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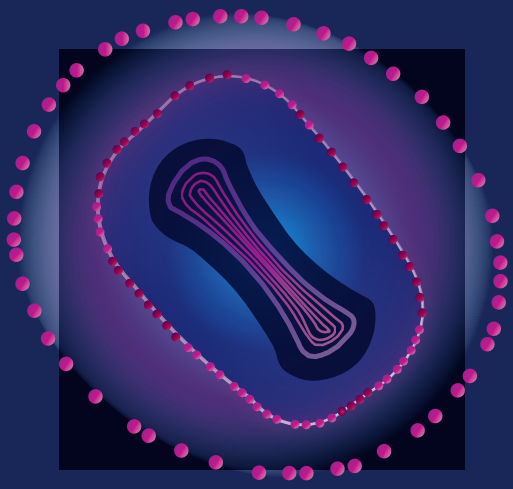
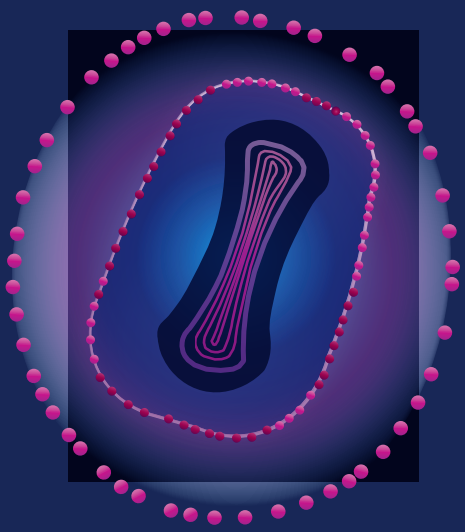
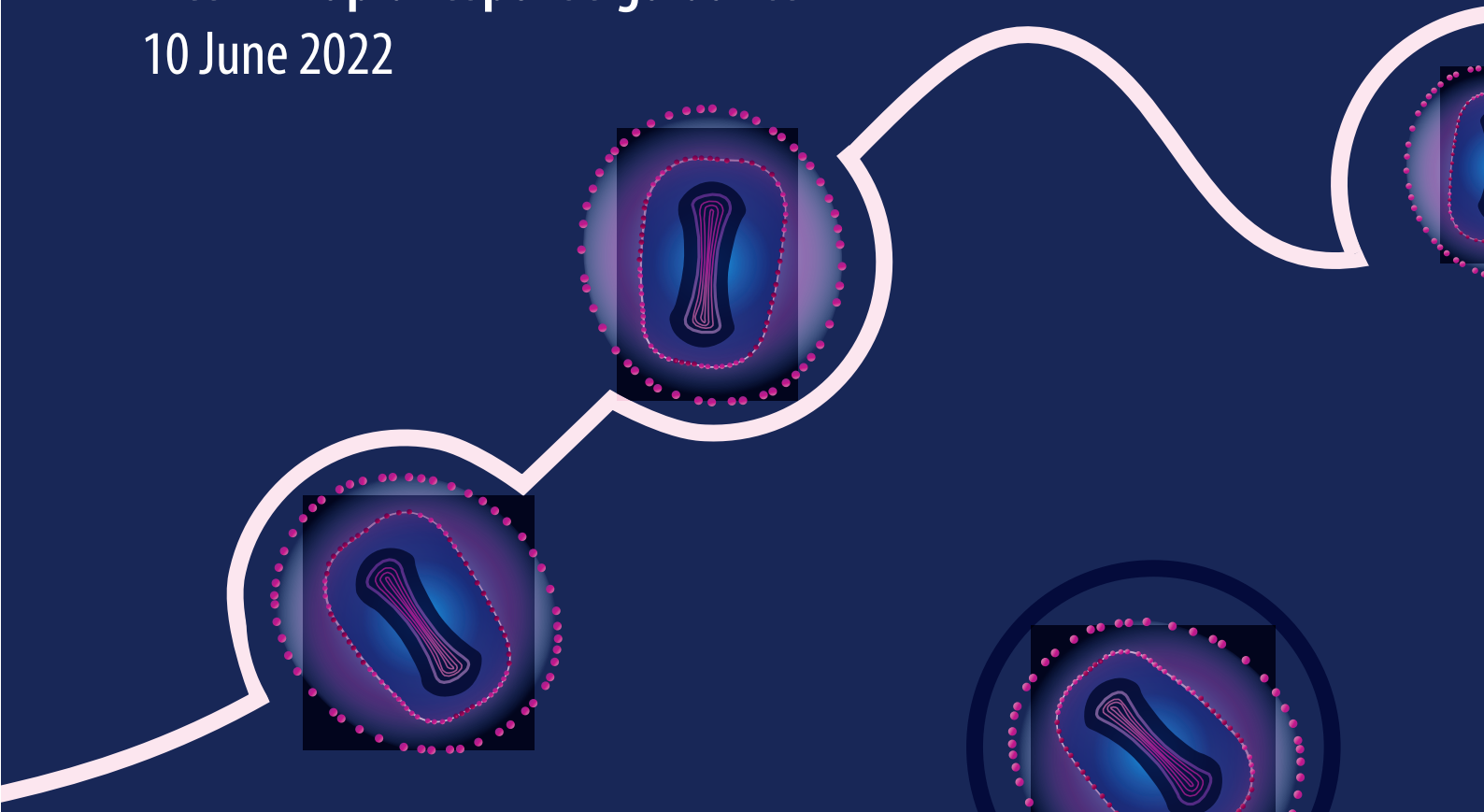




CLINICAL MANAGEMENT AND INFECTION PREVENTION AND CONTROL FOR MONKEYPOX

Interim rapid response guidance

10 June 2022



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ABBREVIATIONS

ABCD	airway, breathing, circulation, disability
ACH	air changes per hour
AGP	aerosol-generating procedure
AII	airborne infection isolation
ARDS	acute respiratory distress syndrome
ART	antiretroviral therapy
AVPU	alert, voice, pain, unresponsive (scale)
BMI	body mass index
CA-MRSA	community-acquired methicillin-resistant *Staphylococcus aureus*
CB	Congo basin
CBT	cognitive behavioural therapy
CDC	Centers for Disease Control and Prevention
CFR	case fatality ratio
CSF	cerebrospinal fluid
DGI	disseminated *gonococcal* infection
DOI	declaration of interest
EMA	European Medicines Agency
GDG	Guideline Development Group
HSV	herpes simplex virus
ID	infectious disease
IFRC	International Federation of Red Cross and Red Crescent Societies
IPC	infection prevention and control
IITT	Interagency Integrated Triage Tool (WHO/IFRC)
IO	intraosseous
IV	intravenous
LGV	lymphogranuloma venereum
MDR	multidrug-resistant
MEURI	Monitored Emergency Use of Unregistered and Investigational Interventions
MPX	monkeypox
MSM	men who have sex with men
MSSA	methicillin-sensitive *Staphylococcus aureus*
MUAC	mid-upper arm circumference (in children)
PAHO	Pan American Health Organization
PCR	polymerase chain reaction
PEP	post-exposure prophylaxis
PPE	personal protective equipment
PTSD	post-traumatic stress disorder
RCT	randomized controlled trial
RT-PCR	real-time polymerase chain reaction

STIs	sexually transmitted infections
US FDA	United States Food and Drug Administration
VIG	vaccina immune globulin
VZV	varicella zoster virus
WA	West Africa
WHE	Health Emergencies Programme (WHO)
WHO	World Health Organization

EXECUTIVE SUMMARY

Twelve years after the new orthopoxvirus was discovered in a Danish laboratory in 1958 the first case of human monkeypox (MPX) was identified in 1970 in a 9-month-old boy in the Democratic Republic of the Congo *(1,2)*. Since then most cases have been reported across Central and West Africa *(1)*. MPX rashes can resemble various infectious diseases such as varicella zoster virus, herpes simplex virus and syphilis. As of 6 June 2022, a total of 1002 laboratory-confirmed laboratory-confirmed cases of MPX have been reported to WHO from 29 Member States from Europe and North America, across four WHO regions and no deaths have been reported. To date, the current MPX outbreak is mostly among men who have sex with men (MSM) and have predominately been identified amongst men seeking care in primary care and sexual health clinics due to symptoms similar to other sexually transmitted infections (STIs). For the most up-to-date case numbers see website ( ).

Due to the multi-country nature of this outbreak, WHO has developed rapid interim guideline for the clinical management and infection prevention and control (IPC) of MPX. See Section 1 on the methodology for more details.

Target audience

This document aims to provide interim guidance for clinicians, health facility managers, health workers and IPC practitioners including but not limited to those working in primary care clinics, sexual health clinics, emergency departments, dental practices, infectious diseases clinics, genitourinary clinics, maternity services, paediatrics, obstetrics and gynaecology, and acute care facilities that provide care for patients with suspected or confirmed MPX. For the entirety of this document, for ease, we will refer to patients that are being assessed and entering the MPX clinical care pathway as suspects, which includes both epidemiological groups (suspected cases and probable cases).

SUMMARY OF RECOMMENDATIONS

Screening, triage, isolation and clinical assessment

WHO recommends:

- At the first point of contact with the health system, screening and triage be performed for all persons who present with a rash and fever or lymphadenopathy, according to locally adapted WHO case definition (), to identify individuals that have suspected or confirmed MPX.
- After screening and isolation, triage patients with suspected MPX using a standardized triage tool (such as the WHO/IFRC Interagency Integrated Triage Tool); and evaluate the patient to determine risk factors and presence of severe disease.
- Test suspected patients for MPX.

Management of mild or uncomplicated monkeypox

WHO recommends:

- Patients with suspected or confirmed MPX with mild, uncomplicated disease and not at high risk for complications can be isolated at home, for the duration of the infectious period, as long as a home assessment determines infection prevention and control (IPC) conditions are fulfilled at home setting.
- A home assessment should be conducted when deciding to isolate and care for a person with suspected or confirmed MPX with mild uncomplicated disease in a home setting.
- A patient with mild, uncomplicated MPX cared for at home should be isolated in an area separate from other household members and away from shared areas of the home (i.e. a separate room or area with a curtain or screen).
- Caution should be taken when handling and cleaning linens, household surfaces and during waste disposal.
- Patients with MPX be given symptomatic treatment such as antipyretics for fever and analgesia for pain.
- Patients with MPX be assessed for their nutritional status and given adequate nutrition and appropriate rehydration.
- Counsel patients with mild MPX about signs and symptoms of complications that should prompt urgent care.
- Conservative treatment of rash lesions should be performed dependent of their stage with aims to relieve discomfort, speed healing and prevention of complications, such as secondary infections or exfoliation.
- Antibiotic therapy or prophylaxis not be used in patients with uncomplicated MPX. However, lesions should be monitored for secondary bacterial infection (i.e. cellulitis, abscess) and if present treated with antibiotics with activity against normal skin flora, including *Streptococcus pyogenes* and methicillin-sensitive *Staphylococcus aureus* (MSSA).

WHO recommends: Mental health care of patients with monkeypox

WHO recommends:

- Prompt identification and assessment for anxiety and depressive symptoms in the context of MPX should be done. Initiation of basic psychosocial support strategies and first-line interventions for the management of new anxiety and depressive symptoms should be taken.
- Psychosocial support strategies should be the first-line interventions for management of sleep problems in the context of acute stress.

Antiviral and other therapies

- In patients with MPX, it is preferable to use antivirals under randomized clinical trials (RCTs) with collection of standardized clinical and outcome data to rapidly increase evidence generation on efficacy and safety and, when not possible, antivirals may be used under expanded access protocols, such as MEURI (Monitored Emergency Use of Unregistered and Investigational Interventions) *(3)*.

Infection prevention and control at health facilities

WHO recommends:

- Contact and droplet precautions be implemented for any suspect patient with MPX. In addition to contact and droplet precautions, airborne precautions should be implemented if varicella zoster virus (i.e. chickenpox) is suspected and until it is excluded.
- Contact and droplet precautions be implemented for any confirmed patient with MPX. In addition to contact and droplet precautions, respirators should be used.
- Airborne precautions be implemented if aerosol-generating procedures (AGPs) are performed.
- Areas within the health care facility frequently used by the patient or where patient care activities occur and patient care equipment should be cleaned and disinfected as per national or facility guidelines.
- Linens, hospital gowns, towels and any other fabric items should be handled and collected carefully.
- All bodily fluids and solid waste of patients with MPX should be treated as infectious waste.
- Patients isolated with MPX should have measures put in place to support patient interaction with family and visitors to promote well-being.

Caring for sexually active populations

WHO recommends:

- All patients should be advised to abstain from sex until ALL skin lesions from MPX have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath.
- Based on the precautionary principle, WHO suggests the use of condoms consistently during sexual activity (receptive and insertive oral/anal/vaginal) for 12 weeks after recovery to prevent the potential transmission of MPX.

Caring for women during and after pregnancy

WHO recommends:

- Pregnant or recently pregnant women with mild or uncomplicated MPX may not require acute care in hospital but monitoring in a health facility may be preferred; those with severe or complicated disease should be admitted to a health facility for care as they require optimized supportive care or interventions to improve maternal and fetal survival.
- Pregnant and recently pregnant women with MPX should have access to woman-centred, respectful, skilled care, including midwifery, obstetric, gynaecologic, fetal medicine and neonatal care, as well as mental health and psychosocial support, with readiness to care for maternal and neonatal complications.
- Mode of birth should be individualized, based on obstetric indications and the woman's preferences. WHO recommends that induction of labour and caesarean section should only be undertaken when medically justified and based on maternal and fetal condition.
- Pregnant and recently pregnant women who have recovered from MPX should be enabled and encouraged to receive routine antenatal, postpartum or abortion care, as appropriate. Additional care should be provided if there are any complications.

Caring for infants and young children with monkeypox

WHO recommends:

- Newborn infants of mothers with MPX should be monitored closely for evidence of potential congenital or perinatal exposure or infection. Mothers and infants or young children can also be exposed through close contact.
- Children exposed to MPX should be fully vaccinated for age according to the routine national immunization schedule and have their vaccinations up to date, when possible.

Feeding of infants in mothers infected with monkeypox

WHO recommends:

- Infant feeding practices, including whether to stop breastfeeding for a mother with MPX, should be assessed on a case-by-case basis, considering the general physical status of the mother and severity of disease, which could impact the risk of transmission of MPX from mother to infant.

Management of high-risk patients and those with complications or severe monkeypox

WHO recommends:

- Patients at high risk for complications (i.e. young children, pregnant women and those who are immunosuppressed) or those with severe or complicated MPX should be admitted to the hospital for closer monitoring and clinical care under appropriate isolation precautions to prevent transmission of MPX virus.
- Patients with MPX who develop complications or severe disease should be managed with optimized supportive care interventions.

Caring for monkeypox patients after acute infection

WHO recommends:

- Patients with suspected or confirmed MPX should have access to follow-up care. All patients with MPX (and their caregivers) should be counselled to monitor for any persistent, new or changing symptoms. If this occurs, they should seek medical care according to national (local) care pathways.

Management of the deceased

WHO recommends:

- The handling of human remains of deceased individuals with MPX should be done with appropriate IPC measures.

Management of exposed health workers

- WHO recommends staff with an occupational exposure to MPX should have an assessment and management plan.

