



Diagnosis, treatment, and prevention of monkeypox in children: an experts' consensus statement

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Abstract

Monkeypox is a zoonotic disease. Since the first human monkeypox case was detected in 1970, it has been prevalent in some countries in central and western Africa. Since May 2022, monkeypox cases have been reported in more than 96 non-endemic countries and regions worldwide. As of September 14, 2022, there have been more than 58,200 human monkeypox cases, and there is community transmission. The cessation of smallpox vaccination in 1980, which had some cross-protection with monkeypox, resulted in a general lack of immunity to monkeypox, which caused global concern and vigilance. As of September 14, 2022, there are four monkeypox cases in China, including three in Taiwan province and one in Hong Kong city. Previous foreign studies have shown that children are vulnerable to monkeypox and are also at high risk for severe disease or complications. In order to improve pediatricians' understanding of monkeypox and achieve early detection, early diagnosis, early treatment, and early disposal, we have organized national authoritative experts in pediatric infection, respiratory, dermatology, critical care medicine, infectious diseases, and public health and others to formulate this expert consensus, on the basis of the latest “*Clinical management and infection prevention and control for monkeypox*” released by The World Health Organization, the “*guidelines for diagnosis and treatment of monkeypox (version 2022)*” issued by National Health Commission of the People's Republic of China and other relevant documents. During the development of this consensus, multidisciplinary experts have repeatedly demonstrated the etiology, epidemiology, transmission, clinical manifestations, laboratory examinations, diagnosis, differential diagnosis, treatment, discharge criteria, prevention, disposal process, and key points of prevention and control of suspected and confirmed cases.

Keywords Children · Consensus · Diagnosis · Monkeypox · Prevention · Treatment

Introduction

In 2022, while the global COVID-19 pandemic has not ended yet, another unexpected outbreak of human monkeypox (MPX) in non-endemic regions has brought a new global threat to light. MPX is a zoonotic infectious disease caused by the monkeypox virus (MPXV). MPX was first discovered in wild monkeys in 1958 and the first human MPX case was identified in a nine-month-old boy in 1970 in the

Democratic Republic of the Congo (DRC) [1]. Since then, most human MPX cases have been prevalent in Central and West African countries. In 2003, MPX cases were detected in the United States, which was the first outbreak of MPX in a non-endemic country and region [2]. In recent years, travel-related MPX cases have occurred in non-endemic countries, such as the United Kingdom, Israel, and Singapore. From January 1 to September 14, 2022, more than 58,200 laboratory confirmed MPX cases and 22 deaths have been reported from 102 countries and regions worldwide [3]. The current MPX outbreak has posed a public health emergency of international concern (PHEIC) on July 23, 2022. MPXV and variola virus (smallpox) belong to the

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genus Orthopoxvirus. Smallpox is one of the most ancient and deadly infectious diseases in history and also the first human disease for which vaccinations were used. Smallpox was declared eradicated in 1980, and vaccination against smallpox was no longer indicated thereafter. The manifestations of MPX are similar to those of smallpox, characterized by fever, lymphadenopathy, and herpes, but MPX is relatively mild and has a low mortality rate. Although the smallpox vaccine provides some cross-immunity against MPX, immunity from smallpox vaccination generally does not last longer than 10 years [4, 5]. People who have been vaccinated against smallpox for more than 10 years and those born after 1980 (i.e., the cessation of smallpox vaccination) generally lack immunity to monkeypox, which has raised worldwide concern and vigilance.

Previous foreign studies have shown that children are vulnerable to MPXV, with children aged 0–15 years accounting for 90% of monkeypox cases [6, 7]. And children were also at high risk for severe disease or complications. In order to improve pediatricians' understanding of MPX and achieve early detection, early diagnosis, early treatment, and early disposal, we hereby formulated an expert consensus on the basis of the latest “*Clinical management and infection prevention and control for monkeypox*” released by the World Health Organization (WHO), the “*guidelines for diagnosis and treatment of monkeypox (version 2022)*” issued by National Health Commission of the People's Republic of China and other relevant documents [8, 9].

