



A REVIEW OF THE MONKEYPOX OUTBREAK IN INDONESIA IN 2022

Meiriani Sari^{1*}, Nany Hairunisa²

¹Department of Pediatrics, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia

²Department of Occupational Medicine, Faculty of Medicine, Universitas Trisakti, Jakarta, Indonesia

* Corresponding Author : E-mail : Meiriani_sari@trisakti.ac.id

ABSTRACT

Monkeypox disease (monkey smallpox) is a disease that has never been found in Indonesia since it was first discovered in humans in the Congo in 1970. So if there is one positive confirmed event, then the disease is an Extraordinary Event (KLB). This disease has become a global concern because since May 13, 2022, WHO has received reports of Monkeypox cases from non-endemic countries. It has expanded to 4 WHO regions: Europe, America, Eastern Mediterranean, and Western Pacific. Until now, further investigations and studies are still being carried out to understand more about the epidemiology, sources of infection, and transmission patterns in non-endemic countries that have reported new cases, such as Indonesia. Until now, no specific treatment has been proven to treat Monkeypox infection. Currently, the therapy used is symptomatic support. The antiviral tecovirimat, or TPOXX, developed by the European Medicines Agency (EMA) as a Monkeypox therapy in 2022 based on research, has not been marketed freely. In addition, antivirals such as cidofovir and brincidofovir have been shown to be effective against orthopox virus in vitro and in animal studies. However, the effectiveness of this drug against monkeypox in humans is not yet known. However, this disease can be prevented by vaccination. In Indonesia, the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine is recommended to prevent Monkeypox disease. The existence of the outbreak report is important to discuss, explore, and understand more about the disease and its management and prevention.

Keywords: *Antivirus, Outbreaks, Monkeypox, Vaccination*

INTRODUCTION

Monkeypox disease has never been found in Indonesia since it was first discovered in humans in the Congo in 1970, caused by the Monkeypox virus. On August 19th, 2022, one positive case was found in a 27-year-old male patient in Jakarta. As of September 15th, 2022, 2 suspects and 63 were discarded. From the distribution of 63 patients with discarded status covering ten provinces in Indonesia.¹

Monkeypox itself was first discovered in 1958 when an outbreak of diseases such as smallpox occurred in a group of monkeys that were kept for research.^{2,3,4} Common symptoms such as fever, headache, enlarged lymph nodes, and skin lesions can cause severe pain.⁵ This disease has clinical relevance in endemic areas of Africa, with outbreaks in the west due to international travel.⁶

According to the WHO, around 3-6% of cases can be fatal; unfortunately, the data on deaths based on cases in Africa before 2022 do not have data that is too representative. Monkeypox virus can heal itself without getting special treatment within a few weeks. As of August 2, 2022, 80 countries have reported approximately 24,000 cases of Monkeypox and five deaths have occurred since May 2022. Monkeypox has since become a disease of global

public health concern, as it was reported in previously non-endemic countries. Since May 13, 2022, WHO has received reports of Monkeypox cases originating from non-endemic countries, and currently, it has expanded to 4 WHO regions, namely Europe, America, Eastern Mediterranean, and Western Pacific.⁷⁻¹⁰

Until now, further investigations and studies are still being carried out to understand better the epidemiology, sources of infection, and transmission patterns in non-endemic countries that have reported new cases, such as Indonesia. There are reports of human-to-human transmission, considering the importance of cases in infected countries. In addition to the possibility of infectious animals in Indonesia, it is important to discuss, explore, and understand how to deal with this disease.^{1,2}

About Monkeypox

Monkeypox is a rare zoonotic disease caused by the Monkeypox virus.³ This virus is in the same family as viruses such as the variola virus that causes smallpox. Monkeypox virus contains double-stranded DNA and has a 200-250 nm brick-shaped envelope. This virus belongs to Poxviridae, subfamily Chordopoxvirinae, and genus

Meiriani Sari, Nany Hairunisa

Orthopoxvirus. Monkeypox symptoms are similar to those of smallpox but are usually milder. Although named Monkeypox, the main cause of this disease is not known with certainty. However, African rodents and primates (such as monkeys) may harbor the virus and transmit it to humans.^{3,11-16}

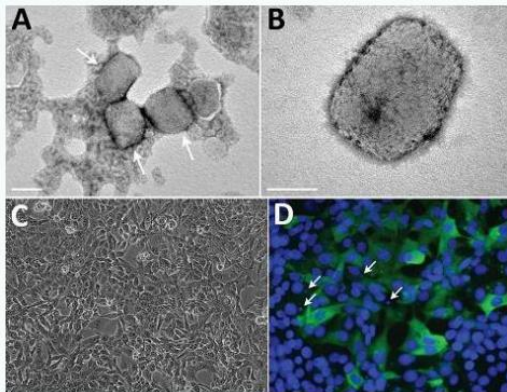


Figure 1. Some forms of Monkeypox virus¹

Epidemiology and Risk Factors (Vulnerable Group)

