with other active exfoliative skin diseases (such as burns, pustulosis, varicella-zoster virus infection, herpes simplex virus infection, severe acne)
6. Those with one or more complications (e.g. secondary bacterial skin infection; bronchopneumonia; concurrent dis- eases, or other comorbidities)
7. Those with abnormal MPXV infection, including accidental implantation into eyes, mouth, or other anatomical parts (such as the genitals or anus), where MPXV infection may pose special hazards.

- Clinical treatment is primarily symptomatic and supportive, including alleviating symptoms, managing complications, and minimizing long-term sequelae.
- Monkeypox can have significant impacts on multiple organ systems in the host, compromising the protective barriers of skin and mucosal surfaces, provoking a robust focal inflammatory response in the lymphatics, and congestion in the lungs.
- In instances of heavy rash burden, exfoliation can be significant, subjecting patients to risks from dehydration and protein losses.
- Serious inflammation and bronchopneumonia can restrict air intake and diminish a patient's wliingness and/or ability to ingest fluids and food. co-infections (HIV, Malaria, varicella) and comorbidities(malnutrition) can also contribute to significant clinical menifestations of illness.[21]

A summary of clinical syndromes associated with monkeypox and potential treatment options for different resource settings is shown in figure 5.

System Affected/Syndrome	Treatment Objective	Therapeutic Considerations/Clinical Setting		Follow-up/Monitoring
		Developed	Low-Resource	
Respiratory tract	Maintain patent airways, prevent respiratory infection, atelectasis, and respiratory compromise	Suctioning of the nasopharynx and airways, incentive spirometry, chest physiotherapy, bronchodilation, oral/intravenous antibiotics for prophylaxis/treatment, nebulizer treatments, bronchoscopy, noninvasive ventilation (e.g., BiPAP or CPAP) [1], intubation/ventilation	Suctioning of the nasopharynx and airways, incentive spirometry, chest physiotherapy, bronchodilation, oral/intravenous antibiotics for prophylaxis/treatment	Respiratory rate, pulse oximetry
Sepsis	Hemodynamic stabilization	Oral/intravenous antibiotics, hemodynamic (e.g., intravenous fluid hydration and vasopressors), supplemental oxygen, corticosteroids, insulin	Oral/intravenous antibiotics, intravenous fluid hydration	Hemodynamic monitoring (e.g., pulse rate, blood pressure)
Gastrointestinal/mouth & throat sores	Minimize mucosal pain and disruption of food intake, promote lesion healing	Oral/topical analgesic medications	Oral/topical analgesic medications	Lesion burden, pain scale, food/fluid intake
Gastrointestinal/vomiting, diarrhea	Minimize gastrointestinal fluid losses	Oral/intravenous antiemetic and antidiarrheal medications, oral/intravenous rehydration	Oral/intravenous antiemetic and antidiarrheal medications, oral/intravenous rehydration	Frequency and volume of emesis and diarrhea, body weight, fluid intake/ouput
Fever	Prevent and treat episodes of fever	Antipyretic medications, external cooling	Antipyretic medications, external cooling	Routine temperature monitoring
Exfoliation, skin compromise	Minimize insensible fluid loss, promote lesion healing	Wash with soap and water or dilute water povidone-iodine solution, moisturized dressings, topical antibiotics (e.g., silver sulfadiazine), surgical debridement, skin grafts	Wash with soap and water or dilute water povidone-iodine solution, moisturized dressings, topical antibiotics (e.g., silver sulfadiazine)	Lesion count/rash burden, body weight, fluid intake/ouput
Superinfection skin	Prevention/treatment of secondary bacterial infections, promote lesion healing	Oral/intravenous antibiotics, incision and drainage, advanced wound management (e.g., negative pressure wound therapy)	Oral/intravenous antibiotics, incision and drainage	Fever, pain/tenderness, erythema, edema, exudate, warmth
Inflammation/lymphadenopathy	Minimize pain and decrease size of lymphadenopathy	Oral/intravenous anti-inflammatory/analgesic medications	Oral/intravenous anti-inflammatory/analgesic medications	Size of lymphadenopathy, pain/tenderness
Ocular infection	Prevent corneal scarring and vision impairment	Ophthalmic antibiotics/antivirals and corticosteroids; slit lamp examination	Ophthalmic antibiotics/antivirals and corticosteroids	Vision testing; repeat examination to assess recrudescence

Fig. 5: **Clinical syndromes associated with MPV and their potential treatments**

Source:
https://www.researchgate.net/publication/321766480/figure/tbl1/AS:669339292299275@1536594331491/Monkeypox-Clinical-syndromes-and-possible-treatment-options.png

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CONCLUSION

The recent apparent increase in human monkeypox cases across a wide geographic and non-endemic area and the potential for further spread have raised the level of concern for this emerging disease. It is now well known how the monkeypox virus (or MPXV) can spread.

More research is required though to better understand if the MPXV can be spread when someone has no symptoms, the frequency of its spread through respiratory secretions, the likelihood of a symptomatic individual spreading the virus through respiratory secretions, and other ways of transmission (i.e. through semen, vaginal fluids, urine, or feces). [22,23]

The most common outcome following an infection is scarring from the rash – however, more serious complications can arise, according to some research of monkeypox in humans. The evidence suggest that more severe complications and sequelae are found tobe more prevalent in particular among unvaccinated patients, which highlights the need to raise awareness and also the need to vaccinate all categories at risk including healthcare and sexual health workers. Therefore, we should pay high attention to scientific arrangement, strengthen the basic research on zoonotic poxvirus disease. To control the spread of MPX, it is critical to strengthen awareness and surveillance. The early diagnosis is key to prevent the epidemic of MPX, and the technical international cooperation is essential to reduce the risk of MPX.

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