Pathogen

MPXV is an enveloped double-stranded DNA virus with a genome size of approximately 190 kb. MPXV belongs to the orthopoxvirus genus of the Poxviridae family and is one of the four orthopoxviruses that are pathogenic to humans; the others are variola virus, cowpox virus, and vaccinia virus [10]. These viruses all contain soluble antigens, nucleoprotein antigens, and hemagglutinin, possess essentially the same antigenic properties and have displayed cross-immunity between them. Therefore, vaccination against smallpox can also provide cross-protection against MPXV infection.

MPXV can be manually isolated and cultured quite easily. It can grow well in cells from humans, monkeys, mice, rabbits, and other sources and in the chorioallantoic membrane of chicken embryos, leading to cytopathic effects. The morphology of MPXV is consistent with other orthopoxviruses; it has a rounded brick or oval shape, a size of 200 nm × 250 nm, and an outer membrane of 30 nm surrounding a homogeneous core body. The MPXV has two distinct genetic branches, the Central African (Congo Basin) clade and the West African clade [11], and the first clade is more contagious and severe in clinical characteristics [12].

Following sequence analysis, the strain of MPXV responsible for the current outbreak has been identified as belonging to the West African clade.

MPXV has shown resistance to low temperatures and drying and can remain infectious for months on fomites (e.g., soil, clothing, and bed linen) and in dermal crusts of infected patients. However, it is sensitive to high temperatures. An increased temperature of 56 °C for 30 min or 60 °C for 10 min can inactivate the virus. Furthermore, ultraviolet rays and general disinfectants can also inactivate MPXV, and MPXV is sensitive to sodium hypochlorite, chloroxylenol, glutaraldehyde, formaldehyde, and paraformaldehyde [9].

Epidemiology

Overview and epidemiological characteristics

MPXV occurs primarily in the partial tropical rainforest areas of Central and West Africa, encompassing 11 African countries, of which the Democratic Republic of Congo and Nigeria have suffered the most severe outbreaks in history [10]. MPXV infections mainly occur in people who did not receive the smallpox vaccination, in particular, children. In 1970, a male infant in the Democratic Republic of Congo was diagnosed as the first human MPX case, resulting in the definition of MPX as a zoonotic disease [1]. From 1970 to 1997, more than 500 confirmed cases with an average age of only 4.4 years were reported in the Democratic Republic of Congo, and from 2001 to 2008, this country reported more than 800 confirmed cases with an average age of 10 years [13]. Since 2017, a total of 249 confirmed cases have been reported in Nigeria, with an average age of 29 years, of which about 70% are males [14]. Previous studies have shown that the basic reproduction number (R_0) of the Congo Basin clade is about 0.6–1.0 [15], which is slightly higher than that of the West African clade, and its secondary attack rate in the unvaccinated population is about 8% [11].

The first MPX outbreak outside of Africa occurred in 2003 in the United States, resulting in 35 MPX cases caused by infected animals [2]. Between 2018 and 2021, sporadic cases associated with travel to Nigeria have been reported in the United Kingdom (the UK, seven cases), Israel (one case), Singapore (one case), and the United States (two cases), after which human-to-human transmission was identified [16–18]. The majority of cases of this current MPXV outbreak were reported after May 2022, and in the three-week period between August 23 and September 14, there were 16,000 laboratory-confirmed cases and 10 deaths increased [3]. Over 85% of confirmed cases were from the Region of the Americas and the European Region, of which the United States had the largest number of confirmed cases, with 22,774 confirmed cases reported as of September 14, 2022.

[19, 20]. Most of the confirmed cases were adult males who did not receive the smallpox vaccination. Among them, gay men, bisexuals, and other men who had sex with men were high-risk groups [3, 21]. Fewer cases have been reported in Asia. As of September 14, 2022, there are 16 cases in Singapore, 10 in India, 7 in Thailand, 4 each in Japan and the Philippines, 3 in Taiwan (China), 1 in Hong Kong (China), 2 in South Korea, and 1 in Indonesia [3].

The current MPX outbreak has already involved many countries and areas around the world rapidly, suggesting that undetected community transmission might have occurred in those countries, which is of high concern. As of 14 September, 2022, a total of 175 cases of monkeypox have been reported in children aged 0–17 years, with 65 cases in Africa Region, 62 in Europe, and 27 in the United States [3, 20, 21]. It is necessary to establish the prevention and control strategy and strengthen monitoring of the imported cases [22].