Fatal cases of Monkeypox are more common in children and are often related to exposure to the virus, the patient's health status and complications. The presence of immune deficiency can worsen the prognosis. Smallpox vaccination can reduce the incidence of this disease. Individuals under 40-50 years old seem more easily infected with Monkeypox. This is thought to occur due to the decreasing number of smallpox vaccines as the disease is eradicated in several countries.^{9,12,14,17,18}

Some groups included in the vulnerable group are pregnant women, children, and immunocompromised patients. Research conducted by the New England Journal of Medicine recently showed that 98% of monkeypox cases diagnosed in 16 countries between April and June occurred in men who had sex with other men. This raises concerns about the stigma of the LGBT community toward Monkeypox.^{19,20}

Transmission

Monkeypox is usually passed from person to person through close contact with an infected person. Contact from person to person, such as direct contact, contact with droplets, contact with infectious body fluids or through media (linen). The virus enters the body through broken/open skin (even if it is not visible), the respiratory tract, or mucous membranes

(eyes, nose, or mouth). Airborne transmission is rare. Transmission through droplets usually requires prolonged contact, so family members who live in the same household or are in close contact with cases are at greater risk of infection. People with Monkeypox are contagious when symptomatic (usually between two to four weeks). Rashes, body fluids (such as fluid, pus or blood from skin lesions) and scabs are highly contagious. Clothes, bedding, towels or eating utensils/plates contaminated with the virus from an infected person can also infect others.¹⁴

In addition, animal-to-person transmission can also occur. Contact with blood, body fluids or skin lesions of infected animals can transmit Monkeypox. Monkeypox's natural reservoir has not been determined, but it is most likely in rodents. Monkeypox infection in Africa has been found in many animal species: tree squirrels, Gambian giant rats, striped rats, dormice and primates. In the case that occurred in the United States, the first case was infected by a prairie dog.^{4,21,22}

Pathophysiology

The entry of the virus from various places of entry, such as the oropharynx, nasopharynx and intradermal; Monkeypox virus will then replicate at the inoculation site and then spread through the lymph nodes. Initial viremia will trigger the viral spread of the infection and focus on other organs. This phase describes the incubation period. This period lasts 7-14 days with a deadline of 21 days. The onset of symptoms correlates with secondary viremia lasting 1-2 days of prodromal symptoms such as fever and lymphadenopathy before the appearance of the lesions. Infected patients are highly contagious during this period. Lesions begin in the oropharynx and then on the skin. Serum antibodies can be detected when lesions appear.^{2,4,5,9,12}

Sign and Symptoms

Monkeypox symptoms vary. Some people can have moderate symptoms, while some can be more severe and require health facilities. The most common symptoms include fever, headache, myalgia, backache, malaise and enlarged lymph nodes. These symptoms can be followed or accompanied by a rash lasting two to three weeks.²³

This rash is commonly found on the face, palms, soles of the feet, eyes, mouth, throat, and

Meiriani Sari, Nany Hairunisa

genital areas such as the penis, vulva, and anus. The number of these rash lesions varies from one to thousands. The evolution of these lesions usually begins with the appearance of macular lesions and then becomes papules, vesicular, pustular to desquamated. These lesions are usually firm and

often form an umbilical cord (a point at the apex of the lesion). These lesions are typically painful to the point that they become itchy during the healing process. The patient will remain infectious until all lesions heal.^{1,3,5,7,12,14,23,24}



Figure 2. Lesions on Monkeypox ¹

In addition, Monkeypox can also be accompanied by rectal symptoms. Purulent or bloody stools, rectal pain or bleeding from the rectum may be seen in patients with Monkeypox. Respiratory symptoms such as sore throat, nasal congestion, and cough can be found in sufferers.^{1,2,8}

Monkeypox infection can be divided into two periods:² The invasion period (lasting 0-5 days) is characterized by fever, severe headache, lymphadenopathy, back pain, myalgia, and severe asthenia. Lymphadenopathy is a distinctive feature of Monkeypox compared to similar diseases. Lymphadenopathy can be felt in the neck, armpit or groin.² The skin eruption usually begins within 1-3 days of the onset of fever. The rash tends to appear on the face and extremities rather than the trunk. Involves the face in 95% of cases, palms and soles in 75% of cases, genitalia in 30% of cases and the conjunctiva in 20% of cases, including the cornea. Lesions develop from macules to papules then vesicles and pustules to crust over and detach from

the skin. The number of lesions varies from a few to several thousand. In severe cases, the lesions may coalesce and cause large patches of skin to peel.^{1,2,8}

