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## A REVIEW OF THE MONKEYPOX OUTBREAK IN INDONESIA IN 2022

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### 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 19<sup>th</sup>, 2022, one positive case was found in a 27-year-old male patient in Jakarta. As of September 15<sup>th</sup>, 2022, 2 suspects and 63 were discarded. From the distribution of 63 patients with discarded status covering ten provinces in Indonesia.<sup>1</sup>

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.<sup>2,3,4</sup> Common symptoms such as fever, headache, enlarged lymph nodes, and skin lesions can cause severe pain.<sup>5</sup> This disease has clinical relevance in endemic areas of Africa, with outbreaks in the west due to international travel.<sup>6</sup>

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.<sup>7-10</sup>

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.<sup>1,2</sup>

### About Monkeypox

Monkeypox is a rare zoonotic disease caused by the Monkeypox virus.<sup>3</sup> 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 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.<sup>3,11-16</sup>

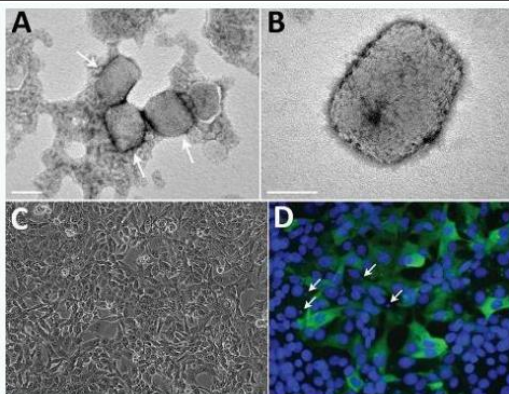


Figure 1. Some forms of Monkeypox virus<sup>1</sup>

### 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.<sup>9,12,14,17,18</sup>

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.<sup>19,20</sup>

### 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.<sup>14</sup>

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.<sup>4,21,22</sup>

### 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.<sup>2,4,5,9,12</sup>

### 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.<sup>23</sup>

This rash is commonly found on the face, palms, soles of the feet, eyes, mouth, throat, and 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.<sup>1,3,5,7,12,14,23,24</sup>





Figure 2. Lesions on Monkeypox <sup>1</sup>

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. <sup>1,2,8</sup>

Monkeypox infection can be divided into two periods: <sup>2</sup> 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. <sup>2</sup> 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. <sup>1,2,8</sup>

Table 1. Monkeypox lesion progression <sup>2</sup>

| 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 Monkeypox<sup>2</sup>

### 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 contagiosus and cryptococcus.<sup>1,3,5,6,8,12,14</sup>

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.<sup>1,3,5,6,8,12,14</sup>

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.<sup>8</sup>



Figure 4. Lymphadenopathy in children with monkeypox<sup>8</sup>

Table 2. Comparison of Monkeypox Symptoms and Signs and Differential Diagnosis<sup>2</sup>

| Symptoms and Signs      | Monkeypox  | Chickenpox (Varicella)                               | Measles                                |
|-------------------------|--|--|--|
| <b>Fever</b>            | 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 |
| <b>Rash</b>             | 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   |
| <b>Rash development</b> | Slow, 3-4 weeks  | Fast, crops appear for a few days                    | Fast, 5-7 days                         |



|                               |   |  |  |
|-------------------------------|---|--|--|
| <b>Rash</b>                   | 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 |
| <b>Duration</b>               |   |  |  |
| <b>Distinctive appearance</b> | Lymphadenopathy   | Itchy rash   | Koplik spots   |
| <b>Mortality</b>              | 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%.<sup>3,5,8-14</sup>

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.<sup>2,4,8,17,20,22</sup>

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.<sup>1</sup>

### 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.<sup>2,3,5,8,24-26</sup>

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.<sup>2,8,27-29</sup>

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. , .<sup>1,2</sup>

### 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.<sup>2,8,30,31</sup>

### 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.

### CONFLICTS OF INTEREST

The authors declare no conflict of interest in this article.

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## 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.