Source of infection

MPXV-infected animals and individuals are both the main sources of infection. The primary hosts of the MPXV are African rodents (African squirrels, tree species of squirrels, Gambian giant rats, dormice, etc.), and primates (a variety of monkeys and apes) can be occasionally infected due to contact with infected rodents [8, 9].

Route of transmission

MPXV invades the body through damaged skin or mucous membranes [8, 9].

Animal to human transmission

People would be infected by handling or eating raw meat from the infected animals, contacting with exudates, blood, and other body fluids of infected animals, either by being scratched or bitten by the infected animals.

Human to human transmission

MPXV is mainly transmitted through close contact, or respiratory droplets during prolonged and close contact with an infected person. Transmission also occurs when person come in contact with contaminated materials. In addition, transmission can also occur via the placenta from mother to fetus. There is no doubt that sexual behavior is actually a form of close contact. Given the high prevalence of gay or bisexual men and detectable MPXV DNA in their seminal fluid during the current outbreak, sexual transmission also appears obvious [23, 24].

Susceptible population

People who have been vaccinated against smallpox for more than 10 years and have not been vaccinated against smallpox are susceptible to the MPXV [8, 9].

Pathogenesis and pathophysiology

The pathogenesis of MPX has not been fully elucidated. The potential mechanisms currently considered are as follows.

- (1) Direct damage: after the MPXV enters the human body through damaged skin or mucosa, the virus can infect epithelial cells of the skin, respiratory tract, and vascular system, and rapidly change the metabolic function of these cells, leading to cell metabolic disorder and lytic death. Numerous viral particles are then released outside the infected cell, inducing new infection. Meanwhile, the MPXV can cause lymphadenopathy by spreading to lymphoid tissues and replicating [25, 26].
- (2) Viraemia: Adler et al. reported seven MPXV-infected cases, of which viral nucleic acids were detectable in the blood sample of six cases, with a maximum duration of more than 20 days [26]. The virus invades the bloodstream and spreads to the skin of the body where it replicates. Pathological manifestations include the swelling of epidermal keratin-forming cells in the form of vacuoles, ballooning and reticular degeneration, local spine layer relaxation or blister formation, small round well-defined inclusion bodies in the epidermis around the blisters, dilated dermal capillaries, and infiltration of mononuclear cells in the dermal papillae [27, 28].
- (3) Inhibition of immune response: the MPXV can escape to the immune system by blocking the synthesis of interferon-induced protein kinases, inhibiting the antigen presentation of MHC-II molecules and the NK- κ B signaling pathway, and evolving a variety of immunomodulatory proteins [29, 30].
- (4) Cytokine storm: MPXV infection promotes the activation of a large number of innate immune cells and specific immune cells, and releases a large number of cytokines. It can cause cytokine storm, leading to a systemic inflammatory response, impairment in the functions of multi-system organs, and even death in severe cases [31, 32].

Clinical presentations

Clinical presentations of monkey pox before the current outbreak

Incubation period is usually 6 to 13 days following exposure but can range from 5 to 21 days [23].

In the early-onset, there are prodromal manifestations such as fever, headache, dorsalgia, myalgia, fatigue, and superficial lymphadenopathy (located at the mandibula, neck, behind the ear, armpit, or/and groin), which lasts for one to three days [33–37], and fever may not be present in some pediatric patients. Among them, swollen lymph nodes are a distinctive feature of MPX that is different from other diseases characterized by fever and rash, such as chicken pox, smallpox, and measles [15]. In addition, patients may also suffer from cough and sore throat.

A rash appears one to three days after the onset of symptoms. The rash is similar to a smallpox rash, first appearing on the face and gradually spreading to the head, trunk, extremities, palms, and soles. The rash tends to be denser (centrifugal distribution) on the face and extremities. The rash can involve the mucous membranes, including the conjunctiva, oral cavity, vulva, vagina, and anus. The rash goes through stages such as macules, papules, blisters or blood blister, pustules, and crusts. Blisters or blood blisters and pustules are mostly spherical, about 0.5–1 cm in diameter, hard in texture, and may be accompanied by obvious itching and pain. The number of herds varies from a few to thousands. Some children start with one or more rashes around the anus and genitals, followed by fever and enlarged lymph node. In severe cases, the rash may merge, and even large pieces of skin may fall off.