Table 1. Monkeypox lesion progression²

Stadium	Duration	Characteristic
Enatem		Lesions sometimes appear first on the tongue and in the mouth
Macula	1-2 days	Macular lesions appear
Papule	1-2 days	The lesion progresses from a macula (flat) to a papule (there is an elevation)
Vesicle	1-2 days	The lesion will become a vesicle, an elevated lesion with elevation and filled with clear fluid
Pustule	5-7 days	The lesion becomes a pustule filled with opaque fluid, elevates, is round and hard on pressure
Crust	7-14 days	At the end of the second week, the pustules become crusty and will last up to 1 week and then peel off



Figure 3. Clinical Manifestations in Monkeypox²

Diagnosis and Differential Diagnosis

In addition to signs and symptoms, Monkeypox's diagnosis is based on real-time polymerase chain reaction (PCR) examination of dry swab samples of lesions or ulcers. Samples from nasopharyngeal swabs, serum samples, scabs, and tissue samples can also be used for PCR or pathological examination. The differential diagnosis includes syphilis, cancrroid, varicella zoster, herpes simplex, hand-foot-and-mouth disease, molluscum contagious and cryptococcus.^{1,3,5,6,8,12,14}

The definition of Monkeypox cases can be divided into four classifications of suspected (suspected), confirmed, probable and possible diagnoses. The Monkeypox case definitions are divided into four classifications: suspected, confirmed, probable and possible diagnoses. Suspected cases are patients with sudden onset of fever followed by vesicular-pustular eruptions predominantly on the face, palms, soles of the feet, and the discovery of at least five smallpox-type crusts. Recent WHO guidelines add the presence of a mucosal lesion as the definition of a suspected case. Confirmed cases are suspected cases that have been confirmed by the laboratory, such as positive IgA antibodies, PCR or virus isolation. A probable case is a suspected case with appropriate epidemiology but no laboratory confirmation access. Cases may be established in patients with vesicular lesions, pustules or crusts who have not been diagnosed with measles, have a history of fever with vesicles or have a crusted rash. This individual also meets epidemiological criteria, has an orthopoxvirus-specific IgM elevation, and has an unexplained febrile rash.^{1,3,5,6,8,12,14}

Clinically, Monkeypox's differential diagnosis can account for diseases with other rashes, such as smallpox, chickenpox, measles, bacterial skin infections, scabies, syphilis, and specific drug-related allergies. In addition, lymphadenopathy during the prodromal phase can be a typical clinical feature to distinguish Monkeypox from other similar smallpox diseases, such as smallpox, chickenpox/varicella (chickenpox), and others.⁸



Figure 4. Lymphadenopathy in children with monkeypox⁸

Table 2. Comparison of Monkeypox Symptoms and Signs and Differential Diagnosis²

Symptoms and Signs	Monkeypox	Chickenpox (Varicella)	Measles
Fever	Fever >38°C, rash after 1-3 days	Fever up to 39°C, rash after 0-2 days	High fever 40.5°C, rash after 2-4 days
Rash	Macules, papules, vesicles, pustules. The type of rash is the same in every phase in all areas of the body	Macules, papules, vesicles. There are various phases	Non-vesicular rash in various phases
Rash development	Slow, 3-4 weeks	Fast, crops appear for a few days	Fast, 5-7 days



Meiriani Sari, Nany Hairunisa

Rash	Starting at the head, denser on the face and limbs; appears on the palms of the hands and soles of the feet	Start at the head; denser on the body; not on the palms of the hands and soles of the feet	Starts in the head and spreads; can reach hands and feet
Distinctive appearance	Lymphadenopathy	Itchy rash	Koplik spots
Mortality	3-6%	Rare	Varies

2022 Monkeypox Outbreak

Monkeypox was first discovered in 1958 when a disease such as the smallpox outbreak occurred in a group of Singaporean monkeys sent to Denmark for research. The first human case of Monkeypox was discovered in 1970 in Congo in a 9-month-old child. As of June 2022, 86% of cases reported to WHO were from the European region. Other regions such as Africa 2%, America 11%, Eastern Mediterranean <1%, and West Pacific region <1%.^{3,5,8-14}

