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Human Monkeypox Virus infection

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Abstract

Monkeypox is a zoonotic disease. First, this infection was found in animals but has been widespread in humans and become a pandemic all over the world including Indonesia with different case fatality rates caused by monkeypox infection among the countries. Some clinical features caused by monkeypox infection are similar to other infections caused by chicken pox and other viruses. Treating and preventing monkeypox infection need holistic management among medical personnel.

***Keywords*:** Monkeypox; virus; infection; transmission

1. INTRODUCTION

Monkeypox (MPX) is a zoonotic disease caused by orthopoxvirus which causes chickenpox in humans.[1,2] The development of MPX has become increasingly widespread since it was discovered to infect humans in 1970 and became one of the global public health emergencies in 2022 due to re-emerging disease occurring at the same time as the COVID-19 epidemic.[3,4,5,6,7] In general, this infection occurs through sexual transmission, direct contact with the source of infection, or indirect contact with an incubation period of 5-15 days.[8] Different with the first time happened, when becoming as an outbreak, MPX was identified all over the world include south east Asia and declared as public health emergency of international concern on July 2022 and impact in economic and health challenges.[6,7] Several countries show different case fatality rates (CFR), namely 8.7% for the total worldwide, with the highest CFR value found on the African continent, namely 10.6%.[9]

2. DISCUSSION

2.1 Definition

MPX is caused by the monkeypox virus which belongs to the poxviridae family, chordopoxvirinae subfamily, and orthopoxvirus genus.[1,6,9,10,11] It is a double-stranded deoxyribonucleic acid (DNA) virus that replicates in the bodies of humans, other primates, rodents and also squirrels.[8]

2.2 Epidemiology and risk factors

MPX infection was discovered in 1959 in monkeys at a research center in Copenhagen, Denmark. Transmission of viruses from animals to humans occurs due to direct contact through body fluids, mucous membranes, open wounds, and objects contaminated with viruses. Human infection was discovered in infants in the Republic of Congo in 1970.[1,3,6,8] From 1970 to 2003, MPX became endemic in 11 countries in Africa. MPX infection outside Africa was first discovered in 2003 in America and is widespread, especially in groups with a history of travel to endemic areas. Since 2017-2019 MPX has increasingly expanded to Europe. In 2022, while COVID-19 is still ongoing, MPX becomes a global public health emergency. In 2022, WHO reported 46,068 confirmed cases of MPX with 15 deaths in 99 WHO countries.[1,6,12,13,14] The first findings in 2022 in a non-endemic country in Europe were found in the United Kingdom in patients who had previously travelled to the

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Nigerian.[5,15] In Indonesia, MPX was first discovered on August 19 2022 in a 27years old man in Jakarta. This infection was spread across ten provinces of Indonesia with 2 suspected cases of MPX and 63 other suspected cases having negative PCR results.[16] In risk groups such as women, pregnant women, children and patients with reduced immune status, more severe clinical symptoms were found. Recent research also found a high prevalence of MPX in homosexual groups. [13,16,17,18,19,20,21] Monkeypox outbreak in Nigeria was found mainly in those aged 21-40 years, besides the absence of a history of smallpox vaccination, changes in behavioural and cultural patterns among humans are believed to be risk factors that aggravate this situation. An increase in the incidence of this infection is also found in nosocomial environments, especially in health workers who provide services to patients infected with MPX.[22]

2.3 Transmission

This MPX virus infection can be transmitted directly or indirectly. Direct transmission usually occurs through close contact with droplets, contact with infected skin lesions can be through sexual contact. Indirect transmission can occur through contact with surrounding objects such as the same bedding and the same food utensils.[23,24] In endemic areas, transmission can occur due to human contact with contaminated animals, whether live or dead animals.[22,25]

Data on the incidence of MPX infection shows a 20-fold increase in 2006-2007 compared to 1981-1986 data, this is due to the increase in population and increasingly improving surveillance programs, apart from that, an increase in the number of infections with MPX 2 was also found, where previously many infections were documented. in MPX 1. In addition, the cessation of smallpox vaccination since 1970 has also increased the incidence of MPX infection.[5,13,22,26,27]