The rash lasts for about 2–4 weeks from the appearance to the scabs falling off. The rash is contagious before decrustation, in particular within one week after the rash appears.

Fever usually resolves on the first day of the rash or within three days; a secondary fever may occur during the pustular phase, suggesting that the patient is getting worse.

Erythema or hyperpigmentation, or even scarring, may remain after the scab falls off, and the scarring may last for several years. Depressed scarring is the most common long-term sequelae in pediatric patients.

Clinical presentations of monkey pox in the current outbreak

Before the rash appears, patients often present with systemic symptoms such as fever, headache, sore throat, back pain, myalgia, and fatigue, lasting 1–5 days. The number of rashes is usually 1–20, rarely > 100. The most common rash sites were the anogenital and perioral areas, less often on the trunk, arms, or legs. There are even some MPX cases with an isolated rash on their face or fingers. Rash can be present without systemic symptoms and swollen lymph nodes. Lymphadenopathy is not common, but there are rashes in the area of lymphadenopathy. The clinical presentation of some MPX cases is atypical, even without a clear epidemiologic background.

Complications before the current outbreak

MPX is mostly self-limiting, and most patients recover spontaneously within two to four weeks. However, some pediatric patients may develop complications. Immunocompromised children, and those who have certain skin conditions, such as eczema, are at risk of severe MPX. Most of the deaths occurred in children under the age of 10, mainly due to complications.

- (1) Secondary bacterial infection: most common, may include furuncle, carbuncle, cellulitis, abscess, necrotizing soft tissue infection, suppurative lymphadenitis, and posterior pharyngeal abscess. Sepsis (bloodstream infection) and septic shock can also occur.
- (2) Respiratory complications: bronchopneumonia and even respiratory distress.
- (3) Gastrointestinal complications: vomiting and/or diarrhea, which can lead to severe dehydration and disturbances in electrolyte and the acid-base balance.
- (4) Encephalitis: crying, feeding deterrence, convulsions, consciousness disorder, and even coma.
- (5) Eye infection and corneal scarring, which can lead to permanent vision loss.

Complications in the current outbreak

- (1) Proctitis/ulcerative pharyngitis or tonsillitis.
- (2) Genital, perianal, or facial lesions that evolve into large plaques, ulcers, or crusts and cellulitis requiring antibiotic treatment.
- (3) Moderate to severe rectal pain or defecation pain caused by proctitis or anal border lesions.
- (4) Edema or severe edema of penile foreskin.

Laboratory tests for monkey pox virus

General examination

The white blood cell count in peripheral blood is within the reference range or above, and the number of platelet counts is within the reference range or below. Some pediatric patients may have abnormal liver and kidney functions, such as elevated transaminase levels, decreased blood urea nitrogen levels, and hypoproteinemia.

Etiological examination

If MPX is suspected, health workers should collect appropriate specimens, such as skin lesions, blister fluid, dry crusts, and oropharyngeal or nasopharyngeal secretions and have

them transported to a laboratory with the certified capability of testing for pathogenic testing in accordance with the safety requirements for biological samples [38].

Nucleic acid test

Polymerase chain reaction (PCR) is the preferred laboratory test for MPXV, due to its high accuracy and sensitivity [39]. Gene sequencing technology can further provide support for virus mutation analysis and traceability. Due to the short duration of viremia, collection of patient blood samples for nucleic acid testing should not be routinely performed.

Serological test

Serological test for the detection of MPX can be used if the result of the nucleic acid test is inconclusive. The patient infected with the monkeypox virus has elevated levels of anti-orthopoxvirus IgM based on acute samples or has a four-fold rise in IgG antibody titer based on acute and convalescent samples [40]. Recent smallpox/monkeypox vaccination or exposure to other known orthopoxviruses may interfere with serological test.

Viral culture/isolation

The MPXV can be isolated from above specimens. Cultures of MPXV are easy to isolate and culture, but they must be handled in a Biosafety Level 3 (BSL-3) or higher-level laboratory.

Diagnosis

Suspected cases

Children with acute rashes of unknown etiology who have one or more of the following symptoms or signs and any of the following epidemiological history should be suspected of MPX [8, 9].