Since May 2022, Monkeypox cases have been reported from non-endemic countries and forwarded to reports from endemic countries. Most confirmed cases had a history of travelling to European and North American countries, compared to Central and South Africa, where Monkeypox is endemic. This is the first time that Monkeypox cases have been found in both endemic and non-endemic countries. Of the cases reported to WHO, most were identified as being transmitted through sexual intercourse or health facilities related to but not exclusively with men who have sex with men.^{2,4,8,17,20,22}

On August 19, 2022, one positive case was found in a 27-year-old male patient in Jakarta. As of September 15, 2022, there are 2 suspects and 63 discarded. From the distribution of 63 patients with discarded status covering 10 provinces in Indonesia.¹

Management and Vaccination

Currently, no specific treatment has been proven to treat Monkeypox infection. Like other viral diseases, Monkeypox therapy is symptomatic supportive therapy. An antiviral tecovirimat or TPOXX was developed by the European Medicines Agency (EMA) as a monkeypox therapy in 2022 based on animal and human studies. This drug has not been marketed freely. In addition, antivirals such

as cidofovir and brincidofovir have been shown to be effective against orthopoxvirus in in-vitro and animal studies. The effectiveness of this drug against monkeypox in humans is unknown.^{2,3,5,8,24-26}

However, there are also precautions that can be taken to prevent an outbreak from occurring. For example, vaccines used during smallpox (smallpox) eradication programs protect Monkeypox. Based on several observational studies, the smallpox vaccine has an effectiveness of 85% for preventing Monkeypox. In addition, receiving this vaccine will result in milder symptoms. A new vaccine developed for smallpox was approved in 2019 to prevent Monkeypox, but global availability is limited.^{2,8,27-29}

The recommended vaccination in Indonesia to reduce the incidence of Monkeypox is the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine. The MVA-BN that will be used as the third generation of smallpox vaccine is effective and safe to give to monkeypox patients with immunocompromised conditions or those with innate immune disorders. In addition, MVA-BN is also safe to use for patients over 18 years, children and also pregnant woman.^{1,2}

Complications and Prognosis

There are data on the relationship between Monkeypox in children. However, based on reports of patients infected with Monkeypox, this disease tends to be more severe in children. Rarely, Monkeypox can cause complications, including encephalitis, cellulitis, pneumonia, sepsis, abscess, airway obstruction due to severe lymphadenopathy, keratitis, hyperpigmentation, pneumonia, and corneal scarring.^{2,8,30,31}

Conclusions

With the outbreak report, it is important to discuss, explore, and understand more about the disease and its management and prevention. Unfortunately, there is currently no specific treatment for Monkeypox. However, this disease can be prevented by vaccination. In Indonesia, the Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine is recommended to prevent Monkeypox disease.



Meiriani Sari, Nany Hairunisa

CONFLICTS OF INTEREST

The authors declare no conflict of interest in this article.

FUNDING

No specific funding was provided for this review.

AUTHORS CONTRIBUTIONS

The authors contributions to this review are as follows: conceptualization, collecting literature, and writing draft: Meiriani Sari; supervision, review and editing: Nany Hairunisa.