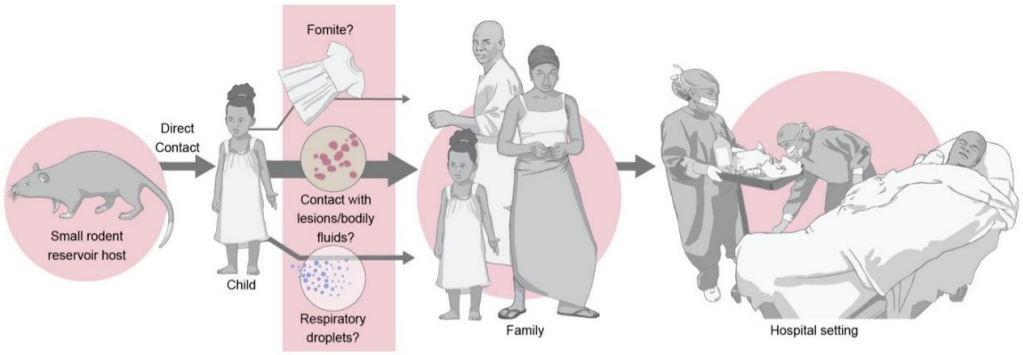

Figure. 1. MPX transmission[22]

2.4 Pathophysiology

This disease begins when the virus enters the body through the oropharynx, nasopharynx and intradermally. The virus replicates on this side of the inoculation and extends through the lymph nodes. The first viremia triggers the spread of the virus to other organs on days 7 to 21 days. After this incubation period, MPX enters a prodromal phase for 1-2 days characterized by fever and lymphadenopathy before the appearance of maculopapular lesions starting in the oropharynx and skin.[3,16] In this phase, human-to-human transmission has begun to occur via droplets.[6,28,29,30,31]