Symptoms or signs: Acute fever (> 38.5 °C), lymphadenopathy, headache, myalgia, back pain, weakness, and other clinical symptoms, and their clinical manifestations cannot be explained by chickenpox, shingles, herpes simplex, measles, hand-foot-mouth disease, bacterial skin infections, disseminated gonococcal infections, syphilis, etc.

Epidemiological history:

- (1) Traveled or resident in an overseas country or region with confirmed cases of MPX within 21 days of illness onset (focus on endemic countries);

- (2) Had close or intimate contact with a confirmed case of MPX within 21 days of illness onset;
- (3) Had contact with the blood, body fluids, or secretions of MPXV-infected animals such as rodents and non-human primates within 21 days of illness onset.

Confirmed cases

Confirmed cases are defined as suspected cases with nucleic acid test results positive for MPXV or isolation of the MPXV in culture from a clinical specimen [8, 9].

The infectious disease report should be handled in accordance with relevant requirements for any case that meet the criteria for suspected or confirmed cases.

Differential diagnosis

In the clinic, epidemiological history is very important for the differential diagnosis of MPX. Detailed observations on the distribution and morphological characteristics of rash are needed when a skin lesion appears, combined with a full-body accompanying performance. First, it should be differentiated from other infectious diseases with skin lesions such as smallpox, chicken pox, herpes zoster, herpes simplex, hand-foot-mouth disease, herpetic whitlow, syphilis, dengue fever, and scabies. In addition, it should also be differentiated from non-infectious diseases such as allergic diseases, including contact dermatitis, papular urticaria, fixed drug eruption, severe drug eruption, such as Steven Johnson syndrome, inflammatory diseases, bullous pemphigoid, allergic purpura, and neoplastic diseases, including bullous Langerhans cell histiocytosis and cutaneous mast cell hyperplasia.

Treatment

The management of MPX infection is mainly supportive and symptomatic treatment, including alleviating discomfort, management of complications, and preventing long-term sequelae.

General treatment and monitoring

For MPX cases, the general treatment strategies include appropriate rest, sufficient calories and liquid intake, maintaining the water–electrolyte balance and homeostasis, and closely monitoring of vital signs, fingertip pulse oxygen saturation, and grade of pain. Signs related to the mental status and diet of children, such as poor spirit, lethargy, irritability,

and paleness should also be closely observed. Complications should be noted. In addition, nutrition, feeding, nursing, and growth and development monitoring should be strengthened in premature babies and infants.

Supportive and symptomatic treatment

Management of compromised skin and/or mucosa

Keep skin, oral surface, ocular system, and nose clean to prevent bacterial infection, and avoid scratching the skin lesions; however, it is not recommended to use prophylactic antibiotics. If skin herpes were ruptured, boric acid solution or 0.5% furacillin solution can be considered for wet compression of the lesions. For significant pruritis from rashes, calamine lotion or oral antihistamine can be used. For lesions of oral mucosa, the mouth should be rinsed with salt water and normal saline daily. The use of chlorhexidine mouthwash for cleaning can be considered as well. Children under one year of age can be wiped with cotton swabs dipped in light saline or physiological saline. In case of genital or anorectal lesions, warm sitz baths may relieve symptoms. For keratitis or corneal ulceration, wearing contact lenses should be avoided and eye drops and Vitamin A supplementation could be adopted. An ophthalmologist should be consulted if symptoms persist [8, 9, 41].

Active control of hyperpyrexia

If the axillary temperature of pediatric patients exceeds 38.5 °C with obvious discomfort, antipyretic drugs should be given, such as ibuprofen or acetaminophen. For infants under two months of age, physical cooling should be used. Children who have febrile convulsions need prompt anti-stunning treatment [42].

Alleviation of pain

Analgesics can be used in the case of bothersome headache and pain from rash and swollen lymph nodes. For mild and moderate pain, non-steroidal anti-inflammatory drugs such as paracetamol (oral, 10–15 mg/kg every 4–6 hours, maximum dose 60 mg/kg/day) or ibuprofen (oral, 10 mg/kg every 6–8 hours) could be selected. For severe pain, tramadol or opioids such as morphine could be considered. Tramadol is limited to children aged six months and older, at a dose of 1–2 mg/kg, orally or intravenously every 4–6 hours, with a maximum daily dose of 400 mg. The dosage of morphine is oral 0.2–0.4 mg/kg/time every 4 hours, or via intravenous drip 0.05–0.1 mg/kg/time, every 4–6 hours [8, 9, 42–44].