REFERENCES

1. Kementerian Kesehatan Republik Indonesia. Kasus Monkeypox Pertama di Indonesia Terkonfirmasi. 2022.
2. Pedoman Pencegahan dan Pengendalian Kementerian Kesehatan RI Direktorat Jenderal dan Pengendalian Penyakit. Pedoman Pencegahan dan Pengendalian Penyakit Monkeypox. Kementerian Kesehatan. 2022.
3. Singhal T, Kabra SK, Lodha R. Monkeypox: A Review. *Indian J Pediatr.* 2022 Oct;89(10):955–60.
4. Nolen LD, Osadebe L, Katomba J, Likofata J, Mukadi D, Monroe B, et al. Extended human-to-human transmission during a monkeypox outbreak in the Democratic Republic of the Congo. *Emerg Infect Dis.* 2016 Jun 1;22(6):1014–21.
5. Cheema AY, Ogedegbe OJ, Munir M, Alugba G, Ojo TK. Monkeypox: A Review of Clinical Features, Diagnosis, and Treatment. *Cureus.* 2022 Jul 11;
6. Veleven TP, Meyer CG. Monkeypox 2022 outbreak An update. *Trop Med Int Health.* 2022;27:604–5.
7. Hraib M, Jouni S, Albitar MM, Alaidi S, Alshehabi Z. The outbreak of monkeypox 2022: An overview. *Annals of Medicine and Surgery.* 2022 Jul 1;79(104069):1–4.
8. Centers for Disease Control and Prevention. Monkeypox Signs and Symptoms. 2022.
9. Beer EM, Bhargavi Rao V. A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. *PLoS Negl Trop Dis.* 2019;13(10).
10. European Centre for Disease Prevention and Control. Monkeypox multi-country outbreak Key messages. 2022.
11. Oladoye MJ. Monkeypox: A Neglected Viral Zoonotic Disease. *European Journal of Medical and Educational Technologies.* 2021 May 15;14(2):em2108.
12. Petersen E, Kantele A, Koopmans M, et al. Human Monkeypox epidemiologic and clinical characteristic, diagnosis and prevention Elsevier Enhanced Reader. *Infect Dis Clin An Am.* 2019;33:1027–43.
13. Kapoor S, Varadharajan A. Monkeypox 2022: Emerging Zoonotic Epidemic Threat, Future Implications, and Way Ahead. *Journal of Public Health and Primary Care.* 2022;20(20):1–4.
14. Pal M, Mengstie F, Kandi V. Epidemiology, Diagnosis, and Control of Monkeypox Disease: A comprehensive Review. *American Journal of Infectious Diseases and Microbiology.* 2017;5(2):94–9.
15. Centre for Emerging Zoonotic and Parasitic Diseases Outbreak Response Unit D of PHS and R. Monkeypox Frequently Asked Questions. 2022.
16. Moore MJ, Rathis B, Zahra F. Monkeypox. In: Abai A, Abu-Gosh A, Acharya AB, editors. *StatPeals.* 4th ed. 2022. p. 1–4.
17. Reardon S. Why is Monkeypox Evolving So Fast - Scientific American. *Scientific American.* 2022. p. 1–2.
18. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox—A potential threat? A systematic review. *PLoS Negl Trop Dis.* 2022 Feb 1;16(2).
19. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, et al. Monkeypox Virus Infection in Humans across 16 Countries — April–June 2022. *New England Journal of Medicine.* 2022 Aug 25;387(8):679–91.
20. Orkin C. Monkeypox an expert explains what gay and bisexual men need to know. *The Conversation.* 2022.



Meiriani Sari, Nany Hairunisa

21. Hutson CL, Carroll DS, Gallardo-Romero N, Drew C, Zaki SR, Nagy T, et al. Comparison of Monkeypox Virus Clade Kinetics and Pathology within the Prairie Dog Animal Model Using a Serial Sacrifice Study Design. *Biomed Res Int.* 2015;2015:1–19.
22. Grant R, Nguyen LBL, Breban R. Modelling human-to-human transmission of monkeypox. *Bulletin of the World Health Organization.* 2020 Sep 1;98(9):638–40.
23. Patel A, Bilinska J, Tam JCH, da Silva Fontoura D, Mason CY, Daunt A, et al. Clinical features and novel presentations of human monkeypox in a central London centre during the 2022 outbreak: Descriptive case series. *The BMJ.* 2022;378(e072410):1–17.
24. Adler H, Gould S, Hine P, et al. Clinical features and management of human monkeypox a retrospective observational study in the UK - PubMed. *The Lancet Dis.* 2022;8:1153–62.
25. Reynolds MG, McCollum AM, Nguete B, Lushima RS, Petersen BW. Improving the care and treatment of monkeypox patients in low-resource settings: Applying evidence from contemporary biomedical and smallpox biodefense research. *Viruses.* 2017 Dec 12;9(380):1–14.
26. Johnson PLF, Bergstrom CT, Regoes RR, Longini IM, Halloran ME, Antia R. Evolutionary consequences of delaying intervention for monkeypox. *The Lancet.* 2022 Sep;1–2.
27. Brooks JT, Marks P, Goldstein RH, Walensky RP. Intradermal Vaccination for Monkeypox — Benefits for Individual and Public Health. *New England Journal of Medicine.* 2022 Aug 31;1–3.
28. Gruber MF. Current status of monkeypox vaccines. *NPJ Vaccines.* 2022 Aug 17;7(94):1–3.
29. Thy M, Peiffer-Smadja N, Mailhe M, Kramer L, Ferré VM, Houhou-Fidouh N, et al. Breakthrough infections after post-exposure vaccination against Monkeypox. *medrxiv.* 2022 Aug 4;1–19.
30. Billieux B.J, Tshiani O, Sejvar J. Neurologic Complications of Smallpox and Monkeypox A Review *Infectious Diseases JAMA Neurology JAMA Network.* *JAMA Neurol.* 2022;3491:1–3.
31. Sousa D, Ftade J, Patrocinio J, et al. Monkeypox infection and bacterial cellulitis a complication to look for Elsevier Enhanced Reader. *International Journal of Infectious Disease.* 2022;123:180–2.