Collection of standardized data collection and the WHO Clinical Platform

1. METHODOLOGY

This rapid response interim guideline was developed according to the standards and methods described in the *WHO Handbook for guideline development (4).* The initial content was derived from a draft version of the *Monkeypox field guide* (unpublished, see acknowledgements) chapters on clinical care and IPC. These chapters were converted into practical "straw-man" recommendations by the WHO Steering Committee, led by the Clinical Management and Operations Unit, and the IPC team, Country Readiness Strengthening Department, WHE. On 25 May 2022, the WHO Steering Committee was convened to agree on the scope of the guideline and the draft "straw-man" recommendations version of the guidance.

Related guidelines: When possible, already published WHO guidelines were used to support rapid recommendations (see References).

Timing: This is published as the *Clinical management and infection prevention and control for monkeypox: interim rapid response guidance*, with a proposed update 2 months from publication and conversion to a GRADE-based guideline that adheres to standards for trustworthy guidelines.

Stepwise approach

Step 1. Evidence monitoring: For the clinical recommendations, a comprehensive search was performed online via PubMed, using the following search criteria: "Monkeypox", "Orthopoxvirus or Poxvirus" "Clinical outcomes" "Maternal outcomes" "Immunosuppression" and "Antivirals or therapeutic". Randomized controlled studies, cohort studies, meta-analysis, case reports and review articles were reviewed. Because of the accelerated timeline and broad scope of the guideline, it was not feasible to undertake a formal GRADE process (PICO questions; systematic reviews; formal documentation of values and preferences; and incorporation of considerations of costs, resources and feasibility).

For IPC recommendations, draft guidance was developed based on transmission-based precautions. This was circulated to an expert panel of IPC and infectious disease (ID) specialists which requested a rapid literature review be conducted. The technical unit then conducted a rapid literature search on PubMed using the search strategy "Monkeypox", "Orthopoxvirus or Poxvirus" AND "transmission". Systematic reviews and relevant papers were included and reviewed. On 25 May 2022 a consultation with IPC and ID experts from all WHO regions was held to discuss IPC measures and the findings of the rapid literature search were shared at this meeting. On 24 May 2022, WHO hosted a clinical network meeting to gather information about clinical characteristics and management from clinicians with recent experiences in the care of patients.

Step 2. Convening the GDG: On 27, 28 and 30 May 2022, WHO convened an expert GDG comprised a multidisciplinary panel of health care providers with experience in the clinical management and IPC of patients with emerging zoonotic diseases, HIV, STIs, as well as sepsis. In preparation for this meeting, the draft guidance was circulated to the panel alongside the primary references used in its development. The technical unit collected and managed declarations of interest (DOIs) and found no GDG member to have a conflict of interest. In addition to the distribution of a DOI form, during the meeting, the WHO Secretariat described the DOI process and an opportunity was given to GDG members to declare any interests not provided in written form. No verbal conflicts were declared. Web searches did not identify any additional interests that could be perceived to affect an individual's objectivity and independence during the development of the recommendations.

Step 3. Final recommendations: The GDG convened and was moderated by two external chairs. Draft "straw-man" recommendations were shared with the panel beforehand and discussion was moderated until consensus was achieved. The following elements of the evidence to decision framework were discussed: benefits and harms, feasibility, resource considerations, equity and patient values and preferences. The available, very low quality evidence (small observational studies) and expert opinion underpinned the discussions. In addition, the precautionary principle was raised due to the limited information that was available and the current uncertainty related to modes of transmission and the potential risks for health workers and the public. The draft document was shared with the GDG in an iterative process every day after the meetings for their review. The draft document was shared with the GDG in an iterative process every day after the meetings for review. The WHO Steering Committee pre-specified voting rules in the case that consensus was not clearly achieved. A simple majority would be used to determine the direction of the recommendation.

Step 4. Review, publication and dissemination: The final document was submitted for expedited Guideline Review Committee (GRC) and approved for executive clearance by Mike Ryan (Executive Director, WHE).

WHO will aim to update this guidance with a GRADE-based, standard WHO guideline within 8–12 weeks of publication.

2. CLINICAL CHARACTERIZATION

2.1 Background

Monkeypox (MPX) is a viral zoonotic disease that belongs to the *Orthopoxvirus* genus of the *Poxviridae* family. Human disease was first identified in 1970 in a 9-month-old boy in the Democratic Republic of the Congo and since then most cases have been reported across Central and West Africa *(1,2)*. There are two known clades of MPX, one in West Africa (WA) and one in the Congo Basin (CB) region *(5)*. Historically, the CB clade appears to be more virulent, with a case fatality ratio (CFR) ranging from 1% to 10% *(2,6,7)*, whilst the WA clade is associated with an overall lower mortality rate of < 3% *(7,8)*. Recent data for the latter report a CFR of 1.4% *(9)*. It is important to note that mortality in different settings may differ substantially.

2.2 Natural history and disease severity

The incubation period of MPX is usually 6 to 13 days following exposure but can range from 5 to 21 days *(10)*. Although most people recover within weeks, severe complications and sequelae have been reported to be more common among those unvaccinated for smallpox compared with those vaccinated (74% vs 39.5%) *(11)*. It is unclear if there is waning immunity to smallpox vaccination over time; however, studies indicate that smallpox vaccination is approximately 85% effective in preventing MPX *(12)*. Since prior smallpox vaccination may result in a milder disease course, it is important to ascertain vaccination status in any person exposed to MPX *(9)*. Evidence of prior vaccination against smallpox can typically be found as a scar on the upper arm. Individuals over 40 to 50 years of age (depending on the country) may have been vaccinated against smallpox prior to cessation of global smallpox vaccination campaigns after the WHO declared eradication of the disease in 1980 *(1)*. Additionally, some laboratory personnel or health workers may have received the vaccine.

To date, most reported deaths have occurred in young children and immunocompromised individuals, such as those with poorly controlled HIV *(8,11,13)*. A recent study from the Democratic Republic of the Congo reported that in a cohort of 216 patients, there were three deaths in patients < 12 years of age. When compared with survivors, patients with fatal disease had higher MPX viral DNA in blood, maximum skin lesion count, and day of admission AST and ALT values *(9)*.

2.3 Signs and symptoms

MPX can cause a range of clinical signs and symptoms. The initial phase of clinical illness typically lasts 1 to 5 days, during which time patients may experience fever, headache, back pain, muscle aches, lack of energy and lymphadenopathy – which is a distinctive feature of this disease *(9)*. This is followed by a second phase, which typically occurs 1 to 3 days after fever subsides with the appearance of a rash *(12,14,15)*. The rash presents in sequential stages – macules, papules, vesicles, pustules, umbilication before crusting over and desquamating over a period of 2 to 3 weeks. The lesions range in size from 0.5 to 1 cm in diameter and from a few to several thousand in number *(1,2)*. The eruption tends to be centrifugal, starting on the face and extending towards the palms and soles of the hands and feet, and can involve the oral mucous membranes, conjunctiva, cornea and/or genitalia *(2,11,16)*. Observations from current outbreaks in European and North American countries describe lesions starting in the genital area, but more information is

needed *(17)*. Patients may develop lymphadenopathy – which was described in 98.6% of a cohort of over 200 patients with MPX in the Democratic Republic of the Congo *(2,9)*. Oral ulcers are common and may affect a patient's ability to eat and drink leading to dehydration and malnutrition *(14,18)*. Inflammation of the pharyngeal, conjunctival and genital mucosae may also occur *(10,14)*. A recent large prospective observational study describing the natural history of 216 patients with MPX in the Democratic Republic of the Congo described the most common clinical symptoms to be rash (96.8%), malaise (85.2%) and sore throat (78.2%). The most common findings on physical examination were the classic MPX rash (99.5%); lymphadenopathy (98.6% – the cervical region was most frequently affected [85.6%], followed by the inguinal region [77.3%]); and mouth/throat lesions (28.7%) *(9)*.

Though uncommon, patients with MPX may develop severe and life-threatening complications. For example, the confluence of skin lesions are susceptible to bacterial skin and soft tissue infections such as cellulitis, abscesses, necrotizing soft tissue infections requiring meticulous local wound care; subcutaneous accumulation of fluid in the crusting phase leading to intravascular depletion and shock; and exfoliation resulting in areas of skin that may require surgical debridement and grafting *(14,15,18)*. Other rarer complications include severe pneumonia and respiratory distress, corneal infection which may lead to vision loss, loss of appetite, vomiting and diarrhoea which may lead to severe dehydration, electrolyte abnormalities and shock, cervical lymphadenopathy which may lead to retropharyngeal abscess or respiratory compromise, sepsis, septic shock, and, encephalitis and death *(8–11,13–15)*.

Small studies looking at laboratory abnormalities in patients with MPX indicate that leucocytosis, elevated transaminases, low blood urea nitrogen and hypoalbuminaemia were common features during illness, and that lymphocytosis and thrombocytopenia were seen in more than one-third of patients evaluated *(2,9,18)*.

2.4 Differential diagnosis

The rash which develops in MPX may resemble other infectious diseases or other conditions, including varicella zoster virus (VZV, chickenpox), herpes simplex virus (HSV), primary or secondary syphilis, disseminated *gonococcal* infection (DGI), foot and mouth disease, chancroid, lymphogranuloma venereum (LGV), granuloma inguinale, molluscum contagiosum, measles, scabies, rickettsia pox, chikungunya, zika virus, dengue fever, vasculitis and other bacterial skin and soft tissue infections.

Often, the rash caused by VZV can be confused with MPX but can be distinguished as the rash in varicella generally progresses quicker, is more centrally located than the centrifugal distribution of MPX, is in multiple stages of development (rather than the same stage as seen in MPX) and patients usually do not have lesions on their palms and soles *(2,11)*. Additionally, patients with VZV typically do not have lymphadenopathy, which is a hallmark of MPX *(11)*. Despite the clinical differences between these two diseases, a study from the Democratic Republic of the Congo reported co-infection with MPX/VZV with an incidence of 10–13% *(19,20)*. Patients with co-infection reported fatigue, chills, headache and myalgias. These individuals were less likely to report signs/symptoms of oral sores, axillary lymphadenopathy, cough or sore throat. Patients with co-infection had a higher lesion burden than seen with VZV alone but a lower rash burden than seen with MPX alone raising the suggestion that co-infection with these two viruses could modulate severity of the overall infection – an area for further investigation *(19,20)*.

2.5 Transmission and viral shedding

Despite decades of circulation in animals with occasional spread to humans, there are limited data available describing transmission and viral shedding of MPX. Available information supports that transmission can occur from animal to human, human to human and from contaminated environments to humans. To date, most information is available from countries in West and Central Africa and less from areas in other WHO regions *(18)*.

MPX virus is transmitted from infected animals to humans via indirect or direct contact *(12)*. Transmission may occur from bites or scratches, or during activities such as hunting, skinning, trapping, cooking, playing with carcasses, or eating animals, such as non-human primates, terrestrial rodents, antelopes and gazelles, and tree squirrels *(14)*. The extent of viral circulation in animal populations is not entirely known and further studies are underway *(11)*.

Human-to-human transmission can occur through direct contact with infectious skin or mucocutaneous lesions, this includes face-to-face, skin-to-skin, mouth-to-mouth or mouth-to-skin contact and respiratory droplets (and possibly short-range aerosols requiring prolonged close contact) *(2,21,22)*. The virus then enters the body through broken skin, mucosal surfaces (e.g. oral, pharyngeal, ocular and genital), or via the respiratory tract *(21,23)*. The infectious period can vary, but generally patients are considered infectious until skin lesions have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath. Transmission can also occur from the environment to humans from contaminated clothing or linens that have infectious skin particles (also described as fomite transmission). If shaken, these particles can disperse into the air and be inhaled, land on broken skin or mucosal membranes and lead to transmission and infection; one documented health worker infection has been published suggesting MPX virus transmitted through contact with contaminated bedding *(15,24)*. Persistence of surrogate pox virus in the environment and on different types of surfaces has been found to last between 1–56 days depending upon the temperature and room humidity *(25,26)*; however, there are currently limited data on surface contamination and fomite transmission, aside from contaminated linens *(15)*. Pox viruses are generally more resistant to environmental conditions and show high environmental stability *(25,26)*. During our literature search, no information on the presence of virus in wastewater was found.

A recent study published in May 2022 from the United Kingdom has reported on the clinical characterization, viral kinetics and polymerase chain reaction (PCR) positivity and response to antivirals in seven patients infected with MPX between 2018 and 2021. All seven patients had MPX viral DNA detected by PCR in skin lesions and in upper respiratory tract samples; six patients had DNA detected in blood; four patients had DNA detected in urine and one person had DNA detected in skin abscesses. Another recent study published in May 2022 on the clinical characterization of 216 patients diagnosed between 2007 and 2011 in the Democratic Republic of the Congo suggested that MPX viral DNA in blood and the upper respiratory tract may be detected prior to onset of rash and that peak viral load may occur very early in the disease course *(9)*. Data also suggest the MPX scabs contain significant quantities of viral DNA until and including when they fall off and that it is higher than the levels found in the blood and throat *(9)*. It should be noted that viral infectivity of specimens was not determined. At this time, the significance of these findings in relation to viral transmission and infectious period remains uncertain *(12)*. More information is needed to better understand other possible modes of transmission and persistence via contact with other bodily fluids (such as breastmilk, semen, vaginal fluid, amniotic fluid or blood) and to better understand transmission by respiratory droplets and aerosols.

In the current outbreak countries and amongst the reported MPX cases, transmission appears to be occurring primarily through close physical contact, including sexual contact (oral, vaginal and anal).

2.6 Women and persons that are pregnant or postpartum

In utero transmission of MPX has been documented as has transmission from mother to child via direct contact *(27,28)*. The former is from a longitudinal case series that reported outcomes of four pregnant women: one delivered a healthy baby, two had early miscarriages and one a fetal death where the stillborn was covered with diffuse rash with virologic confirmation of MPX. This suggests that MPX virus infection may lead to adverse outcomes for the fetus, such as death or spontaneous abortion *(9,28)*. The association between severity of maternal illness and these outcomes is unclear *(28,29)*.

2.7 Mid- and long-term effects

More information is needed about the clinical characterization of mid- and long-term effects of MPX. A study has reported > 90% of MPX survivors have no complications, regardless of smallpox vaccination status *(14)*. Of those who do develop long-term complications, most common sequelae are disfiguring scarring of the skin and blindness *(11,14,30)*. Pitted scars can develop called pockmarks *(11,14)*. Data also suggest that patients may be at risk for developing mental health complications *(15)*.

2.8 Summary of clinical care and infection prevention and control

Caring for patients with suspected or confirmed MPX requires early recognition of suspects, rapid implementation of appropriate IPC measures, testing of likely pathogens to confirm diagnosis, symptomatic management of patients with mild or uncomplicated MPX and monitoring for and treatment of complications and life-threatening conditions such as severe dehydration, severe pneumonia and sepsis. The role of MPX-specific therapeutics remains experimental and can be used under RCTs (preferred) or expanded access protocols. Implementation of appropriate IPC measures with engineering, administrative and personal protective equipment (PPE) controls is essential to mitigate and control transmission of MPX in health care and community settings *(31)*. All patients with MPX should receive respectful, patient-centred care that maintains dignity, privacy and confidentiality.

3. SCREENING, TRIAGE, ISOLATION AND CLINICAL ASSESSMENT (3 RECOMMENDATIONS)

WHO recommends, at the first point of contact with health system, screening and triage be performed for all persons who present with a rash and fever or lymphadenopathy, according to locally adapted WHO case definition (☝) (see Annex 1), to identify individuals that have suspected or confirmed MPX.