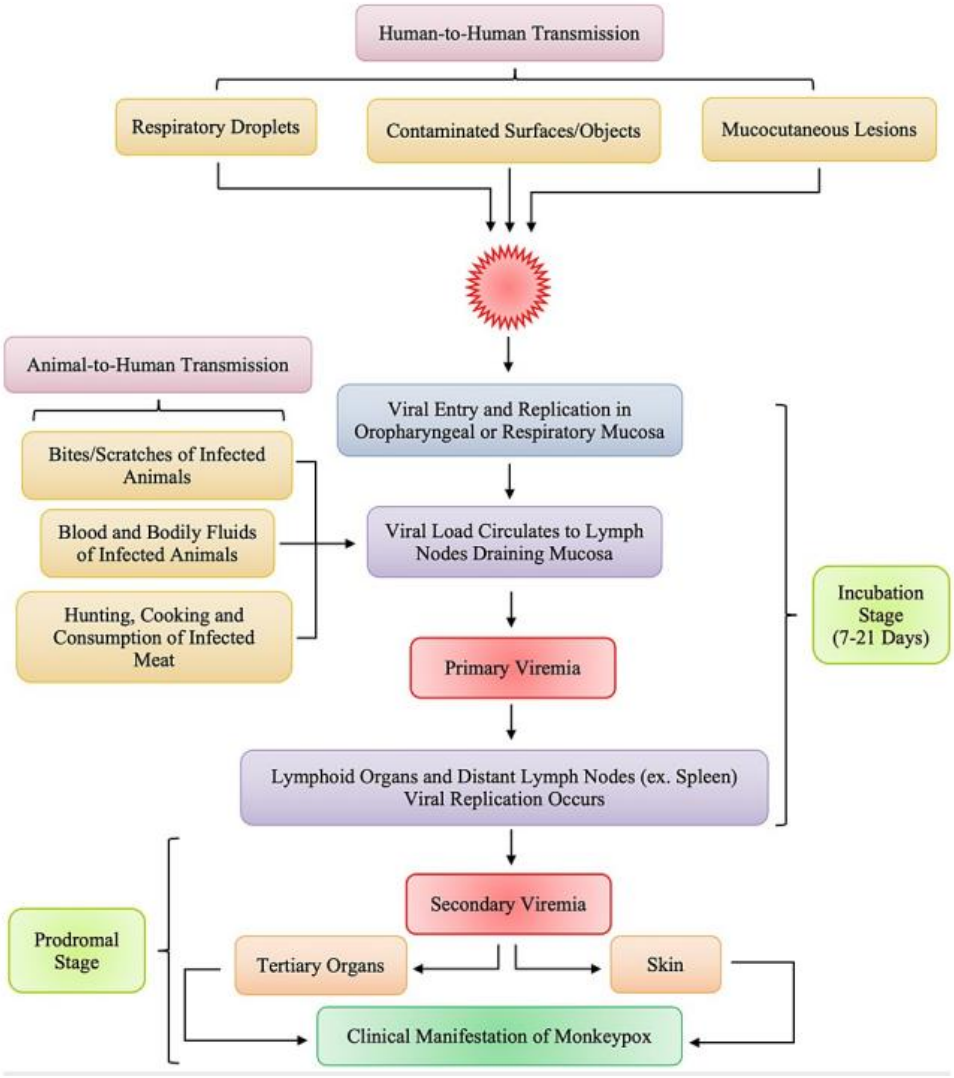

Figure. 2. Pathophysiology of MPX infection[22,23]

2.5 Clinical Symptoms

The clinical symptoms of MPX infection vary greatly, ranging from mild symptoms to symptoms that are quite severe and require treatment at a health facility. The MPOX infection phase is divided into several phases, namely: [14,16,32,33,34]

1. Incubation period

   The incubation period begins when the virus enters the human body. In this phase, sufferers do not show symptoms and do not cause infection. The incubation phase varies between each person from 5 days to 3 weeks. Generally, lasts up to 12 days.

   1. Prodromal period

      The prodromal period can be divided into 3 phases up to the healing phase. These phases include:

      a. Invasion phase

         This phase is characterized by non-specific symptoms and resembles other viral infections. Symptoms that occur in sufferers include fever, headache, muscle aches and weakness in the body. In some patients it can also be accompanied by coughing and decreased appetite due to ulcer lesions in the mouth. In this phase there is also enlargement of the lymph nodes, especially in the maxilla, cervical and inguinal. In general, this phase lasts up to three days before the next phase. The presence of enlarged lymph nodes in monkeypox infection can be used to differentiate it from the smallpox virus. Quite severe clinical manifestations can include pneumonitis, ocular disorders and encephalitis with mortality reaching 10%.[3,16]

b. Eruption phase

The eruption phase begins with the appearance of reddish lesions with a centrifugal pattern starting on the face, especially in the area around the eyes, mouth and tongue and spreading to the extremities (arms and legs) especially on the palms of the hands. Reddish lesions begin with enanthema lesions. This enanthem lesion will turn into a reddish macule followed by a papule which is a lesion with a protrusion on the skin. This papular lesion will then turn into a vesicular lesion with clear fluid on top. The clear fluid becomes thicker over time and turns into a pustule. All of these lesions will feel painful until desquamation occurs accompanied by dry crusting. In this phase, sufferers generally feel itchy.

In several cases, atypical symptoms were found in MPX sufferers, including the presence of only one or a few lesions; pain in the anus and surrounding areas; lesions in the anus without spread to other sites; lesions in atypical locations and the presence of lesions without being preceded by fever or other prodromal symptoms.[20,23]