Antivirals

Currently, there are no specific drugs that have been clinically tested for use in MPX, and antiviral drugs used to treat smallpox may be beneficial in the treatment of MPXV infection. Tecovirimat oral dosage form has been approved by the European Medicines Agency (EMA) for the treatment of MPXV infection in adults and children weighing ≥ 13 kg [45]. The recommended treatment dose and duration of Tecovirimat are as follows: 200 mg for children weighing 13–25 kg, 400 mg for 25–40 kg and 600 mg for > 40 kg orally; 6 mg/kg for 3–35 kg, 200 mg for 35–200 kg and 300 mg for > 120 kg intravenously, twice daily for 14 days [8]. In 2021, an adult MPX patient in the UK received Tecovirimat and had a shorter duration of viral shedding and symptoms compared with other patients [26]. In 2022, an adult immunocompromised man with MPXV infection in the USA received a two-week course of Tecovirimat twice a day. He did not report any significant adverse effects, and the skin lesions healed quickly [46]. Brincidofovir is an antiviral drug that inhibits nucleotide analog DNA polymerase in orthopoxviruses and also inhibits the replication of MPXV [47]. Its efficacy has been proved in a lethal MPXV animal model [48]. Brincidofovir is available as an oral tablet or suspension administered in two doses one week apart, 6 mg/kg for children weighing less than 10 kg, 4 mg/kg for children weighing 10–48 kg, and 200 mg for children weighing more than 48 kg [8]. However, in 2018 in the UK, no significant clinical benefit was found in three adult cases of MPX who received Brincidofovir, and all patients had elevated transaminases [26]. More clinical studies are needed to determine the safety and efficacy of Tecovirimat and Brincidofovir in MPX. In addition, experimental animal studies have shown that Cidofovir and NiOCH-14, an analog of tecoviride, have anti-MPXV activity, but the clinical efficacy of the MPX treatment is uncertain [47, 49]. Cidofovir is administered intravenously at 5 mg/kg, once weekly for two weeks [8]. According to the CDC in the USA, tecovirimat is currently being used as the first-line treatment for infection with MPXV, which may be considered for treatment in people infected with MPXV who have severe disease, who are at high risk of severe disease, and those with aberrant infections involving eyes, the mouth, or other anatomic areas (e.g., the genitals or anus); the use of brincidofovir and cidofovir may be considered in unusual circumstances, such as very severe infections, disease progression despite Tecovirimat treatment, or when Tecovirimat is contraindicated or unavailable [50–52].

Vaccinia immune globulin

There are no data available on the effectiveness of vaccinia immune globulin (VIG) in the treatment of MPX, and intravenous VIG may be considered for severe cases or post-exposure prophylaxis in patients with severe immunodeficiency who are unable to receive smallpox vaccine [50, 52, 53].

Management of complications

Secondary bacterial infection of skin (cellulitis, abscess)

Wet compresses with 3% boric acid solution or 1:5000 furcillin solution, or 0.5% neomycin ointment or 2% mupirocin ointment should be applied. Initial oral antibiotics should be sensitive to *Staphylococcus aureus* and Streptococcus, and antimicrobial therapy should be adjusted according to the results of pathogen culture, isolation and identification, and drug susceptibility. If necessary, the debridement of the skin, incision, and drainage may need to be performed in surgery.

Respiratory complications

For pneumonia, symptomatic support is given in priority and the use of antibiotics or antivirals are indicated for co-infections. If the child has acute respiratory distress syndrome, oxygen, non-invasive ventilation, mechanical ventilation, and symptomatic support should be given. Further injury to the heart, lungs, and other organs should be prevented.

Gastrointestinal complications

For children with vomiting and/or diarrhea, intravenous or intraosseous fluid resuscitation should be given to maintain water and electrolyte balance.

Sepsis and septic shock

Fluid resuscitation should be given actively, and vasopressors, as well as antimicrobials, may also be required.

Encephalitis

Sedation and dehydration should be given to reduce intracranial pressure. In case of combined infections, the patient should receive corresponding antibiotics and/or antivirals.