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# A REVIEW OF THE MONKEYPOX OUTBREAK IN INDONESIA IN 2022

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## A REVIEW OF THE MONKEYPOX OUTBREAK IN INDONESIA IN 2022

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### 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 19<sup>th</sup>, 2022, one positive case was found in a 27-year-old male patient in Jakarta. As of September 15<sup>th</sup>, 2022, 2 suspects and 63 were discarded. From the distribution of 63 patients with discarded status covering ten provinces in Indonesia.<sup>1</sup>

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.<sup>2,3,4</sup> Common symptoms such as fever, headache, enlarged lymph nodes, and skin lesions can cause severe pain.<sup>5</sup> This disease has clinical relevance in endemic areas of Africa, with outbreaks in the west due to international travel.<sup>6</sup>

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.<sup>7-10</sup>

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.<sup>1,2</sup>

### About Monkeypox

Monkeypox is a rare zoonotic disease caused by the Monkeypox virus.<sup>3</sup> 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 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.<sup>3,11-16</sup>

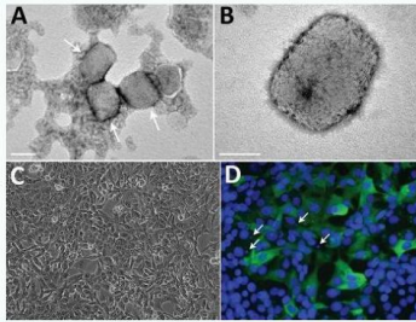


Figure 1. Some forms of Monkeypox virus<sup>1</sup>

### 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.<sup>9,12,14,17,18</sup>

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<sup>21</sup> of the LGBT community toward Monkeypox.<sup>19,20</sup>

### 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<sup>6</sup>. Clothes, bedding, towels or eating utensils/plates contaminated with the virus from an infected person can also infect others.<sup>14</sup>

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.<sup>4,21,22</sup>

### 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.<sup>2,4,5,9,12</sup>

### 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.<sup>23</sup>

This rash is commonly found on the face, palms, soles of the feet, eyes, mouth, throat, and 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.<sup>1,3,5,7,12,14,23,24</sup>

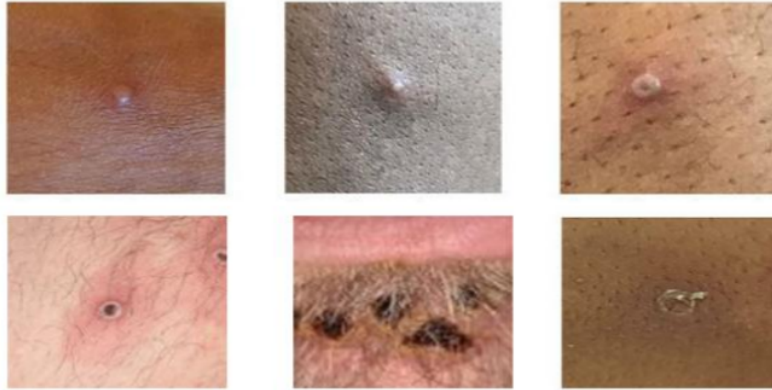


Figure 2. Lesions on Monkeypox <sup>1</sup>

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 <sup>1</sup>ufferers. <sup>1,2,8</sup>

Monkeypox infection can be divided into two periods: <sup>2</sup> 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. <sup>2</sup> 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. <sup>1,2,8</sup>

Table 1. Monkeypox lesion progression <sup>2</sup>

| 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 Monkeypox<sup>2</sup>

### 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.<sup>1,3,5,6,8,12,14</sup>

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.<sup>1,3,5,6,8,12,14</sup>

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.<sup>8</sup>



Figure 4. Lymphadenopathy in children with monkeypox<sup>8</sup>

Table 2. Comparison of Monkeypox Symptoms and Signs and Differential Diagnosis<sup>2</sup>

| Symptoms and Signs      | Monkeypox  | Chickenpox (Varicella)                               | Measles                                |
|-------------------------|--|--|--|
| <b>Fever</b>            | 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 |
| <b>Rash</b>             | 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   |
| <b>Rash development</b> | Slow, 3-4 weeks  | Fast, crops appear for a few days                    | Fast, 5-7 days                         |



Meiriani Sari, Nany Hairunisa

|                               |   |  |  |
|-------------------------------|---|--|--|
| <b>Rash</b>                   | 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 body; not on the palms of the hands and soles of the feet | Starts in the head and spreads; can reach hands and feet |
| <b>Duration</b>               |   |  |  |
| <b>Distinctive appearance</b> | Lymphadenopathy   | Itchy rash   | Koplik spots   |
| <b>Mortality</b>              | 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%.<sup>3,5,8,14</sup>

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.<sup>2,4,8,17,20,22</sup>

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.<sup>1</sup>

### 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.<sup>2,3,5,8,24-26</sup>

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.<sup>2,8,27-29</sup>

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.<sup>1,2</sup>

### 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.<sup>2,8,30,31</sup>

### 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.

### CONFLICTS OF INTEREST

The authors declare no conflict of interest in this article.

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**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.

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