Remarks:

- A simplified questionnaire and screening protocol based on the WHO case definition adapted to local epidemiology can be implemented at the point of entry to health care (or during contact tracing) to screen patients based on the WHO case definition and local epidemiology. For example, during this outbreak, this can be done at primary care clinics, sexual health clinics, emergency departments, infectious diseases clinics, genitourinary clinics, dermatology clinics, maternity and paediatrics clinics and others.
- Depending on national (local) coordination pathways, telemedicine may be considered as a means of screening patients.
- Medical masks and alcohol-based hand sanitizer should be available for patients presenting at screening areas. Signs should be posted for both respiratory hygiene and hand hygiene and instructions to put on a well-fitting medical mask if any respiratory symptoms.
- Screening activities should be conducted maintaining a distance of at least 1 m from patients and using a "no touch" approach. Where these measures cannot be implemented or maintained then the facility should conduct a risk assessment to determine the level of PPE required according to the IPC recommendations for health facilities in the context of MPX (see Section 7 on IPC). Health workers performing screening should follow the WHO Your 5 moments for hand hygiene *(31,32)* (☝).
- While waiting, crowding should be prevented between patients and a distance of at least 1 m should be maintained between patients *(32).*
- Persons with symptoms that meet the case definition for suspected MPX should enter the MPX clinical care pathway and immediately be given a well-fitting medical mask and isolated in a well-ventilated single room. If a well-ventilated single room is not available, then group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation (at least 1 m between patients). Suspected cases should not be cohorted together with confirmed cases (see Section 7 on IPC).
- Consider implementing in-patient surveillance for MPX depending upon local epidemiology.

WHO recommends after screening and isolation, triage patients with suspected MPX using a standardized triage tool (such as the WHO/IFRC Interagency Integrated Triage Tool); and evaluate the patient to determine risk factors and presence of severe disease.

Remarks:

- Triage refers to the sorting of patients by priority after screening, based on specific criteria (e.g. severity) and can be performed at any point of access to the health care system, including in both pre-health care and facility-based settings *(33)*. This can also be done on hospital wards, during monitoring of patients.
- Acuity based triage is the action of sorting and prioritizing patients based on the estimation of their severity. This is used to identify patients who require immediate medical intervention and those who can safely wait or who may need to be transported to a specific destination based on their condition *(33)*.
- The Interagency Integrated Triage Tool (IITT) is a novel triage tool developed to provide an integrated set of protocols for routine triage of adults and children. The tool focuses on a three-tier triage system and can be found in the WHO *Clinical care for severe acute respiratory infection toolkit* (👆) *(33)*.
- Clinical assessment should focus on identifying signs and symptoms of severe or complicated disease and those at higher risk for severe disease (see Table 3.1).

Table 3.1. Risk factors and clinical findings described as being associated with severe disease and poor outcomes (based on small, uncontrolled, observational studies)

Patient groups at higher risk of severe disease or complications	• Children, pregnant women, persons who are immunosuppressed such as persons living with HIV having poorly controlled disease *(5,6,10,11,13,26)*. • Though data are lacking, patients with chronic skin conditions (e.g. atopic dermatitis), acute skin conditions (i.e. burns) may also be at higher risk for complications, such as bacterial infection *(33)*.
Clinical signs and symptoms of complications	• Nausea and vomiting *(11,16)*, painful cervical lymphadenopathy causing dysphagia, poor oral intake, eye pain, vision abnormalities, hepatomegaly, sepsis, dehydration, respiratory distress/pneumonia, and/or confusion.
Laboratory abnormalities	• Elevated hepatic transaminases (AST and/or ALT), low blood urea nitrogen (BUN), low albumin, elevated white blood count (WBC), or low platelet count *(16)*.
Skin lesion severity score	• From smallpox experience *(28,94)*: – Mild (< 25 skin lesions) – Moderate (25–99 skin lesions) – Severe (100–250 skin lesions) – Very severe (> 250 skin lesions).

WHO recommends to test suspected patients for MPX.

Remarks:

- Testing for MPX should be conducted as soon as possible to confirm diagnosis (see *Laboratory testing for the monkeypox virus: interim guidance* (), updated 23 May 2022).
- In areas with other endemic infections that cause rash and fever or lymphadenopathy, or if patient has risk factors for other diseases, as part of screening, febrile patients should be tested and treated per routine protocols (e.g. STIs such as syphilis, HSV and HIV for sexually active persons, malaria testing in endemic areas for patients with fever, and other infectious diseases per clinical context and local epidemiology) (see Section 2) *(9,34,35)*. Co-infection may coexist (see Section 1), but prevalence remains unknown *(13,19)*. Co-infection has been reported in up to 13% of patients in the Democratic Republic of the Congo.

4. MANAGEMENT OF MILD OR UNCOMPLICATED MONKEYPOX (9 RECOMMENDATIONS)

4.1 General considerations for community care

Health ministries and intersectoral partners at national and subnational levels should engage with communities and other actors to identify and provide the resources needed, implement risk communication strategies to provide support, and look to other contexts for possible solutions to ensure that IPC measures can be met to provide safe care in settings where patients will be cared for *(36)*.

WHO recommends that patients with suspected or confirmed MPX with mild, uncomplicated disease and not at high risk for complications can be isolated at home, for the duration of the infectious period, as long as a home assessment determines IPC conditions are fulfilled at home setting.

Rationale:

- The guidance panel agreed that for patients with mild or uncomplicated MPX home isolation was reasonable provided IPC measures could be implemented to reduce the risk of transmission and that this may be preferred by patients, and by health systems to reduce burden on hospitals. National or subnational health authorities may recommend isolation in community or health facility based on their analysis of benefits and harms.

Clinical considerations:

- Decision to isolate and monitor a patient at home should be made on a case-by-case basis and be based on their clinical severity, presence of complications, care needs, risk factors for severe disease and access to referral for hospitalization if condition deteriorates.
- Patients isolating at home should be ambulatory, have good food and water intake, be able to feed, bathe and dress themselves, and require minimal to no assistance from a caregiver.
- Those at higher risk for severe disease such as children, pregnant women or immunosuppressed patients should be considered for admission to a health facility for closer monitoring due to concern for clinical deterioration.
- If vulnerable populations are living in the home setting and adequate IPC requirements cannot be met, consider isolation in a health facility *(36)*. Vulnerable persons that should be identified in the home due to their increased risk of adverse outcomes if infected with MPX include young children, pregnant women and persons who are immunosuppressed, such as persons living with HIV not on antiretroviral therapy (ART) *(7,8,13,15,28)*. Though data are lacking, patients with chronic skin conditions (e.g. atopic dermatitis) or acute skin condition (i.e. burns) may also be at higher risk for complications *(37)*.

WHO recommends that a home assessment should be conducted when deciding to isolate and care for a person with suspected MPX or confirmed MPX with mild uncomplicated disease in a home setting.

IPC remarks:

- A trained health worker should assess and counsel whether the home in question is suitable for the isolation and provision of care of a patient with MPX, including whether the patient and/or other household members have the capacity and required provisions (see Annex 5). This includes the ability to adhere to home isolation. Limited or no access to water, sanitation or resources for personal hygiene and limited ability to maintain isolation and IPC measures pose risks for household and community members. This assessment can be done at the initial health visit or via telephone or telemedicine and does not require a home visit.
- The patient and designated person that is facilitating self-care should be counselled regarding the risks of transmission. It is preferred that the designated person be previously vaccinated against smallpox or MPX and not be from a high-risk group.
- If adequate isolation and IPC measures cannot be ensured at home, then isolation may need to be arranged, with informed consent from the patient and agreement from the caregiver and members of the household, in a health care facility or other designated facility *(36)*.
- If vulnerable persons (those at higher risk for complications, see Table 3.1) are present in the home setting and cannot be kept apart from the patient, then the health worker should offer to arrange for an alternative location for isolation for the patient if available.

4.2 IPC considerations in community

WHO recommends that a patient with mild, uncomplicated MPX cared for at home should be isolated in an area separate from other household members and away from shared areas of the home (i.e. a separate room, or area with a curtain or screen).

Remarks:

- Patients at home with MPX should be able to manage their self-care. Clinical follow up should be conducted using methods other than in-person visits (e.g. telemedicine, telephone).
- Designate one person to facilitate the self-care of the patient with mild, uncomplicated MPX: preferably someone who is in good health, has no underlying chronic conditions and has had previous smallpox vaccination or MPX virus infection. For example, this may include preparing meals, going to grocery store, getting medications, etc.
- The patient with MPX should stay in a dedicated, well-ventilated room (e.g. with windows that can be opened frequently) separate from others in the household.
- Household members and the patients with MPX should clean their hands with soap and water or an alcohol-based hand sanitizer frequently. In addition, household members should avoid entering the room.
- If the designated person that is facilitating self-care needs to enter the isolation area, they should maintain a distance of at least 1 m from patient. When distance cannot be maintained, the designated person is to wear a well-fitting medical mask and disposable gloves. They should clean their hands with either soap and water or an alcohol-based hand sanitizer, before and after contact with the patient or surrounding environment and before putting on and after removing their gloves.

- Items such as eating utensils, linens, towels, electronic devices or beds should be dedicated to the person with MPX. Avoid sharing personal items.
- The patient with MPX should wear a well-fitting medical mask and cover lesions when in close proximity of others, and when moving outside of the designated isolation area (e.g. to use the toilet).
- If a health worker is required to provide care to persons with MPX in the home, they should wear appropriate PPE (gloves, gown, eye protection and respirator), perform hand hygiene (according to the WHO 5 moments and before putting on and after removing PPE) and clean and disinfect any patient care equipment used.
- If persons with MPX leave their household to seek medical attention, they should preferably inform their health practitioner or the facility they will visit in advance of arrival (so the facility can implement transmission-based precautions), wear a well-fitting medical mask, ensure all lesions are covered and refrain from close contact such as in crowded, public transportation.
- Patients with MPX who are cared for at home should remain in isolation and refrain from close contact until their skin lesions have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath.

WHO recommends, that caution should be taken when handling and cleaning linens, household surfaces and during waste disposal.

Remarks:

- Linens and bedding should be carefully lifted and rolled to prevent dispersion of infectious particles from lesions and body fluids. They should not be shaken. Only the patient with MPX should handle and launder their bedding, clothing etc.
- Linens, towels, and clothing from the patient with MPX should be laundered separately from other household laundry. Clothing and linens of the person with MPX can be reused after washing with soap and preferably hot water (> 60°C) or soaked in chlorine* if hot water is not available *(25,26,38)*.
- Dishes and utensils and household surfaces, such as furniture, beds, toilets or floors, or any location where the patient has had contact should be cleaned with water and soap and disinfected regularly (e.g. common household disinfectant or bleach products). Pay particular attention to frequently touched surfaces.
- Use damp mopping, avoid dry sweeping to prevent dispersion of particles. Carpeting and household furnishing should be steam cleaned where possible. Avoid vacuuming.
- Waste that is generated from caring for a patient with MPX, such as bandages and PPE, should be placed in strong bags and securely tied before disposal and eventual collection by municipal waste services. If such services are not available, as an interim measure and according to local policies, safely burying or controlled burning may be done until more sustainable and environmentally friendly measures can be put in place.

* Due to the lack of available research with the MPX virus, there is uncertainty about the precise concentration of chlorine or the amount of risk reduction which might be achieved. However, there is general consensus based on evidence from other viruses that the addition of chlorine is likely to reduce residual contamination and this may be particularly useful where thermal disinfection, dilution and mechanical action is suboptimal *(39–41)*.

4.3 Clinical considerations

4.3.1 Pain and nutrition

WHO recommends patients with MPX be given symptomatic treatment such as antipyretics for fever and analgesia for pain.

Remarks for symptomatic treatment of pain:

- Headache and pain from skin rash, oral, ocular and genital lesions, swollen lymph nodes, and generalized muscle aches are common. Pruritis from rashes can also be bothersome. See Annex 2 for common medicines that can be used.
- For oral lesions, rinse the mouth with clean, salt water at least four times a day *(42)*. Consider use of oral antiseptic to keep lesions clean (e.g. chlorhexidine mouthwash) or local anaesthetic (e.g. viscous lidocaine) *(43)*.
- Symptomatic and supportive care is essential to maintain good nutrition and hydration. For genital or ano-rectal lesions warm sitz baths (warm bath made up of water and baking soda or epsom salt to heal and cleanse the perineal area) and/or topical lidocaine may offer symptomatic relief *(42)*.

WHO recommends patients with MPX be assessed for their nutritional status and given adequate nutrition and appropriate rehydration.

Remarks (key actions):

- Assess the nutritional and hydration status of all patients with MPX whether on admission to a health facility or when seen in the community. Nutritional intake can be compromised due to oropharyngeal lesions and/or painful cervical lymphadenopathy. Nutritional support is described as an important intervention *(9)*.
  - **Adults:** history of reduced appetite or weight loss, body weight, height, calculation of body mass index (BMI), look for signs of malnutrition (e.g. muscle wasting, nutritional oedema etc.); a standardized tool can be used (e.g. Malnutrition Universal Screening Tool ( )) *(44)*.
  - **Children:** same as above plus mid-upper arm circumference (MUAC) (6–59 months). A nutrition specialist or trained clinician should evaluate children and those with severe malnutrition.
  - See Table 9.2 for classification of dehydration.
- Oral nutrition should be encouraged daily, as patients need sufficient energy (kcal) and essential nutrients, in addition to fluids and electrolytes. If the patient is well enough for oral food intake, offer nutrient dense therapeutic foods; especially for children and those at risk of malnutrition per the WHO *Pocket book of hospital care for children*: Section 10.1 ( ) *(45)*.
- If food intake is not tolerated, evaluate for reason and treat appropriately. For example, if poor feeding is a result of nausea or vomiting, antiemetic medication can improve intake ability; if it is due to weakness, the patient should be assisted with feeding by a health care provider; or, if tolerated, due to pain from oral lesions or cervical adenopathy, treat pain.
- Provide vitamin A supplements according to standard recommendations, especially for children who have not recently received a dose. It plays an important role in all stages of wound healing and eye health *(48)*.

4.3.2 Monitoring

WHO recommends to counsel patients with mild MPX about signs and symptoms of complications that should prompt urgent care.

Remarks:

- Communication between the patient and trained health workers, should be established for the duration of the home-care period.
- Monitoring patients and caregivers in the home can be done by trained community workers or outreach teams by telephone, telemedicine or email initially on a daily basis (when possible) or as considered clinically necessary after initial assessments. The patient's willingness to engage in medical assessments should also be considered.
- Patients with MPX and their families should be counselled about the signs and symptoms of complications and how to recognize a deterioration in their health status that requires medical attention. For example, patients should be informed to contact their health worker immediately if their lesions get worse or increase in quantity, if they develop worsening pain, persistent fever, nausea or vomiting and decreased oral intake, visual symptoms, difficulty breathing or dizziness or confusion.
- If a pregnant woman has chosen to be cared for at home, then counsel the woman about maternal, fetal and newborn signs and to seek care if they develop worsening illness or danger signs. Self-care interventions should be encouraged.
- Counsel women about healthy behaviours including diet, physical activity, intake of micronutrients, tobacco alcohol and other substance use, per WHO recommendations on antenatal (👆) and postnatal (👆) care *(49,50)*.
- For women requiring abortion services, consider alternative modes of service delivery, including self-management of medical abortion up to 12 weeks' gestation, where women have access to accurate information and to a health care provider at any stage of the process, per the WHO *Abortion care guideline* (👆) *(51)*.