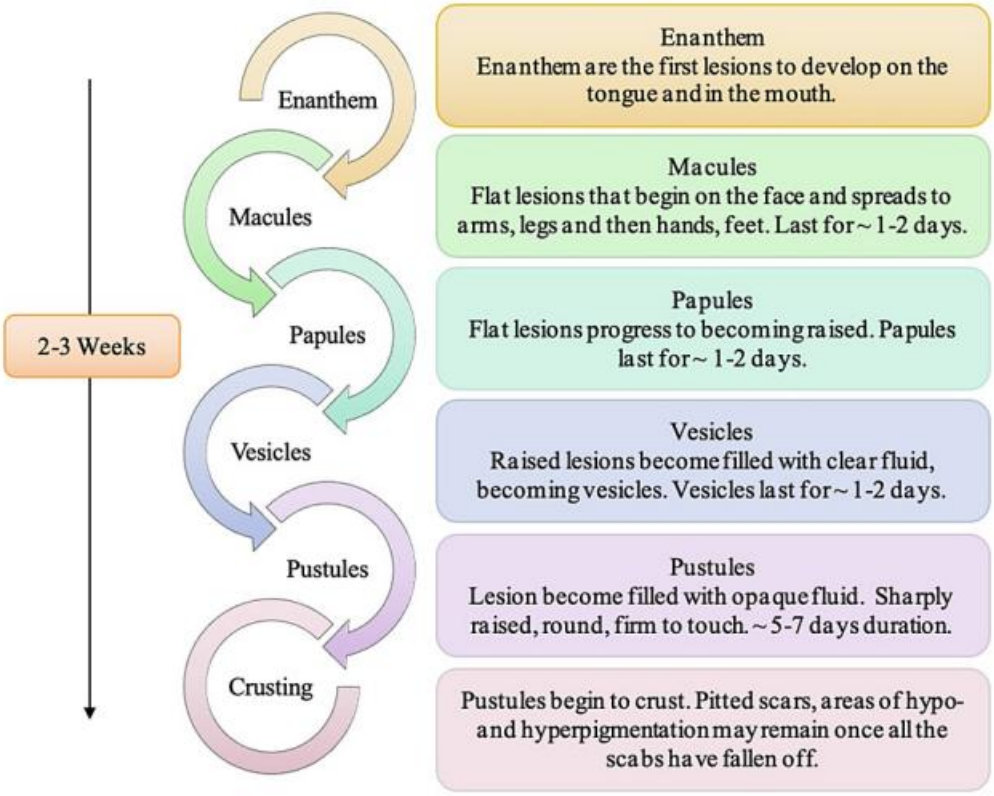

Figure. 3. Stages of the eruption phase in MPX infection.[32]

Figure 4. Clinical symptoms of MPX infection[16]

c. Convalescent phase
In general, the convalescent phase or sustained healing phase occurs after 3 weeks from the eruption phase. This healing period will be different for each individual depending on the individual's level of vulnerability and endurance.

2.6 Diagnosis and differential diagnosis

Diagnosis of MPX infection can be done through

a. Clinical Symptoms
These clinical symptoms are difficult to differentiate from clinical symptoms due to other viral infections, but MPX infections are often accompanied by lymphadenopathy.[3,26,35]

b. Laboratory examination
Further examination to confirm MPX infection through polymerase chain reaction (PCR) examination with high accuracy and sensitivity values. This examination can be carried out with specimens originating from throat swabs, serum or infected tissue. Immunoglobulin M (IgM) serological examination is also considered useful for confirming ongoing monkeypox infection.[3,16]
Research by Thornhill et al showed that the highest positive PCR test results were in nasopharyngeal swabs (23%), compared to blood (7%) and urine (3%). In men who have sex with men (MSM) patients, positive results on semen examination reached 90.6%.[36,37]

Several other infections such as syphilis, cancer, varicella zoster, herpes simplex, hand-foot and mouth disease, molluscum, and cryptococcus are in the differential diagnosis of MPX. The reddish lesions that often appear in monkeypox themselves resemble the appearance of lesions in smallpox, chickenpox, measles, bacterial skin infections, scabies and lesions caused by skin allergies.[16]

Table 1. Differences in clinical features of MPOX, varicella and measles[16,24,38]

Symptoms and Signs	Momkeypox	Chickenpox/Varicella	Measles
Fever	>38ºC followed by rash after 1-3 days	Fever >39ºC followed by rash for 0-2 days	High fever >40ºC followed by rash after 2-4 days
Appearance of rash	Macule-papule-vesicle-pustule with the same phase	Macula-papula-vesicles with different phases	Non-vesicular rash with various phases
Development of rash	3-4 weeks	Fast	Fast
Distribution of rash	Starting on the face, palms and feet	Starting from the head and not on the palms of the hands and feet	Starting from the head and spreading to the extremities
Typical sign	KGB enlargement	Rash and itching	Koplik spots
Death	1%-10%	Seldom	Varies

2.7 Management

a. Symptomatic and supportive therapy

Until now there is no specific therapy used to treat monkeypox infection. Like other viral infections, monkeypox therapy includes symptomatic therapy and supportive therapy. Some supportive treatments such as antipyretics to treat fever and analgesics for pain.[3,16] Patients with gastrointestinal symptoms often require rehydration or intravenous therapy.