Keratitis or keratohectosis

Contact lenses should be avoided. Eye drops, supplemented with vitamin A and others can be applied, and severe cases should further be referred to ophthalmologists.

Psychosocial support

Pediatric patients with MPX are prone to discrimination and social exclusion due to its obvious manifestations of vesicular rash and purulent herpes, resulting in psychological disorders, emotional impairment, and social distress in children. Scarring and disability associated with the disease can also cause psychological distress. For children with emotional instability, fear, or psychological disorders, psychological interventions based on the principles of psychological guidance, behavioral therapy, and family therapy could be considered. Furthermore, anti-anxiety or antidepressant drugs can be used if necessary.

Management of comorbidities

Patients with underlying diseases (such as congenital cardiopulmonary and airway diseases, chronic cardio-renal diseases, malnutrition, hereditary diseases, immune deficiency diseases, and tumors), who are prone to severe disease and higher case-fatality after MPXV infection, should be given active treatment for MPX to control the primary disease.

Traditional Chinese medicine

MPX belongs to the category of "plague" in traditional Chinese medicine. According to traditional Chinese medicine, it could be treated dialectically in stages by combining the clinical manifestations and physiological characteristics of children.

Discharge criteria

The following criteria can be met for discharge: normal body temperature, significant improvement of clinical symptoms, and crusting off.

Infection prevention and control

Non-pharmaceutical intervention measures

The comprehensive control measures of MPX prevention are generally based on the management of infectious sources. Non-pharmaceutical intervention (NPI) measures, such as surveillance, isolation, and close contact tracing,

are currently the main measures of MPX prevention and control, aimed at slowing down the spread of the transmission. Surveillance and early detection of cases are crucial in containing the epidemic. All healthcare institutions at different levels should pay more attention to the epidemiological history of patients with fever and rash during their daily medical consultation, while simultaneously conducting pathogenic screening tests to exclude varicella, herpes zoster, herpes simplex, hand-foot-mouth disease, or other potential pathogens [40]. The designated isolation hotel or settings should conduct active surveillance and screening of MPX symptoms such as skin rash among their inbound personnel, especially those who had a history of residence in MPX epidemic countries within 21 days before entry. Individuals meeting the definition of suspected cases need to be promptly interviewed and investigated, and transferred to a designated hospital for isolation, medical observation, diagnosis, confirmation, and treatment. If MPX is confirmed, the patients should be immediately isolated in designated wards for treatment until all skin lesions have crusted and the scabs have fallen off [9].

Close contact with MPX patients is the most important risk factor. During a MPX outbreak response, identification, tracing, and management of close contacts are critical measures to prevent and control the transmission chain and should be initiated immediately after the detection and report of any suspected MPX case. Close contacts should be closely monitored for any signs or symptoms from the date of last exposure to the MPX case or contaminated objects of the MPX case [54].

Furthermore, to prevent MPXV transmittance from animals to humans, it is recommended to halt the import of rodents and non-human primates unless absolutely necessary, and the import trade of rodents and primates from MPX endemic areas in Africa should be restricted or banned. A quarantine period for carried and shipped animals should be reinforced at the border entry. Any animals that may have had contact with an animal infected with the MPXV should be quarantined, handled with standard precautions, and observed for MPX symptoms for 30 days [55].

Vaccination

Smallpox vaccine may provide some protection against MPX [56]. ACAM2000 (second-generation smallpox vaccine) is a replication-competent vaccine that can cause infection and serious adverse events after inoculation. The MVA-BN (Imvanex/JYNNEOS) vaccine, a third-generation smallpox vaccine (replication defective), has been licensed by the Food and Drug Administration (FDA) in the US and European Medicines Agency for the prevention of monkeypox [44, 50, 51]. In the USA, ACAM2000 and JYNNEOS are allowed for use against MPX for pediatric cases

under Expanded Access to Investigational Drugs authorization [52]. Efficacy and safety of these vaccines for the prevention of MPX in humans remain to be explored, specifically for children or adolescents.

Mass vaccination against smallpox or MPX is not advocated for the general population at this stage. The WHO recommends that vaccination should be decided through a joint risk assessment including health care personnel and the patient [57]. Pre-exposure vaccination is recommended for populations with occupational exposure risk to MPX, including laboratory personnel, clinical health care workers, epidemic management workers, and other high-risk groups, including gay, bisexual, and other men who have sex with men. Pre-exposure vaccination is also necessary for children who may be at increased risk of exposure. Post-exposure prophylaxis is recommended with second or third-generation vaccines for unprotected high-risk exposures; particularly close contacts of MPX cases is recommended preferably within four days (and up to 14 days for asymptomatic cases) after the last exposure [57, 58].