4.4 Clinical management of skin lesions

WHO recommends conservative treatment of rash lesions dependent of their stage with aims to relieve discomfort, speed healing and prevention of complications, such as secondary infections or exfoliation.

Remarks:

- Counsel patient not to scratch skin.
- Patients should be instructed to keep skin lesions clean and dry to prevent bacterial infection. They should be instructed to wash hands with soap and water or use alcohol-based hand sanitizer before and after touching the skin rash to prevent infection. Then lesions may be cleaned gently with sterile water or antiseptic solution. Rash should not be covered but rather left to open air to dry.
- For complications of skin lesions such as exfoliation or suspicion of deeper soft tissue infection (pyomyositis, abscess, necrotizing infection), consider consultation with appropriate specialist (i.e. wound care specialist, ID specialist, and/or surgeon). Debridement of the skin should not be done unless performed by an expert wearing appropriate PPE *(21)*.
- Optimal management of skin lesions is uncertain and needs further research.

WHO recommends that antibiotic therapy or prophylaxis not be used in patients with uncomplicated MPX. However, lesions should be monitored for secondary bacterial infection (i.e. cellulitis, abscess) and if present be treated with antibiotics with activity against normal skin flora, including *Streptococcus pyogenes* and methicillin-sensitive *Staphylococcus aureus* (MSSA).

Remarks:

- The skin lesions in patients with MPX may be inflamed causing mild erythema and/or skin hyperpigmentation – this does not need to be treated with antimicrobial therapy *(10)*. Empiric or prophylactic use of antibiotics should be discouraged, as it increases the risk of emergence and transmission of multidrug-resistant (MDR) bacteria and places individuals at risk to possible side-effects of antibiotics such as *Clostridium difficile* associated diarrhoea. Infections with MDR bacteria are more difficult to treat, and associated with increased morbidity and mortality *(52–54)*.
- Secondary bacterial infection of skin lesions has been reported as a common complication of MPX and patients should be monitored closely *(10,13,16,21)*.
- A swab of a superficial skin infection is unlikely to be helpful unless the patient has had a prolonged hospitalization and there is concern for MDR organism. Signs of bacterial infection include erythema, induration, warmth, worsening pain, a purulent drainage, malodorous discharge, or recurrence of fever. See Annex 3 for oral options of antibiotics. In selected cases based on individual risk factors, known colonization and local prevalence, consideration may be given to initiate treatment for community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA).
- Patients with bacterial superinfection of MPX rashes may develop an abscess which is the collection of pus within the dermis or subcutaneous tissue and most commonly due to bacteria from the skin (*Streptococcus* spp. and *Staphylococcus* spp.) *(55)*. An abscess may appear as a painful, red, shiny nodule with or without fluctuance. This may be associated with surrounding cellulitis, fever, and worsening pain at the site of infection.
  - Treatment of an abscess is incision and drainage done by sterile aseptic technique by a qualified health worker using appropriate IPC measures, to prevent complications related to untreated abscess such as osteomyelitis, septic arthritis, pyomyositis, sepsis and shock. Depending on the location in the body (e.g. adjacent to major blood vessels), size and complexity of the abscess, the incision and drainage may need to be performed in the operating theatre. Fluid should be aspirated and sent for microbiology and culture to help target antimicrobial therapy *(55)*.
- The decision to initiate antimicrobial therapy should be based on individual clinical assessment and local antimicrobial resistance patterns. If the patient does not clinically improve or the infection continues to spread, reassess the patient and the antibiotic regimen to consider if adjustments are necessary. See WHO *Essential Medicines List: antibiotic book* () for more information regarding selection of antimicrobials and appropriate use *(56)*.

5. MENTAL HEALTH CARE OF PATIENTS WITH MONKEYPOX (2 RECOMMENDATIONS)

WHO recommends prompt identification and assessment for anxiety and depressive symptoms in the context of MPX and to initiate basic psychosocial support strategies and first-line interventions for the management of new anxiety and depressive symptoms.

Remarks:

- The MPX outbreak can lead to significant mental and psychosocial effects, including *(42,57)*:
  - Fear of the disease or death, loss of sense of meaning of life, or loss of faith.
  - Physical and social isolation from family or community.
  - Stigma associated with diagnosis and returning to the community.
  - Scarring and disability (e.g. blindness) associated with the disease.
- Patients with MPX should receive compassionate, respectful, people-centred care consistently, while ensuring appropriate and adequate protection of household members, visitors and health workers.
- Basic psychosocial support skills are essential for management of all patients and represent an integral part of care that should be provided for all. When a patient with MPX arrives at a health facility, the patient and family members should be informed about MPX and encouraged to remain calm. They should be informed about how the disease is transmitted and educated about the precautions that should be taken to prevent the disease from spreading. Families should be updated on the patient's condition and provide any additional information.
- Ideally, a psychologist, social worker, or nurse psychosocial provider fluent in the local language will be involved from the onset of the disease to counsel the patient on what will happen while in isolation. If this is not possible, then general nurses in the health centre should be trained and supervised to provide basic psychological support, using standardized resources (WHO *Psychological first aid* (☞) and Inter-Agency Standing Committee (☞) guidance on basic psychosocial skills) *(58,59)* as follows to:
  - Provide non-intrusive, practical care and support.
  - Assess needs and concerns.
  - Help to address basic needs (food, water, information).
  - Listen to patients and families, but not pressure them to talk.
  - Provide accurate information on the patient's condition and treatment plan in easily understood and non-technical language, as lack of information can be a major source of stress.
  - Help people address urgent needs and concerns and help with decision-making as necessary.
  - Comfort patients and families while helping them feel calm. Inform them that the vast majority of MPX patients survive, so be sure to communicate to patients and their families that recovery is expected.
  - Help people connect to information, services, and social supports. Information about MPX is important as it helps to dispel myths, share clear messages about healthy behaviour, and improve understanding of the disease.

  - Encourage patients and caregivers to use evidence-based stress management and self-help tools such as the WHO stress management guide *Problem management plus (PM+)* (👆) *(60)*.
  - Following recovery, patients may suffer from lingering scars or disfigurement and psychological distress as a result. Psychological and social care should be included in the follow-up care plan and as part of a multidisciplinary team of care.
- For people who are experiencing symptoms of depression, brief psychological interventions based on the principles of cognitive behavioural therapy (CBT), problem management and relaxation training can be considered *(61)*. Consider using remote mental health support (i.e. telephone therapy) when access to regular services is disrupted.
- If a person's anxiety or depressive symptoms persist beyond recovery from MPX, then an underlying anxiety or depressive disorder may be suspected, and a mental health professional should be consulted, and these conditions should be managed appropriately. Refer to the *mhGAP Humanitarian Intervention Guide for mental, neurological and substance use disorders in non-specialized health settings* (👆) *(62,63)*.
- It is important to ask about thoughts or acts of self-harm, particularly during MPX, due to risk factors for self-harm and suicide such as sense of isolation, loss of a loved one, job, or financial loss and hopelessness. Remove possible means of self-harm, activate psychosocial support, follow up with the person, and consult a mental health professional as necessary. Refer to the *mhGAP Humanitarian Intervention Guide for mental, neurological and substance use disorders in non-specialized health settings* (👆) *(62,63)*.
- To ensure comprehensive care and based on the initial assessment, following discharge, link the person to employment, education, social services (including housing) and other relevant sectors *(64)*.
- CBT with a trauma focus, eye movement desensitization and reprocessing or stress management should be considered for adults with post-traumatic stress disorder (PTSD) (👆) *(58,62)*.

WHO recommends psychosocial support strategies as the first-line interventions for management of sleep problems in the context of acute stress.

Remarks:

- Sleep hygiene advice (including avoiding the use of psychostimulants such as caffeine, nicotine or alcohol), and stress management (including relaxation techniques and mindfulness practices) are effective in reducing sleep problems and may be offered. Psychological interventions based on the principles of CBT may also be considered.
- For people who are hospitalized for MPX, additional causes of insomnia may include environmental factors (e.g. excessive light and noise at night), anxiety, persistent cough, delirium, agitation or pain. Identifying and promptly addressing underlying causes should be prioritized before using any pharmacological sleep aids.

6. ANTIVIRALS AND OTHER THERAPIES (1 RECOMMENDATION)

6.1 Antivirals

In patients with MPX, it is preferable to use antivirals under randomized clinical trials (RCTs) with collection of standardized clinical and outcome data to rapidly increase evidence generation on efficacy and safety and, when not possible, antivirals may be used under expanded access protocols, such as MEURI (Monitored Emergency Use of Unregistered and Investigational Interventions) *(3)*.

Remarks:

- Due to limited supply of antivirals, use may be considered as treatment for those at risk for severe disease, or those that present or develop severe MPX. The optimal use of antivirals, including as post-exposure prophylaxis (PEP), will need to be reconsidered pending more available information.
- WHO has developed a standardized case record form located on our Clinical Platform () that can support Member States in the collection, data management and analysis to accelerate our understanding of clinical characterization and response to therapeutics, for more information, see our website ().
- **Tecovirimat** is licensed by the European Medicines Agency (EMA) for the treatment of smallpox, MPX, cowpox and complications from immunization with vaccinia and by the United States Food and Drug Administration (FDA) and Health Canada for smallpox *(65–67)*. The effectiveness of tecovirimat was evaluated based on studies in animals infected with lethal doses of orthopoxviruses, in studies on the medicine's effects in the human body, and on the way the medicine is absorbed, modified and removed from the body in humans and animals (pharmacodynamics and pharmacokinetics) *(65,68,69)*.
- Tecovirimat, inhibits viral envelope formation of MPX virus by targeting the viral protein p37, which is highly conserved among orthopoxviruses *(69)*. It is available as immediate release oral capsules administered twice daily for 14 days *(65,70)*. An intravenous formulation was approved by the US FDA on 19 May 2022 *(71)*. Preclinical studies suggest tecovirimat was effective in non-human primates *(15)*.
- A recent study from the United Kingdom described a patient who had blood and upper respiratory tract PCR negative 48 hours after starting treatment and remained PCR negative at 72 hours. Her haematological, renal and liver profile remained within normal limits and she was discharged home to complete therapy *(15)*. Reported side-effects of tecovirimat include headache, nausea, abdominal pain and vomiting *(70,72)*. It is a weak inducer of cytochrome P450 and thus may have drug interactions with other medications metabolized through the same pathway *(15,74)*. More studies are needed on safety and efficacy for the treatment of MPX in field settings *(15,74)*.
- **Brincidofovir** is approved by the EMA and FDA for treatment of smallpox and has been shown to have antiviral activity against double-stranded DNA viruses, including poxviruses *(73,75)*. It inhibits replication of MPX virus by inhibiting polymerase-mediated synthesis of DNA and is available as an oral tablet or suspension administered to patients as two doses 1 week apart *(11)*. Reported side-effects of this medication include elevation of hepatic transaminases, diarrhoea, nausea, vomiting and abdominal pain *(73)*. Brincidofovir is not recommended in women who are pregnant due to risk of embryo-fetal toxicity. It is advised that individuals of childbearing

potential avoid becoming pregnant and that they use effective contraception during treatment and for at least 2 months after last dose *(15)*. It has been used in three cases of MPX that have been reported in the United Kingdom since 2018. In all cases the patients developed elevated transaminases and none completed a full course of therapy *(15)*. No consistent association was seen between dose of brincidofovir and clinical or virological parameters *(15)*.

- **Cidofovir** is approved by the FDA for the treatment of cytomegalovirus *(76)*. It inhibits replication of MPX virus by inhibiting DNA polymerase and is administered intravenously *(11)*. It has showed activity against poxviruses in laboratory and animal studies *(75)*. Cidofovir associated renal toxicity and electrolyte abnormalities have been reported *(79)*.
- **NIOCH-14** is a chemically synthesized compound being developed by the State Research Center of Virology and Biotechnology Vector since 2001 *(79,80)*. NIOCH-14 is an analogue of tecovirimat with comparable activity against orthopoxviruses *(79,80)*. Animal challenge studies with MPX comparing NIOCH-14 and tecovirimat showed significant reduction of virus production in the lungs and infected animals 7 days post infection when compared with controls *(79,80)*. Due to the small numbers of patients treated, the clinical efficacy of this therapeutic for MPX is uncertain.

This is a rapidly emerging field. For more up-to-date information about therapeutics and the WHO R&D Blueprint roadmap, visit website (). See Annex 4 for more details.

6.2 Immune globulin

Vaccina immune globulin (VIG) is composed of antibodies from individuals inoculated with the smallpox vaccine. It is unknown if a person with exposure to MPX or with severe infection would benefit from VIG – if used it should be in a clinical research context with prospective data collection *(81,82)*.

7. INFECTION PREVENTION AND CONTROL AT HEALTH FACILITIES (7 RECOMMENDATIONS)

Implementation of appropriate IPC measures is essential to mitigate and control risks of transmission of MPX in health care and community settings *(31,83)*. Implementing a hierarchy of controls is central to reducing the risk of exposure to MPX within health care settings. As such, considerations for the application of engineering and administrative controls and the use of PPE have been integrated throughout the recommendations outlined.

In countries where IPC programmes are limited or non-existent, it is critical to ensure that basic IPC standards are put in place at the national and health facility level to provide minimum protection to patients, health workers, caregivers and visitors and thereby protect the community. WHO provides guidance on the minimum requirements *(82)* for IPC at the national level and in health care facilities. Achieving the IPC minimum requirements and more robust and comprehensive IPC programmes based on WHO *Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level* () across whole health systems is essential to sustaining efforts to control emerging infectious diseases, health care-associated infections and antimicrobial resistance *(81)*.

Health workers should always follow standard precautions and perform a risk assessment to evaluate the need to use additional precautions. Standard precautions include:

- hand hygiene
- respiratory hygiene and cough etiquette
- patient placement
- personal protective equipment
- aseptic technique
- safe injections and sharps injury prevention
- environmental cleaning and disinfection
- handling of laundry and linen
- decontamination and reprocessing or reusable patient care items and equipment
- waste management.

7.1 IPC considerations for suspected patients with MPX

WHO recommends that contact and droplet precautions be implemented for any suspect patient with MPX. In addition to contact and droplet precautions airborne precautions should be implemented if varicella zoster virus (i.e chickenpox) is suspected and until it is excluded.

Remarks:

- Health workers should perform hand hygiene according to the WHO Your 5 moments for hand hygiene, including prior to putting on and after removing PPE.
- If varicella zoster virus (i.e. chickenpox) is suspected, place the patient in an airborne infection isolation (AII) room with a dedicated bathroom or toilet.
  - If an AII room is not available, place patient in a well-ventilated single room with a dedicated bathroom or toilet and keep the door closed.