b. Antiviral therapy[39,40,41,42,43,44,45]

i. Tecovirimat

Several vulnerable groups such as patients with a reduced immune status, babies under 8 years of age and pregnant women are advised to receive antiviral therapy. The first antiviral used to treat this infection was tecovirimat with the potential to prevent the formation of the virus envelope through inhibition of the p37 protein in orthopoxvirus and virus maturation in infected cells. The use of this drug has started since 2018 to treat smallpox in America, while in Europe it has been used to treat monkeypox since 2022.[14,16,41]

Research to assess the safety of tecovirimat in 359 volunteers showed there was no difference in the side effects experienced by the group using tecovirimat compared to placebo.[43,46] The dose of tecovirimat used as therapy is adjusted to the patient's body weight, namely 600 mg with two doses per day for 40kg-120kg and 600 mg with three doses per day for body weight above 120kg for 14 days.[47,48]

ii. Brincidofovir and cidofovir

The use of oral brincidofovir as therapy for monkeypox infections is still in the animal research stage, but this drug has been proven effective in treating other orthopoxvirus infections and smallpox with a better level of safety than cidofovir. This drug works by inhibiting viral DNA polymerization. The side effects that arise are an increase in transaminase and bilirubin enzymes. The use of cidofovir in the management of monkeypox infections is still very small, but animal studies have shown good results.[48]

iii. *Vaccinia immune globulin* (VIG)

VIG is a hyperimmune globulin that is usually used as a therapy for several vaccine complications such as eczema, general weakness after vaccination, and vaccine-related infections. The use of VIG to treat monkeypox or smallpox infections has not yet been studied in humans.[30,48]

c. Advanced antiviral research

Considering the high number of monkeypox cases in 2022, currently it is being considered to develop research into several antivirals to treat monkeypox, namely ribavirin and tiazofurin as inhibitors of inosine monophosphate dehydrogenase (IMP).[31,47]

2.8 Prevention

a. Preexposure prevention

i. Prevention in the community[15,22,25,49]

Avoid direct contact with MPX infected lesions through disinfection and standard hygiene procedures as well as on materials used by patients such as clothing or towels by using gloves when cleaning the tools used. Transmission of this virus increases through sexual contact in homosexual groups so it is recommended not to have unsafe sexual contact.

ii. Prevention in health facilities

Medical personnel have a high risk of close contact with patients with suspected MPX. Before contact with suspected MPX patients, health workers must apply universal precaution procedures by using gowns, N95 masks, gloves and eye protection. This is done until all the crusts on the patient's body are gone.[3]

iii. Vaccination

1. Human monkeypox vaccination[44,50,51]

Apart from avoiding direct contact, monkeypox virus vaccination is an important effort to prevent transmission. Currently there is no vaccination specifically for the MPX virus, but smallpox virus vaccination is believed to cause a cross-reaction to MPX of 85% which can be used for prevention. Currently in America there are two vaccines that have been accepted as prevention of smallpox infections, namely ACAM2000 and JYNNEOS (imvanune or imvanex) and only JYNNEOS is accepted as prevention of MPX. Currently, several novel mRNA vaccination studies are also developing that utilize the MPX virus spike protein.[14]

2. Human monkeypox vaccination in Indonesia

The recommended vaccination in Indonesia during the pandemic is Modified Vaccinia Ankara-Bavarian Nordic (MVABN), which is a smallpox vaccination and can be tolerated in patients with immune system disorders, children and pregnant women.[16]

b. Postexposure prevention

i. Self-isolation and quarantine

Groups of patients with suspected or diagnosed monkeypox should be placed in separate isolation rooms, preferably with negative pressure rooms.[14]

ii. Vaccination

Monkeypox transmission requires prolonged exposure. The CDC recommends that the first dose of vaccination be given immediately four days after exposure. If vaccination is given four to 14 days after exposure, the effectiveness of vaccination for prevention is reduced, but can reduce the clinical symptoms that occur.[48]

3 CONCLUSION

Monkeypox (MPX) is a zoonotic disease and will become a re-emerging disease in 2022. The clinical picture resembles smallpox infection but, in some cases, it can cause severe clinical symptoms. Supportive and antiviral therapy is used to treat this infection. Vaccination and universal precaution procedures are one of the prevention efforts for MPX infection.

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