People without a history of smallpox vaccination should be given two doses of subcutaneous injections at four-week intervals, while people with a smallpox vaccination history may be given only one dose of subcutaneous injection [57, 58].

General prevention

To reduce the risk of exposure and infection, in addition to the vaccination and NPI measures, individuals should try to avoid unprotected contact with wild animals, especially sick or dead animals, including their flesh and blood. All food containing animal flesh or organs must be thoroughly cooked before consumption. People working or traveling in MPX epidemic areas should avoid close contact with wild animals and avoid sexual activity (e.g., men who have sex with men) with persons suspected of infection [59]. If contact with MPX patients is necessary, avoid close physical contact or sharing household items (e.g., bedding or clothing), and take good personal protection measures when caring for or visiting patients (e.g., wear disposable latex gloves, medical protective masks, and disposable isolation clothing). Pay attention to hand hygiene and wash hands under running water with soap and hand sanitizer in time [8].

Key points of nosocomial infection prevention and control

Disposal actions for MPX case

Healthcare workers should strictly implement the pre-examination triage and are responsible for the initial diagnosis.

When receiving people who present with fever and rash as initial symptoms, healthcare workers should carefully inquire about their epidemiological history and screen for pathology to diagnose in time. Suspected or confirmed cases should be reported to the China Information System of Disease Prevention and Control institutions within 24 hours.

Both suspected and confirmed cases should be isolated in a single isolation room, and their movements should be limited. To minimize the risk of contact transmission, it is recommended that one appointed family member stay with the child in isolation if necessary.

Patients are advised to wear surgical masks and replace them on time. Skin lesions should be unexposed as much as possible to avoid infection. Cover with dressing if there are few skin lesions and wear long-sleeve clothes and trousers if there are many lesions involved. For pediatric patients with extensive skin lesions who are in a severe condition and require bed rest, it is recommended to cover their skin lesions with scald gauze and to use a blanket to avoid secondary skin damage. Bed sheets and clothing should be changed every day and sterilized at a high temperature and high pressure. Ultraviolet disinfection is required daily in the isolation room.

It is necessary to register those who have been in close contact with suspected and confirmed cases, and implementation of isolation and medical surveillance should be done in time, usually for 21 days [9, 38, 59].

Personnel protection measures

If permitted by the patient's condition, a surgical mask should be recommended and replaced regularly. When patients leave the isolation room, the skin lesions should be covered as much as possible to minimize the risk of contact transmission. Caregivers should wear surgical masks and gloves and perform hand hygiene when touching the patient. In addition, caregivers should avoid sharing personal items with patients and reduce skin exposure.

Healthcare workers should take contact prevention and droplet prevention measures, such as wearing disposable latex gloves, medical masks, protective face shields or eye protection, and disposable isolation gowns, as well as perform hand hygiene [9, 38, 59].

Disinfection measures

According to the route of MPXV transmission, it is important to disinfect personal items, such as clothing, towels, sheets, and tableware. Other items contaminated by secretions, as well as the environment and surfaces that may be contaminated also need to be disinfected.

According to the resistance of MPXV, thermal disinfection, chlorine disinfectant, chlorine dioxide, peracetic

acid, hydrogen peroxide, etc. can be selected to disinfect by wiping, spraying, or soaking. Disposable medical supplies should be used as much as possible; for non-disposable medical supplies, pressure steam sterilization is preferred; for thermolabile items, chemical disinfectants or low-temperature sterilization should be used for disinfection or sterilization.

For hand hygiene, quick-drying hand sanitizer or directly applying 75% ethanol is recommended. For those who are allergic to alcohol, other effective alcohol-free hand sanitizers such as quaternary ammonium salts can be used. When contaminants are visible to the naked eye, hands should be washed immediately with washing solution or soap under running water according to the six-step washing method, followed by disinfection.

Patients' secretions, feces, and blood pollutants should be strictly disinfected [9, 38, 59].

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Declarations

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