  - Health workers should wear the following PPE: gloves, gown, respirator (e.g. N95, FFP2) and eye protection.
  - Isolation room/area should have signage posted at the entrance indicating that patient is under contact/droplet/airborne precautions and the required PPE in the correct order for health workers.
- When varicella zoster virus (i.e. chickenpox) is not suspected, place patient in a well-ventilated single room with a dedicated bathroom or toilet.
  - Health workers should wear PPE according to the PPE recommendation for confirmed patients (gown, gloves, respirator (e.g. N95, FFP2) and eye protection).
- Health workers should be trained on procedures for safe putting on and removing PPE.
- Use dedicated footwear that can be decontaminated. Disposable shoe covers are not recommended *(84–86)*.
- Instruct the patient to wear a well-fitting medical mask and follow respiratory hygiene and cough etiquette when transport is necessary.
- Avoid unnecessary movement of suspect patients. If the suspect patient must be moved or transported within or beyond the facility, ensure transmission-based precautions are maintained (droplet/contact/airborne), place a well-fitting medical mask on the patient and cover lesions.
- The receiving facility/ward/unit should be aware that transmission-based precautions are required and, pending arrival, the need to prepare the isolation or designated area.

7.2 IPC considerations for confirmed patients with MPX

WHO recommends that contact and droplet precautions be implemented for any confirmed patient with MPX. In addition to contact and droplet precautions, respirators should be used.

Rationale: In the context of the ongoing multi-country outbreak and evolving evidence on the modes of transmission there is currently not enough information to support a recommendation for continuous use of airborne precautions. Although not the dominant form of transmission, the panel recognized the current uncertainty related to the potential for aerosol transmission and risks to health workers providing direct care to confirmed patients with MPX. As a result, the guidance panel voted for the use of respirators as additional respiratory protection, in the context of a well-ventilated room as a precautionary measure at this time.

The panel emphasized that the modes of MPX transmission and disease severity need to be better understood and prioritized for research.

WHO will update this guidance within a short timeframe (8–12 weeks) based on emerging evidence.

Remarks:

- Health workers should perform hand hygiene according to the WHO Your 5 moments for hand hygiene (), including prior to putting on and after removing PPE.
- Place patient in a well-ventilated, single patient room with dedicated bathroom or toilet.
- If single patient rooms are not available, consider cohorting confirmed cases, maintaining a distance of at least 1 m between patients *(83)*.
- Isolation room/area should have signage posted at the entrance indicating contact/droplet precautions.
- Wear PPE including: gloves, gown, a respirator (e.g. N95, FFP2) and eye protection.
- Use dedicated footwear that can be decontaminated. Disposable shoe covers are not recommended *(84–86)*.
- Health workers should be trained on procedures for safe donning and doffing of PPE.

- Cover exposed lesions when others are in the room and if the patient can tolerate.
- Avoid unnecessary movement of confirmed patients. If the patient must be moved or transported within or beyond the facility, ensure transmission-based precautions are maintained, place a well-fitting medical mask on the patient and cover lesions (provided the patient is able to tolerate).
- The receiving facility/ward/unit should be aware that transmission-based precautions are required and, pending arrival, the need to prepare the isolation or designated area.
- Precautions should remain in place until lesions have crusted, scabs have fallen off and a fresh layer of skin has formed underneath.
- Severe cases (including immunosuppressed) who may experience prolonged viral shedding from the upper respiratory tract may require clinical evaluation to determine when transmission-based precautions may be discontinued.

WHO recommends airborne precautions be implemented if aerosol-generating procedures (AGPs) are performed.

Remarks:

- AGPs should be performed in an AII room. If AII room is not available or if it is not feasible, perform AGPs in a well-ventilated, single patient room with the door closed.
- Health workers should wear a respirator (e.g. N95, FFP2) as well as eye protection, gown and gloves when performing AGPs.

WHO recommends that areas within the health care facility frequently used by the patient or where patient care activities occur* and patient care equipment should be cleaned and disinfected as per national or facility guidelines.

Remarks:

- PPE (gloves [heavy duty], gown, respirator [e.g. N95, FFP2] and eye protection) should be worn by health workers while cleaning and disinfecting patient care equipment and patient care areas or isolation rooms where patients were suspected or confirmed to have MPX.
- Use dedicated footwear that can be decontaminated. Disposable shoe covers are not recommended *(84–86)*
- Always clean surfaces first with detergent and water followed by disinfection with an approved disinfectant with virucidal activities (follow national or facility guidelines). Disinfectants should be prepared and applied to surfaces according to manufacturers' instructions *(87)*.
- To prevent cross-contamination, cleaning must always be carried out from the cleanest area first and finish in the dirtiest area last, and always clean from top to bottom.
- Particular attention should be paid to toilets and frequently touched surfaces *(88)*.
- Use disposable or dedicated patient care equipment and clean and disinfect equipment before use on other patients.

* Patient care areas include, for example, outpatient departments, waiting rooms, bathrooms, patient rooms the patient environment.

WHO recommends that linens, hospital gowns, towels and any other fabric items should be handled and collected carefully.

Remarks:

- Carefully lift and roll linens. Do not shake linen or laundry.
- These items should be carefully placed into designated container or bag for transport to laundry services.
- Linens can be machine washed with hot water at > 60°C with laundry detergent and dried according to routine procedures, preferably at high heat *(25,26,38)*. If machine washing is not possible and hot water is not available, linens can be soaked in a large drum using a stick to stir with care taken to avoid splashing. The linens should be soaked in chlorine*, rinsed with clean water and allowed to fully dry.
- Workers in laundry area should follow standard and transmission-based precautions including:
  - minimize handling, in particular avoid shaking of linen and laundry;
  - wear gloves, apron or gown, a respirator (e.g. N95, FFP2) and eye protection.

* Due to the lack of available research with the MPX virus, there is uncertainty about the precise concentration of chlorine or the amount of risk reduction which might be achieved. However, there is general consensus based on evidence from other viruses that the addition of chlorine is likely to reduce residual contamination and this may be particularly useful where thermal disinfection, dilution and mechanical action is suboptimal *(39–41)*.

WHO recommends that all bodily fluids and solid waste of patients with MPX should be treated as infectious waste.

Remarks:

- Waste should be segregated (general waste, infectious waste and sharps) and placed in appropriate bins at point of use *(89)*.
- Management and disposal of waste (including PPE) should be done in accordance with local regulations for infectious waste.
- Ensure health workers wear appropriate PPE (e.g. gloves, gown, respirator [e.g. N95, FFP2], eye protection) during handling of waste.

WHO recommends that for patients isolated with MPX measures should be put in place to support patient interaction with family and visitors to promote well-being.

Remarks:

- Visitors or caregivers should perform appropriate hand hygiene before and after entering/exiting the patient room, receive instruction and be closely supervised on the use (putting on and removal) of PPE for contact and droplet precautions.
- Vulnerable individuals should be counselled regarding the risks in order to make an informed decision on whether to visit the patient.
- Alternate modes of communication such as videoconference to be offered.

8. CONSIDERATIONS FOR CERTAIN POPULATIONS (9 RECOMMENDATIONS)

8.1 Caring for sexually active populations (2 recommendations)

WHO recommends all patients should be advised to abstain from sex until ALL skin lesions from MPX have crusted, the scabs have fallen off and a fresh layer of skin has formed underneath.

Rationale:

- The GDG acknowledged that the risk of transmission from direct contact with infected skin or mucocutaneous lesions can amplify transmission, and thus abstaining from sexual activity during the infectious period would curtail transmission. As well, the potential for sexual transmission is unknown and subject to further research.

Remarks:

- For patients who are sexually active: among persons presenting with rash that are suspected to have MPX, co-infection with other STIs should also be considered. The patient should have the following:
  - Thorough sexual history.
  - Full physical examination using appropriate IPC measures with special attention on examination for:
    - lymphadenopathy;
    - rash in oral mucosae, genitals, ano-genital region, and other parts of skin;
    - testing should be performed for HIV, syphilis, genital HSV, and screening for STIs and managed per WHO *Guidelines for the management of symptomatic sexually transmitted infections* (👆) *(34)*;
    - patients should be encouraged to use condoms consistently during sexual activity for prevention of HIV and other STIs but should be made aware that the use of condoms alone cannot offer protection against acquisition and transmission of disease.
- For persons living with HIV: particularly those with poorly controlled disease who have MPX may be at greater risk for severe disease. Data suggest they may be at risk for genital ulcers, secondary bacterial infection, and prolonged duration of illness *(13)*.
  - If a person living with HIV is diagnosed with MPX, they should continue ART as before.
  - For persons living with HIV who are recently diagnosed with HIV, WHO recommends starting ART as soon as the person is ready and within 7 days per the WHO *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach* (👆) *(90)*. People with lower CD4 counts are possibly at greater risk of complications related to MPX so should be prioritized for starting ART *(13)*.
  - Should a person be diagnosed with both MPX and HIV at the same time, address the most urgent issues and treatment for MPX (see Section 6). It should be noted that the antivirals for MPX have important drug-drug interactions with some of the antivirals used to treat HIV.
  - People living with HIV on ART with suppressed viral load are not considered to be immunosuppressed *(90)*.

Based on the precautionary principle, WHO suggests the use of condoms consistently during sexual activity (receptive and insertive oral/anal/vaginal) for 12 weeks after recovery to prevent the potential transmission of MPX.

Remarks:

- Small case series have reported MPX virus DNA detection in bodily fluids after healing of skin lesions; this raises uncertainty about the persistence of MPX virus in bodily fluids such as semen, vaginal fluids, saliva and blood, and the risk of onward transmission.
- As this is an emergency guidance produced in a quickly evolving situation the precautionary principle is being applied for this public health intervention. As more information becomes available and our understanding related to transmission improves the guidance will be updated accordingly.

8.2 Caring for women during and after pregnancy (4 recommendations)

WHO recommends pregnant or recently pregnant women with mild or uncomplicated MPX may not require acute care in hospital but monitoring in a health facility may be preferred; those with severe or complicated disease should be admitted to a health facility for care as they require optimized supportive care and/or interventions to improve maternal and fetal survival.

Remarks:

- Limited data suggest that MPX virus infection in pregnant women may lead to vertical transmission as well as adverse outcome for the fetus, such as spontaneous abortion and stillbirths *(9,28,29,91)*. This is an area where more research and data are needed.
- Given these potential risks, pregnant women with MPX with mild/uncomplicated disease may be considered for care in a health facility for closer monitoring of disease progression and, if complications occur, to recognize and treat these complications with optimized supportive care (see Section 4 for further considerations).
- Counsel women about healthy diet, mobility and exercise, intake of micronutrients for herself and her infant, tobacco use and second-hand smoke exposure, use of alcohol and other substances, as per WHO guidelines on antenatal care for a positive pregnancy experience () and WHO recommendations on maternal and newborn care for a positive postnatal experience () *(49,50)*.
- Counsel women as per Section 8.1.

WHO recommends that pregnant and recently pregnant women with MPX should have access to woman-centred, respectful, skilled care, including midwifery, obstetric, gynaecologic, fetal medicine and neonatal care, as well as mental health and psychosocial support, with readiness to care for maternal and neonatal complications.

Remarks:

- Woman-centred, respectful, skilled care refers to care organized for and provided to all women in a manner that maintains their dignity, privacy and confidentiality, ensures freedom from harm and mistreatment, and enables informed choice. During labour and childbirth this includes a companion of choice, pain relief, mobility during labour and birth position of choice.
- Screen birth companions using the WHO case definition for MPX (see Annex 1).
- If the companion has suspected or confirmed MPX, arrange for an alternative, healthy birth companion in consultation with the woman. Emphasize to any and all companions the importance of IPC measures during labour, childbirth and during the woman's and newborn's postnatal stay in the health facility. Include appropriate training on and use of PPE and limit movement in the health care facility.

WHO recommends that mode of birth should be individualized, based on obstetric indications and the woman's preferences. WHO recommends that induction of labour and caesarean section should only be undertaken when medically justified and based on maternal and fetal condition.

Remarks:

- Emergency birth and pregnancy termination decisions are challenging and based on many factors such as gestational age, severity of maternal condition, and fetal viability and well-being.
- Interventions to accelerate labour and childbirth (e.g. augmentation, episiotomy, operative vaginal birth) should only be undertaken if medically justified and based on maternal and fetal clinical condition per the WHO recommendations for intrapartum care (🖱) *(92)*.
- Delayed umbilical cord clamping (not earlier than 1 minute after birth) is recommended for improved maternal and infant health and nutrition outcomes. There is no evidence that delaying cord clamping increases the possibility of viral transmission from the mother to the newborn. The proven benefits of a 1–3 minute delay, at least, in clamping the cord outweigh the theoretical, and unproven, harms.
- Individualized decisions should be taken about postponing planned (elective) induction or caesarean section in pregnant women with suspected or confirmed mild MPX *(93)*.
- Placenta and any pregnancy related tissue or fluids, such as amniotic or fetal tissue fluid, must be disposed of following specific IPC protocols for potentially infectious materials (see Section 7).

WHO recommends that pregnant and recently pregnant women who have recovered from MPX should be enabled and encouraged to receive routine antenatal, postpartum, or abortion care, as appropriate. Additional care should be provided if there are any complications.

Remarks:

- Limited data suggest that MPX virus infection in pregnant women may lead to vertical transmission as well as adverse outcome for the fetus, such as spontaneous abortion and stillbirths *(9,28,29,91)*. This is an area where more research and data are needed.
- Although information is currently emerging, pregnant women with or recovering from MPX should be provided with information related to the potential risk of adverse pregnancy outcomes and offered counselling should they request or desire it.
- Women's choices and rights to sexual and reproductive health care should be respected, including access to contraception and safe abortion per the WHO *Abortion care guideline* (🖱) *(51)*.
- Pregnant women with MPX should be informed that it is unknown whether transmission can occur if others are exposed to pregnancy-related fluids or tissues, such as amniotic fluid, placenta or fetal tissue. Instructions should be provided on how to handle potentially infectious specimens (see Section 7).
- Counsel women on safe sexual practices (see Section 8.1).
- All pregnant women with confirmed MPX and their infants should be followed up through national registries for signs of complications (see Section 13).

8.3 Caring for infants and young children with monkeypox (2 recommendations)

WHO recommends that newborn infants of mothers with MPX should be monitored closely for evidence of potential congenital or perinatal exposure or infection. Mothers and infants or young children can also be exposed through close contact.

WHO recommends that children exposed to MPX should be fully vaccinated for age according to the routine national immunization schedule and should have their vaccinations up to date, when possible.

Remarks:

- Transmission of MPX to children occurs the same way it does to adults; animal-human, human-human, and from contaminated environments-to-humans with most information generated from countries in West and Central Africa *(5)*.
- Children should not sleep in the same room or bed or drink/eat from the same utensils as an individual with MPX.
- Data from small studies and case reports suggest that children may be at greater risk than adults for severe disease such as encephalitis and sepsis as well as death *(9–11,16,28)*.
- This is especially important for any situation where MPX may have been caused by an animal bite or scratch, or where integrity of the skin is compromised for any reason. Not only are children at risk for more severe disease but data suggest that infection which compromises the integrity of the skin may also be a risk for more severe disease *(23)*.

- Given these potential risks, young children may be considered for care in health facility to monitor for disease progression, and if they occur to recognize and treat these complications with optimized supportive care. Young children should not be isolated alone. There should be one person (parent or caregiver), who is healthy and not at high risk, providing care to the child with MPX with appropriate IPC measures (see Section 7.2).
- Administer an age-appropriate tetanus toxoid-containing vaccine for infants and children with incomplete childhood vaccination, and for any person who has not completed the recommended tetanus vaccination schedule.

8.4 Feeding of infants in mothers infected with MPX (1 recommendation)

WHO recommends that infant feeding practices, including whether to stop breastfeeding in a mother with MPX, should be assessed on a case-by-case basis, considering the general physical status of the mother and severity of disease, which could impact on the risk of transmission of MPX from mother to infant.

Remarks:

- It is currently unknown whether the MPX virus or antibodies are present in the breastmilk of lactating women.
- The known risks associated with withholding the protections conferred by breastfeeding and the distress caused by separation of mother and infant, must be given greater weight in a risk/benefit calculation than the potential and unknown risk of infection from MPX in the infant.
- Protecting the child's survival while maintaining the nutritional intake of the infant is the priority (e.g. avoiding diarrhoeal illness associated with contaminated formula milk due to unclean water or unhygienic practices).
- Infants of mothers with MPX should be closely monitored for signs and symptoms with the main goal of early supportive care to prevent the development of severe disease and poor outcomes.
- General protective IPC measures should be taken by mothers with MPX when handling and feeding their infants, e.g. washing hands before and after each feeding, wearing a mask (if possible) and covering any lesions on the areola or on areas which have direct contact with the infant. Alternatively, if only one breast has lesions, mothers can express/pump from the breast with lesions on the areola and discard the milk and feed from the non-affected breast. In all cases, monitor the mother-infant pair closely for development of signs and symptoms of MPX and treat accordingly.
- If the infant is less than 6 months and is separated from their mother who has MPX, the infant should be fed with donor human milk or appropriate breastmilk substitutes, informed by feasibility, safety, sustainability, cultural context, acceptability to mother and service availability.
- For infants 6–23 months of age who cannot access donor human milk or appropriate breastmilk substitutes, whole cream animal pasteurised milk is appropriate as part a balanced diet along with complementary foods.
- Comprehensive assistance should be provided for any mother who stopped breastfeeding due to MPX (or any other reason) for re-lactation to re-establish a milk supply and continue breastfeeding.
- In the event of replacement feeding with breastmilk substitute, it is essential to track the infant's growth, development and other illnesses as well as for signs and symptoms of MPX.
- If the mother of an infant or young child has been exposed to MPX and has no symptoms suggestive of infection, the infant or child should not be separated. They should continue breastfeeding while closely monitoring for signs and symptoms of MPX.

9. MANAGEMENT OF HIGH-RISK PATIENTS AND THOSE WITH COMPLICATIONS OR SEVERE MONKEYPOX (2 RECOMMENDATIONS)

WHO recommends that patients at high risk for complications (i.e. young children, pregnant women, and those who are immunosuppressed) or those with severe or complicated MPX be admitted to the hospital for closer monitoring and clinical care under appropriate isolation precautions to prevent transmission of MPX virus.

Remarks:

- See Table 9.1 for systematic evaluation to be conducted in hospitalized patients.

Table 9.1 Vital signs and clinical features to monitor systematically

Vital signs and pain assessment	• Temperature, heart rate, blood pressure, respiratory rate, peripheral oxygen saturation, level of consciousness using the alert, voice, pain, unresponsive scale (AVPU), point of care glucose, and body weight and height to calculate BMI and children's mid-upper arm circumference (MUAC) • Pain scale
General condition	• Is the patient able to eat and drink without support? • Is the patient able to sit and walk independently? • Has the patient had recent weight loss since onset of symptoms?
Rash characterization	• Stage of rash: macules, papules, vesicles, pustules, crusted over, exfoliation • Location of the rash (face, arms, torso, genitals, legs, mucosa) • Number of lesions *(28,94)*: – Mild (< 25 skin lesions) – Moderate (25–99 skin lesions) – Severe (100–250 skin lesions) – Very severe (> 250 skin lesions) • If exfoliation present: % body affected (> 10% is concerning)
Presence of bacterial secondary infection	• Cellulitis, abscess, pyomyositis, necrotizing soft tissue infection
Neurologic status	• AVPU, seizures, coma
Volume status	• Presence of dehydration: mild, moderate, or severe (see Table 9.2 for more details)
Signs of perfusion	• Pulse rate, strength, capillary refill • Urine output (> 0.5 mL/kg/hr = good in adults; 1.0 mL/kg/hr in children) • Mottling of skin
Respiratory system	• Respiratory rate, SpO_2, signs of respiratory distress
Nutritional assessment	• Change in appetite, weight loss, body weight, height, calculation of BMI, MUAC in children • Signs of malnutrition – use standardized tool (e.g. Malnutrition Universal Screening Tool)
Laboratory tests	• Na, K, HCO_3, BUN, creatinine, AST, ALT, glucose, white blood count, Hg, platelet, PT/INR, Cl, calcium, albumin

Source: This table is modified from the WHO *Optimized supportive care for Ebola virus disease (57)* and includes information from WHO *Pocket book of hospital care for children (45)*.

Table 9.2 Classification of dehydration

	Mild (3–5% volume depletion)	Moderate (6–9% volume depletion)	Severe (> 10% volume depletion)
Pulse	Normal	Rapid	Rapid and weak or thready
Systolic blood pressure	Normal	Normal to low	Low
Buccal mucosa	Slightly dry	Dry	Parched
Skin turgor	Normal	—	Reduced
Urine output	Normal Adult (> 0.5 mL/kg/hr) Child (> 1 mL/kg/hr)	At or below Adult (< 0.5 mL/kg/hr) Child (< 1 mL/kg/hr) × 3 hours	Markedly reduced to anuric (< 0.5 mL/kg/hr x 3 hours)
Respiratory rate	No change	Increased	Increased
Ins and outs	Outs > ins	Outs > ins	Outs >> ins
Other	Increased thirst	Increased thirst	In infant, depressed fontanelle, cold skin

Source: This table is modified from the WHO *Optimized supportive care for Ebola virus disease (57)*.

WHO recommends that patients with MPX that develop complications or severe disease be managed with optimized supportive care interventions.

Remarks:

- See Table 9.3.

Table 9.3 Clinical management of complications and severe forms of MPX

Complication	Treatment
Skin exfoliation	• Patients with heavy rash burden may develop exfoliation (in severe cases similar to partial thickness burns), which can be significant leading to dehydration and protein loss *(21)*. • Estimate % skin affected and consider treatment like burns. • Minimize insensible fluid loss and promote skin healing. • Ensure adequate hydration and nutrition. • Obtain consultation with appropriate consultants such as surgeon, dermatologist and/or wound care specialists. • Bedside or surgical debridement as needed. • Skin grafting in rare and severe cases.
Necrotizing soft tissue infection	• This is a life-threatening condition of the deep soft tissue that affects the muscle fascia which causes necrosis, tissue destruction and systemic toxicity. Suspect if patient develops oedema, crepitus, malodorous discharge or pain out of proportion to appearance of infection. Though can be caused by MPX virus, consider bacterial pathogens as well. Start broad spectrum antibiotics to cover *Staphylococcus* sp. and *Streptococcus* sp. Consult surgeon for this surgical emergency *(55)*. • See the WHO *Essential Medicines List antibiotic book* (📖) for guidance on correct antimicrobial selection and appropriate use *(56)*.

Complication	Treatment
Pyomyositis	• This occurs when pus develops within the muscle and should be suspected when the patient has muscle tenderness. Though this can be caused by MPX virus, it may also commonly be caused by skin flora such as *Staphylococcus* sp. or *Streptococcus* sp. *(45,56)*. Ultrasound can assist in diagnosis. Collect blood cultures, start broad spectrum antibiotics, and proceed to surgical incision and drainage. Send sample for microbiology and culture to support antimicrobial therapy selection *(55)*. • See the WHO *Essential Medicines List antibiotic book* (👆) for guidance on correct antimicrobial selection and appropriate use *(56)*.
Cervical adenopathy	• Can occur in up to 85.65% of cases with lymphadenopathy *(9)*. • When large cervical adenopathy is combined with multiple oropharyngeal lesions patients may be at risk for complications such as respiratory compromise and retropharyngeal abscesses. Patients are also at risk for dehydration due to decreased food and water intake *(9,21)*. • Obtain consultation with appropriate specialists, such as surgeon, anaesthesiologist and infectious disease clinicians. Under their care, in severe cases, steroids may be used *(9)*.
Ocular lesions	• One of the most significant sequelae of MPX is corneal scarring and loss of vision *(11,21,30,42)*. • Patients may present with non-specific ocular symptoms such as conjunctivitis. • Eye care with ophthalmologist evaluation *(42)*. • Ophthalmic antibiotics/antivirals if indicated for co-infection. • Vitamin A supplementation, especially to malnourished children *(45)*. • Good eye care that includes eye lubrication and saline-soaked protective eye pads *(45)*. • Avoid steroid ointments (may prolong presence of MPX in ocular tissue) *(21,95)*. • Trifluridine eye drops (sometimes used for other orthopoxviruses or herpetic eye infections) may be considered to hasten resolution of symptoms and prevent long-term damage from scarring, where available *(21,30,95,96)*.
Pneumonia	• Manage according to the WHO *Clinical care for severe acute respiratory infections toolkit* (👆). • See the WHO *Essential Medicines List antibiotic book* (👆) for guidance on correct antimicrobial selection and appropriate use (56).
Acute respiratory distress syndrome (ARDS)	• Oxygen, non-invasive ventilation, mechanical ventilation. • Manage according to the WHO *Clinical care for severe acute respiratory infections toolkit* (👆).
Severe dehydration	• Severe dehydration and hypovolaemic shock can be seen in patients with MPX due to intravascular volume loss due to extensive rash and/or gastrointestinal losses due to diarrhoea and vomiting accompanied by poor oral intake. • The treatment for severe dehydration is resuscitation with intravenous or intraosseous (IV/IO) fluid, given as one or multiple boluses with close monitoring of fluid responsiveness. Adequate IV fluid intake refers to the volume that will correct signs of hypovolaemia. See *Pocket book of hospital care for children* (👆) (21,45).
Sepsis and septic shock	• Sepsis and septic shock differ from severe dehydration as it results from an immune response to an infection. Management of sepsis requires early identification, management of infection and supportive care, including fluid resuscitation to maintain organ perfusion to reduce and prevent further organ injury; and may also require vasopressors as well as control of infection *(21)*. • See the WHO *Clinical care for severe acute respiratory infections toolkit* (👆) for more information about sepsis *(33)*. • See the WHO *Essential Medicines List antibiotic book* (👆) for guidance on correct antimicrobial selection and appropriate use *(56)*.
Encephalitis	• Consider lumbar puncture for cerebrospinal fluid (CSF) evaluation to evaluate for other treatable conditions. • Monitor and assess airway, breathing, circulation, disability (ABCD) and give emergency treatments. • Monitor neurological status (AVPU). • Control seizures with anti-epileptics *(42)*. • Antibiotics/antivirals if indicated for co-infections. • See The WHO *Essential Medicines List antibiotic book* (👆) for guidance on correct antimicrobial selection and appropriate use *(56)*.

Complication	Treatment
Nutritional considerations	• Assess the nutritional status of all patients. If food intake is limited due to weakness, the patient should be assisted with feeding by a health care provider. If the patient is unable to tolerate oral nutrition, consider enteral nutrition. The placement of a nasogastric tube by an experienced provider could be considered along with nasogastric feeding. Always ensure proper placement of nasogastric tube before administering feeds to avoid risk of aspiration. • Take special care with patients at risk for refeeding (critically unwell, low BMI, reduced food intake for > 5 days, a history of alcohol abuse or receiving the following drugs: insulin, chemotherapy, antacids or diuretics) and start enteral feeding slowly with close monitoring. • Patients with reduced levels of consciousness are at risk for aspiration and should not be forced to eat. If severe malnutrition is present, refer to WHO published guideline () *(42,45,47)*.

10. CARING FOR MONKEYPOX PATIENTS AFTER ACUTE INFECTION (1 RECOMMENDATION)

WHO recommends that patients with suspected or confirmed MPX should have access to follow-up care. All patients (and their caregivers) with MPX should be counselled to monitor for any persistent, new, or changing symptoms. If this occurs, they should seek medical care according to national (local) care pathways.

Remarks:

- National (local), coordinated care pathways should be established that can include primary care providers (e.g. general practitioners), relevant specialists (e.g. sexual health, infectious diseases, dermatologist, surgeons, wound care specialists), mental health and psychosocial providers, nutritionists and social care services for patients and families.
- Management should be tailored according to patient needs and be coordinated. Management interventions may entail education, advice on self-management strategies, caregiver support and education, peer-to-peer groups, stress management, stigma mitigation and home medication, and/or specialty management.

11. MANAGEMENT OF DECEASED PATIENTS (1 RECOMMENDATION)

WHO recommends that the handling of human remains of deceased individuals with MPX should be done with appropriate IPC measures.

Remarks:

- Handling of the deceased should be kept to a minimum.
- Perform hand hygiene and wear PPE according to contact and droplet precautions (gloves, gown, respirator [e.g. N95, FFP2] and eye protection) as patients with rashes that have not healed may still have infectious virus.
- Ensure that any leakage of body fluids is contained.
- The body should be wrapped in a cloth or shroud and transferred to the mortuary as soon as possible.
- The dignity of the dead, their cultural and religious traditions, and their families should be respected and protected. Family and friends may view the body after it has been prepared for burial, in accordance with local customs. They should not touch or kiss the body and should clean their hands with soap and water or alcohol-based hand sanitizer after the viewing *(97,98)*.

12. MANAGEMENT OF EXPOSED HEALTH WORKERS (1 RECOMMENDATION)

WHO recommends staff with an occupational exposure to MPX should have an assessment and management plan.

Remarks:

- These plans should be in accordance with national or subnational policies. The term national describes a government entity at national level and subnational describes any government entity below the national level (regardless of the political, financial and administrative design of the country) involved in the management of health personnel in the context of MPX.
- Health workers should notify infection control, occupational health and public health authorities of possible exposures to receive a medical evaluation and instructions on follow up.
- Health workers who have had an occupational exposure (i.e. not wearing appropriate PPE) do not need to be excluded from work if they are asymptomatic, but should undergo active surveillance for symptoms for 21 days post-exposure; and be instructed not to work with vulnerable patients.
- Health workers who have had an exposure to a person with confirmed MPX should undergo medical evaluation and consideration for possible interventions (vaccination or PEP) under prospective data collection protocol or clinical trial.

13. COLLECTION OF STANDARDIZED DATA COLLECTION AND THE WHO CLINICAL PLATFORM

As the cluster of MPX cases continues to expand in countries across WHO regions it is important that we understand the clinical features, prognostic factors and outcomes in patients so we can better inform our clinical management guidelines and inform public health. The WHO Global Clinical Platform ( ) collects patient level anonymized clinical data and has been used to understand various emerging pathogens such as Ebola virus disease and COVID-19. As we work to understand more about the current cases, we have developed a case report form and invite Member States to contribute data to this platform.

The objectives of the platform are to:

- Describe the clinical characteristics of MPX.
- Assess the variations in clinical characteristics of MPX.
- Identify the association of clinical characteristics of MPX with symptoms.
- Describe temporal trends in clinical characteristics of MPX.

14. UNCERTAINTIES AND AREAS FOR RESEARCH

- Transmission:
  - Understand if there is a pre-symptomatic or asymptomatic phase of disease.
  - Understanding routes for human-human transmission to include studies on how viral dynamics and trajectories correlate with viral culture in the various bodily fluids and impact of this on transmission, infectious periods, subgroup by disease manifestation and disease severity.
  - Potential for reverse zoonosis and spillback events.
  - Natural history of disease: disease severity and risk factors for severe, disease in different subpopulations (neonates, children and young people, immunosuppressed, pregnant women and older persons).
- Co-infection: other viruses (VZV, HIV), STIs (such as HSV, syphilis, chancroid, LGV), and others, parasitic infections (malaria, dengue, filariasis) etc. Understand if co-infection impacts transmission, disease severity.
- Best symptomatic care for skin care, rash management, nutrition.
- Best optimized care package for complications such as ocular complications, central nervous system infections.
- Long-term outcomes for recovered patients, including mothers and babies, immunosuppressed. Is there a post-viral syndrome?
- Efficacy and safety of therapeutics, including in pregnant and breastfeeding women and children.
- Health worker exposure risk categories and PEP.
- Understanding the susceptibility of the MPX virus to disinfectants and their virucidal properties (i.e. active ingredients and concentrations, contact time).
- Stability of virus in the environment and on surfaces.
- Wastewater sampling and predicting trends for outbreak response.
- Understand optimal ventilation to reduce disease transmission.
- Duration of transmission-based precautions to maintain patients in isolation (when can transmission-based precautions be lifted).
- Effects of home-based care (what can be learned, models of care, etc.).
- Characterization of viral evolution.

DEFINITIONS

Aerosol-generating procedures: Medical procedures that have been reported to be aerosol generating and consistently associated with an increased risk of pathogen transmission. The current list of procedures recognized by WHO as aerosol generating includes aspiration or open suctioning of respiratory tract specimens, bronchoscopy, intubation, cardiopulmonary resuscitation *(99,100)*.

Airborne infection isolation (precaution) room: A room with a high ventilation rate and controlled direction of airflow that can be used to contain airborne infections and acute respiratory infections caused by a novel agent with the potential to pose a public health risk. Such rooms can be naturally or mechanically ventilated *(99)*:

- **Naturally ventilated airborne precaution room:** the airflow should be directed to areas free of transit, or should permit the rapid dilution of contaminated air into the surrounding areas and the open air; the average ventilation rate should be 160 L/s per patient.
- **Mechanically ventilated airborne precaution room:** negative pressure is created to control the direction of airflow; the ventilation rate should be at least 12 air changes per hour (ACH).

Such a room is equivalent to the "airborne infection isolation room" described by CDC.

Airborne transmission: The spread of an infectious agent caused by the dissemination of droplet nuclei that remain infectious when suspended in air over long distances and time. Airborne transmission can be further categorized into obligate, preferential or opportunistic airborne transmission *(99)*:

- **Obligate airborne transmission:** pathogens that are transmitted only by deposition of droplet nuclei under natural conditions (e.g. pulmonary tuberculosis).
- **Preferential airborne transmission:** pathogens that can initiate infection by multiple routes, but are predominantly transmitted by droplet nuclei (e.g. measles and chickenpox).
- **Opportunistic airborne transmission:** agents that naturally cause disease through other routes, but under special circumstances may be transmitted via fine particle aerosols *(101)*.

Definition from *Infection prevention and control of epidemic-and pandemic-prone acute respiratory infections in health care* (WHO, 2014). WHO will host a global consultation in 2022 to further review this definition.

Contact transmission: The spread of an infectious agent caused by physical contact of a susceptible host with people or objects. Direct contact transmission involves both a direct body-surface-to-body-surface contact and physical transfer of microorganisms between an infected or colonized person and a susceptible host. Indirect contact transmission involves contact of a susceptible host with a contaminated intermediate object (e.g. contaminated hands) that carries and transfers the microorganisms *(99)*.

Droplet transmission: The spread of an infectious agent caused by the dissemination of droplets. Droplets are primarily generated from an infected (source) person during coughing, sneezing and talking. Transmission occurs when these droplets that contain microorganisms are propelled (usually < 1 m) through the air and deposited on the conjunctivae, mouth, nasal, throat or pharynx mucosa of another person. Most of the volume (> 99%) comprises large droplets that travel short distances (< 1 m) and do not remain suspended in the air. Thus, special air handling and ventilation are not required to prevent droplet transmission *(99)*.

Health worker: People primarily engaged in actions with the primary intent of enhancing health. This includes health service providers, such as doctors, nursing and midwifery professionals, public health professionals, technicians (laboratory, health, medical, and non-medical), personal care workers, healers and practitioners of traditional medicine. It also includes health management and support workers, such as cleaners, drivers, hospital administrators, district health managers, social workers and other occupational groups in health-related activities. This group includes those who work in acute care facilities and long-term care, public health, community-based care and other occupations in the health and social care sectors *(102)*.

Respirator: Also known as a filtering facepiece respirator. A type of personal protective equipment that uses a filter as an integral part of the facepiece, or in which the entire facepiece is composed of the filtering medium and a means of sealing to the face. Respirators offer a balance of filtration, breathability and fit. Whereas medical masks filter 3-micrometre droplets, "N95" and"FFP2" rated FFRs must filter more challenging 0.075-micrometre particles or particulates and do so across the entire surface of the respirator as a result of the fitted design. European "FFP2" FFRs, according to EN 149 standard, filter at least 94% sodium chloride salt particles and paraffin oil droplets *(100)*.

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ANNEX 1. **WHO CASE DEFINITIONS FOR MONKEYPOX OUTBREAK IN NON-ENDEMIC COUNTRIES** (AS OF 21 MAY 2022) (SEE WEBSITE FOR CURRENT DEFINITIONS)

Suspected case

A person of any age presenting in a monkeypox non-endemic country with an unexplained acute rash

AND

one or more of the following signs or symptoms, since 15 March 2022:

- headache
- acute **onset of fever (> 38.5ºC)**
- **lymphadenopathy (swollen lymph nodes)**
- **myalgia (muscle pain/body aches)**
- back pain
- asthenia (profound weakness)

AND

for which the following common causes of acute rash do not explain the clinical picture: varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, molluscum contagiosum, allergic reaction (e.g. to plants); and any other locally relevant common causes of papular or vesicular rash.

Note: It is not necessary to obtain negative laboratory results for listed common causes of rash illness in order to classify a case as suspected.

Probable case

A person meeting the case definition for a suspected case

AND

one or more of the following:

- has an epidemiological link (face-to-face exposure, including health care workers without appropriate PPE; direct physical contact with skin or skin lesions, including sexual contact; or contact with contaminated materials such as clothing, bedding or utensils) to a probable or confirmed case of monkeypox in the 21 days before symptom onset;
- reported travel history to a monkeypox endemic country[1] in the 21 days before symptom onset;
- has had multiple or anonymous sexual partners in the 21 days before symptom onset;
- has a positive result of an orthopoxvirus serological assay, in the absence of smallpox vaccination or other known exposure to orthopoxviruses;
- is hospitalized due to the illness.

[1] Countries endemic for monkeypox: Cameroon, Central African Republic, Côte d'Ivoire, Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Congo and Sierra Leone. In Ghana, the monkeypox virus was identified in animals only. Benin and South Sudan have documented imported cases in the past. Countries currently reporting cases of the West African clade are Cameroon and Nigeria; and of the Congo Basin clade are Cameroon, Central African Republic and Democratic Republic of the Congo. With the case definition, all countries, except these four (Cameroon, Central African Republic, Democratic Republic of the Congo and Nigeria) should report new cases of monkeypox as part of the current multi-country outbreak. Should countries of Central Africa identify any case of monkeypox due to the West Africa clade, these should also be reported.

Confirmed case

A case meeting the definition of either a suspected or probable case

AND

is laboratory confirmed for monkeypox virus by detection of unique sequences of viral DNA either by real-time polymerase chain reaction (RT- PCR) and/or sequencing.

Discarded case

A suspected or probable case for which laboratory testing of lesion fluid, skin specimens or crusts by PCR and/or sequencing is negative for MPX virus. Conversely, for example, a retrospectively detected probably case for which lesion testing can no longer be adequately performed (i.e. after the crusts fall off) would remain classified as a probable case.

ANNEX 2. **MEDICATIONS AND DOSAGES FOR SYMPTOMATIC CARE**

Fever – paracetamol
- **Adults:** 1g PO/IV every 6–8 hours. Maximum dose 4g every 24 hours or (2 g if history of chronic liver disease).
- **Neonates:** Oral dose 10–15 mg/kg every 6 hours. Maximum dose 40 mg/kg/day; IV dose 7.5 mg/kg every 6 hours, maximum dose 30 mg/kg day.
- **All other children:** 10–15 mg/kg every 6 hours, maximum dose 60 mg/kg /day.

Mild pain control – paracetamol
- **Adults:** 1g PO/IV every 6–8 hours. Maximum dose 4g every 24 hours or (2 g if history of chronic liver disease).
- **Children:** Orally or IV 10–15 mg/kg/dose every 4–6 hours as required, maximum usual dose 60 mg/kg/day, but 90 mg/kg/day can be given for short period with medical supervision.

Severe pain control – tramadol
- **Adults:** 50–100 mg PO/IV every 4–6 hours as needed, daily maximum 400 mg/day.
- **Children > 6 months:** 1–2 mg/kg every 4–6 hours, maximum 400 mg/day.

Severe pain control – morphine (oral dose preferred if patient can tolerate; only use immediate release tablets for acute pain)
- **Adults:** Oral dose is 10 mg every 4 hours as needed; maximum dose is 60 mg/day. IV dose is 1–4 mg SQ/IV every 4 hours as needed – monitor SBP and RR prior to administration of morphine (hold for low SBP or respiratory rate).
- **Children:** Oral dose is 0.2–0.4 mg/kg/dose every 4 hours. Titrate dose to pain. IV dose is 0.05–0.1 mg/kg/dose every 4–6 hours as required.

Antihistamine
- **Adults:** Loratadine 10 mg PO once daily.
- **Children (> 30 kg):** Loratadine 10 mg PO once daily.

Nausea and vomiting

1. Ondansetron (associated with QT prolongation, thus it is important to note other medications that may also prolong the QT interval and to monitor regularly with ECGs if available).
   - **Adults:** 8 mg PO every 12 hours or 4 mg IV every 8 hours as needed.
   - **Children:** 0.15 mg/kg orally or IV 0.15 mg/kg every 12 hours, maximum dose 8 mg.
2. Promethazine
   - **Only for adults:** 12.5–25 mg orally every 4–6 hours as needed (can prolong QT interval).

Dyspepsia
- **Adult:** Omeprazole 40 mg PO/IV every 24 hours.
- **Child:** Omeprazole: 5–10 kg: 5 mg once daily; 10–20 kg: 10 mg once daily; ≥ 20 kg: 20 mg once daily.

Diarrhoea
- Diarrhoea should be managed conservatively. The use of anti-motility agents is not generally recommended given the potential for ileus.

Anxiety

This may be a symptom patients experience particularly related to being in isolation or due to worsening symptoms.
- First-line therapy is to talk with a mental health counsellor.
- For moderate to severe anxiety, diazepam can be considered, but an evaluation of the patient's mental status should precede its use. Benzodiazepines should not be given to patients with altered mentation.
  - **Adults:** Diazepam 5–10 mg PO every 8 hours as needed as long as mentation is unaffected.
  - **Children:** Diazepam 0.05–0.1 mg/kg PO every 6 hours as needed. Continual supervision by a health aid is indicated to keep the child calm. Sedatives should only be used if necessary to perform procedures and give interventions.

Agitation

If patient is agitated and becomes a danger to self, health care providers or other patients, consider pharmacotherapy.

- **Adults:** Diazepam 2–10 mg PO/IV every 6–8 hours as needed as long as patient can protect their airway.
- **Adults:** Haloperidol 0.5–5 mg every 4–6 hours, as needed.
- **Children > 6 years:** Haloperidol IM 1–3 mg every 4–8 hours, as needed.
- **Children 3–6 years:** Haloperidol PO 0.01–0.03 mg/kg once daily.
- Haloperidol is associated with QT prolongation, thus it is important to note other medications that may also prolong the QT interval and to monitor with ECG regularly if available.

Note: Avoid the use of salicylates (e.g. aspirin) in children and adolescents < 18 years of age to avoid the development of Reye's Syndrome.

ANNEX 3. **ANTIMICROBIAL RECOMMENDATIONS AND DOSAGES FOR BACTERIAL SKIN INFECTION**

This is for the treatment of impetigo, erysipelas or cellulitis caused by a bacterial pathogen. It excludes skin infections caused by viral, fungal or parasitic pathogens; necrotizing fasciitis; pyomyositis; severe infections with sepsis; and surgical site infections.

For further guidance on WHO recommendations for antimicrobial therapy please consult *The WHO Essential Medicines List antibiotic book: improving antibiotic AWaReness* and *The WHO Essential Medicines List antibiotic book: infographics*.

Adults

Antibiotic	Dose
Cloxacillin (flucloxacillin)	500 mg orally every 8 hours
Cefalexin	500 mg orally every 8 hours
Amoxicillin-clavulanic acid	500–125 mg orally every 8 hours
If concern for community acquired MRSA consider following treatment:	
Clindamycin	600 mg orally every 8 hours
Trimethoprim-sulfamethoxazole	800–160 mg orally every 12 hours
Doxycycline	100 mg orally every 12 hours

Note: **In the case of penicillin or beta-lactam allergy:** use clindamycin or trimethoprim-sulfamethoxazole.

Children

Weight	Amoxicillin-clavulanic acid 40–50 mg/kg/dose of amoxicillin component every 12 hours OR 30 mg/kg/dose every 8 hours orally	Cefalexin 25 mg/kg/dose every 12 hours orally	Cloxacillin (flucloxacillin) in neonates: 25–50 mg/kg/dose twice daily; in children: 25 mg/kg/dose every 6 hours
3 < 6 kg	250 mg of amoxicillin/dose twice daily	125 mg every 12 hours	125 mg every 6 hours
6 < 10 kg	375 mg of amoxicillin/dose twice daily	250 mg every 12 hours	250 mg every 6 hours
10 < 15 kg	500 mg of amoxicillin/dose twice daily	375 mg every 12 hours	250 mg every 6 hours
15 < 20 kg	750 mg of amoxicillin/dose twice daily	500 mg every 12 hours	500 mg every 6 hours
20 < 30 kg	1000 mg of amoxicillin/dose twice daily	625 mg every 12 hours	750 mg every 6 hours
> 30 kg	Use adult dose	Use adult dose	Use adult dose

Note: **If concern for community-acquired MRSA consider clindamycin:** neonates 5 mg/kg/dose every 8 hours; children 10 mg/kg/dose every 8 hours.

ANNEX 4. **SUMMARY OF REGULATORY LICENSING OF ANTIVIRALS FOR MONKEYPOX**

	Tecovirimat	Brincidofovir	Cidofovir
Treatment dose, route, duration (adults) *(65,66,71,73,76)*	**Dose** Oral 600mg PO every 12 hours Intravenous* 3 kg to < 35 kg: 6 mg/kg every 12 hours 35 kg to < 120 kg: 200 mg every 12 hours > 120 kg: 300 mg every 12 hours *Must be administered over 6 hours **Duration** 14 days	**Dose** Oral < 10 kg: 6 mg/kg 10–48 kg: 4 mg/kg > 48 kg: 200 mg (20 mL) **Duration** Once weekly for 2 doses, on days 1 and 8	**Dose** Intravenous 5 mg/kg IV once weekly Must be given with oral probenecid: 2 grams 3 hours prior to each dose and 1 gram at 2 and 8 hours after completion of the infusion Must be given with at least 1 L of 0.9% normal saline over a 1–2 hour period before each infusion **Duration** Once weekly × 2 weeks, then once every other week (based on treatment for CMV retinitis)
Treatment dose, route, duration (paediatrics) *(65,66,71,73,76)*	**Dose** Oral 13–25 kg: 200 mg every 12 hours 25–40 kg: 400 mg every 12 hours > 40 kg: 600 mg every 12 hours Intravenous* 3–35 kg: 6 mg/kg every 12 hours 35–120 kg: 200 mg every 12 hours > 120 kg: 300 mg every 12 hours *Must be given over 6 hours **Duration** 14 days	**Dose** Oral < 10 kg: 6 mg/kg 10–48 kg: 4 mg/kg > 48 kg: 200 mg (20 mL) **Duration** Once weekly for 2 doses, on days 1 and 8	**Dose** Intravenous 5 mg/kg IV once weekly Must be given with oral probenecid: 2 grams 3 hours prior to each dose and 1 gram at 2 and 8 hours after completion of the infusion Must be given with at least 1 L of 0.9% normal saline over a 1–2 hour period prior to each infusion. **Duration** Once weekly × 2 weeks, then once every other week (based on treatment for CMV retinitis)
Dosage forms and strength	**Capsules:** 200 mg orange and black *(65)* **Intravenous:** IV injection single-dose 200 mg/20mL *(71)*	**Tablets:** 100 mg, blue, oval shaped *(73)* **Suspension:** lemon-lime flavoured suspension containing 10 mg/mL *(73)*	**Intravenous:** supplied as single-use vials 75 mg/mL for intravenous infusion *(76)*

	Tecovirimat	Brincidofovir	Cidofovir
Use in pregnancy	No data from the use in pregnant women *(65,66)*	Not recommended Administration to small animals resulted in embryotoxicity, decreased embryo-fetal survival, and/or structural malformations. It is recommended to use an alternative therapy if feasible *(73)*	Pregnancy class C No adequate well controlled studies in pregnant women *(76)*
Use in breastfeeding	Unknown whether medicine or metabolites are excreted in human milk *(65,66,70)*	In studies with lactating rates, brincidofovir was detected in milk but not plasma of nursing pups *(73)*	Unknown *(76)*
PEP dose, route, duration (adult)	No data	No data	No data
Mechanism of action	Inhibits activity of the orthopoxvirus VP37 protein and inhibits viral envelope formation *(65,69,70,72)*	Inhibits polymerase mediated synthesis of DNA *(73)*	Inhibits DNA polymerase *(79,80)*
Licensed for smallpox	European Medicines Agency (2022)*(65)* US Food and Drug Administration (2021)*(66)* Health Canada (2021)*(67)*	US FDA (2021) *(73)* EMA (2016)	US CDC (EA-IND)
Licensed for monkeypox	European Medicines Agency (2022) *(65,70)* US CDC (EA-IND protocol)	US CDC (EA-IND protocol)	US CDC (EA-IND)

Note: NIOCH-14: Analogue of tecovirimat *(79,80)*.

	Tecovirimat	Brincidofovir	Cidofovir
NHP data (if human trials not available)	NHP and small animal data showed survival of 80–100% when treated with minimum effective dose Delay in treatment was associated with decreased survival Increasing dose of drug did not lead to survival benefit but did result in the following: • lower circulating viral load • fewer lesions • less clinical signs of infection • unresponsiveness • dyspnoea • fever • lymphadenopathy *(65,68–70)*	Small animal data showed statistically significant improvement in survival compared with placebo in those treated with brincidofovir *(73)*	Small animal models have shown decreased severity of infection with decreased tiers of virus in the nose/sinus and lungs *(76)*. Survival rates of 80–100% *(76)* **Carcinogenesis** 26-week study evaluating once weekly subcutaneous injection in rats was terminated at 19 weeks because in females a palpable mass was detected after six doses. The masses were diagnosed as mammary adenocarcinoma. In a 26-week IV toxicology study in rats, a significant increase in mammary adenocarcinoma as well as significant incidence of Zymbal's gland carcinoma in males *(76)* **Spermatogenesis** In rats and monkeys cidofovir caused inhibition of spermatogenesis No adverse effects on fertility in male rats *(79,80)*

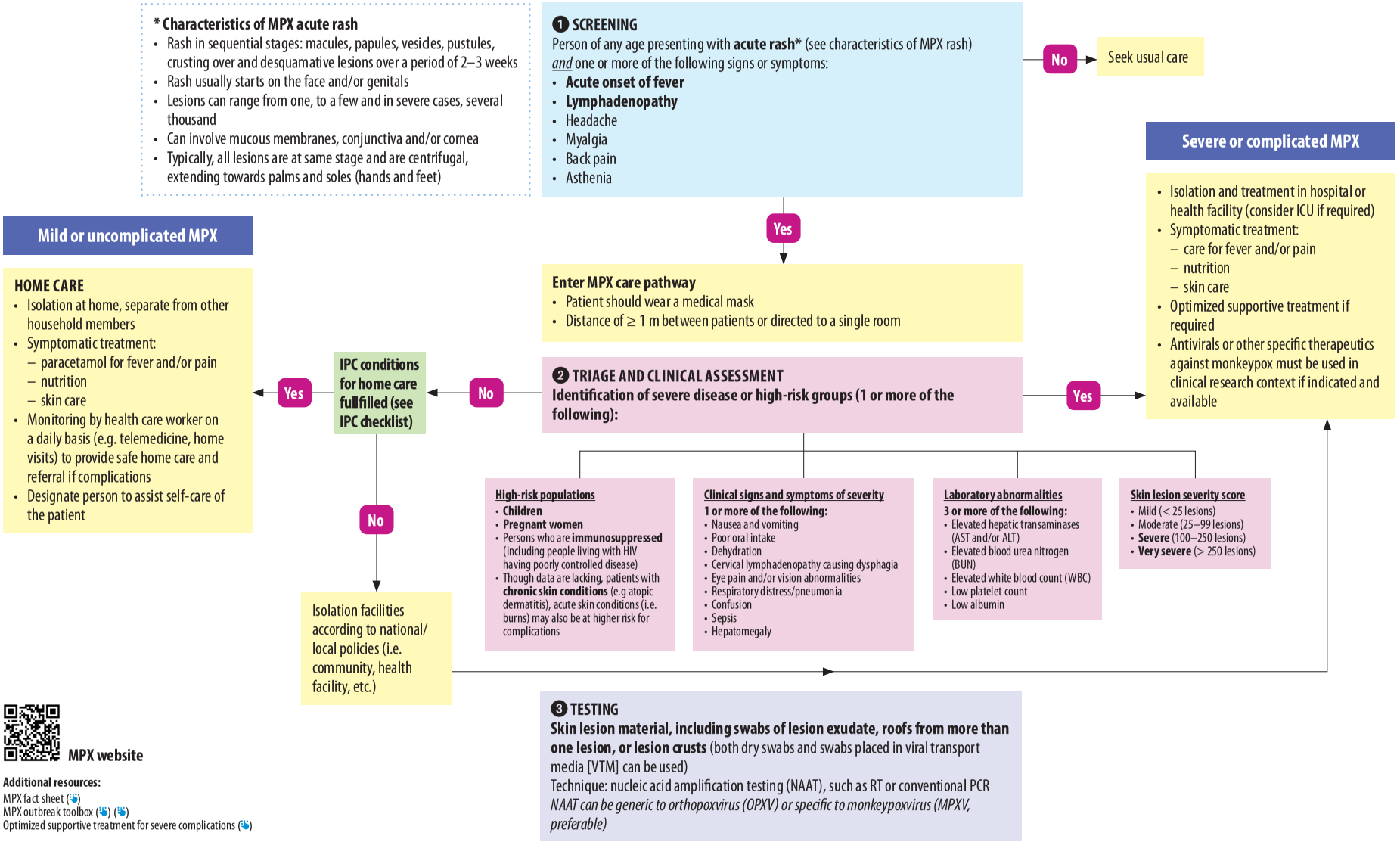
Note: NIOCH-14: Small animal studies showed reduction of virus concentration in primary target organs (lungs, trachea, nose) and secondary organs (brain, liver, kidney, spleen, pancreas) *(79,80)*.

	Tecovirimat	Brincidofovir	Cidofovir
Human data trials	Phase 1 clinical trial: co-administration with repaglinide caused mild-moderate hypoglycaemia in 10/30 patients *(65,66,70)*. Phase 3 clinical trial: expanded safety trial, 359 patients received tecovirimat and 90 received placebo Adverse events: headache, nausea, abdominal pain *(15)* **Case report** *(15)*: 1 patient: Blood and upper respiratory tract PCR negative 48 hours after starting drug Remained PCR negative at 72 hours Haematological, renal, and liver profiles remained normal Discharged home to complete therapy	Safety based on use of brincidofovir for prevention of CMV and adenovirus *(15)* CMX001-201: Phase 2, double-blind, placebo controlled study in adults for prevention of CMV CMX001-202: Phase 2, randomized, double-blind, placebo controlled, multicentre study for prevention of adenovirus disease CMX001-301: Phase 3, randomized, double-blind, placebo controlled parallel-group study in adults for prevention of CMV **Case reports** *(15)*: 3 patients: All developed elevated transaminases None completed a full course of therapy No consistent association between medication and clinical or virological parameters	Three phase 2/3 trials conducted in HIV-infected patients with CMV retinitis*(76)* Study 105: Patients with CMV retinitis randomized to immediate treatment vs delayed treatment until progression of CMV retinitis Study 106: Open-label trial, 48 patients previously untreated with CMV retinitis randomized to immediate treatment or delayed until progression of CMV retinitis Study 107: Open-label trial, 100 patients with relapsing CMV retinitis randomized to 5 mg/kg once a week for 2 weeks and then 5 mg/kg or 3 mg/kg every other week 26/43 receiving 5 mg/kg and 21/41 receiving 3 mg/kg discontinued due to adverse event, intercurrent illness, excluded medication, or withdrawn consent
Toxicity/side-effects *(65,66,70,73,77)*	Well tolerated Very common: headache Common: dizziness, upper abdominal pain, abdominal discomfort, diarrhoea, nausea, vomiting **Drug interactions:** • Repaglinide • Omeprazole • Midazolam • Buproprion • Atorvastatin • Flurbiprofen • Methadone • Darunavir • Maraviroc • Rilpivirine • Sildenafil • Tadalafil • Vardenafil • Voriconazole • Tacrolimus	**GI toxicity:** • Diarrhoea • Nausea • Vomiting • Abdominal pain **Hepatic toxicity:** • Elevated transaminases • Elevated total bilirubin	Nephrotoxicity Neutropenia Decreased intraocular pressure Anterior uveitis/iritis Metabolic acidosis Nausea Fever Alopecia Myalgia Probenecid Hypersensitivity

	Tecovirimat	Brincidofovir	Cidofovir
Monitoring (VS)	Per usual clinical care No enhanced monitoring required	Per usual clinical care No enhanced monitoring required	Closely monitor renal function
Minimal lab monitoring	Haematology Renal function Liver function	Hepatic testing should be performed before starting and while receiving brincidofovir at regular intervals as clinically appropriate	Renal function Haematology Urine protein Within 48 hours prior to each dose
Other	Intravenous formulation approved by US FDA on 19 May 2022 for smallpox *(71)*	**Carcinogenesis** *(73)* Data from rats showed palpable small masses in rats after as few as 26 oral doses at systemic levels less than the expected human exposure based on the recommended dose of brincidofovir The masses were diagnosed as mammary adenocarcinomas, carcinoma in squamous cell, Zymbal's gland, uterus and small intestine and hemangiosarcomas in mesenteric and mediastinal lymph node, liver and abdominal cavity were observed No tumors occurred in rats after 9 twice-weekly intravenous doses **Fertility** *(73)* Individuals of childbearing potential should use effective contraception during treatment and for at least 2 months following last dose **Testicular toxicity** *(73)* Due to animal findings of testicular toxicity, individuals of reproductive potential with partners of childbearing potential should use condoms during treatment for at least 4 months after last dose	Must be given with probenecid and intravenous saline pre-hydration *(76)* **Contraindications** *(76)* CrCl $\leq$ 55 mL/min Creatinine $>$ 1.5 mg/dL Urine protein $\geq$ 100 mg/dL Patients receiving agents with nephrotoxic potential Such agents should be discontinued at least 7 days prior to starting therapy Hypersensitivity to cidofovir Hypersensitivity to probenecid or other sulfa-containing medications **Spectrum of activity** *(76)* Herpes viruses (CMV, VZV) JC virus Adenovirus Papillomavirus

Monkeypox (MPX) clinical care pathway – decision-making algorithm to be used at any health care point

For contacts of suspected or confirmed patients, please refer to WHO guidance *Surveillance, case investigation and contact tracing for monkeypox: interim guidance*.

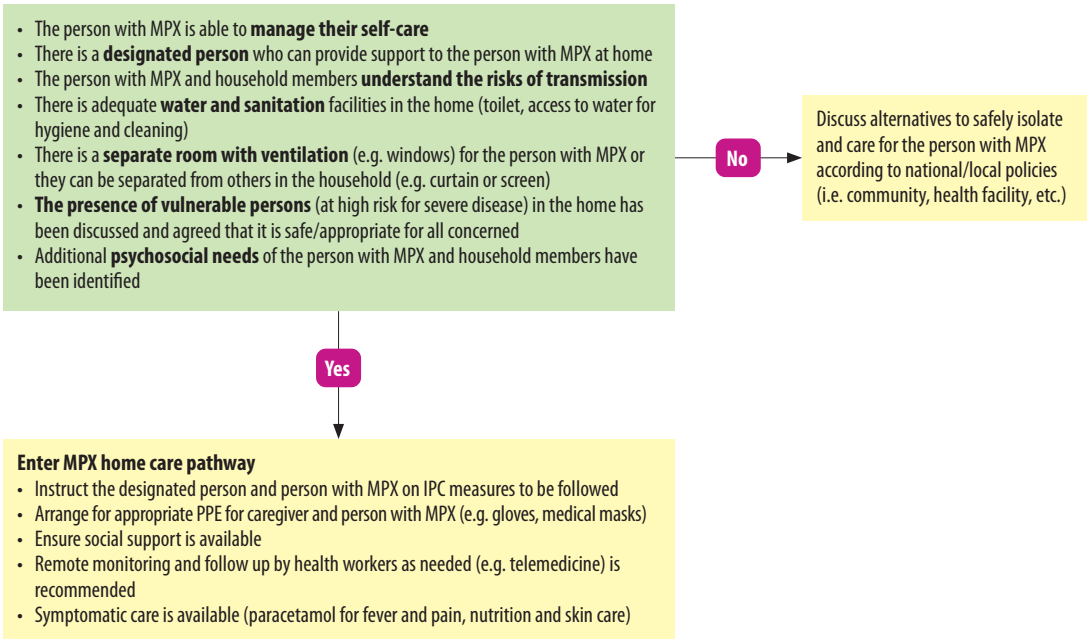


MPX website

Additional resources:

MPX fact sheet
MPX outbreak toolbox
Optimized supportive treatment for severe complications

Checklist for IPC conditions for home care in the management of persons with non-severe or uncomplicated monkeypox (MPX) to be implemented at first point of contact, either at health access point or remotely via telephone or telemedicine



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