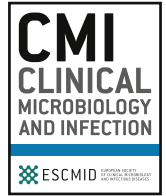




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Guidelines

Management of patients with monkeypox virus infection and contacts in the community and in healthcare settings: a French position paper

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ABSTRACT

Scope: Since April 2022, a large number of monkeypox (MPX) cases have emerged across the globe in regions that are known to be totally free of zoonotic reservoir. The High Council for Public Health is a national institute commissioned to provide guidelines to the French Ministry of Health. The objective of these guidelines and recommendations is to inform the public, people at risk of severe MPX infection, infected patients and their families and contacts and healthcare workers in charge of infected patients.

Methods: A review of the literature from the MEDLINE database was carried out using the single keyword 'monkeypox', including recent and older articles from January 2000 to June 2022. There was no filter for the type of study, except English language. The titles and summaries of all the articles were read by the experts to select articles of interest. The High Council for Public Health brought together specialists with expertise in the field to analyse the scientific literature and international recommendations. Recommendations were classified with clinical practice methodology using four levels (strong recommendation, recommendation, optional recommendation and no recommendation) without grading the level of evidence. To develop and methodologically validate the recommendations, the Appraisal of Guidelines for Research and Evaluation Instrument (AGREE-II) chart was partially used.

Questions addressed by the guidelines and recommendations: (a) What are the therapeutic management measures for hospitalized patients with severe forms of MPX infection, and what are the preventive measures to protect healthcare professionals? (b) What are the isolation and prevention measures in the community for patients with mild or moderate severity MPX infection? (c) what are the preventive measures for contacts of an MPX-infected person? (d) Who should be vaccinated? (e) What are the specific prevention measures for children and schools? **Didier Lepelletier, Clin Microbiol Infect 2022;28:1572**

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Introduction

The current monkeypox (MPX) epidemic, affecting non-endemic countries, is occurring in the midst of the coronavirus disease 2019 pandemic. MPX epidemics have been described for years in East and Central Africa where the virus is endemic within an indigenous zoonotic reservoir, particularly in Nigeria in 2017 that presents primarily with lesions in the genital areas [1]. Occasionally, cases have been observed outside these regions but always

in relation with an animal or human source from the endemic areas. Since the end of April 2022, a large number of MPX cases have emerged across the globe in regions that are known to be totally free of zoonotic reservoir [2–4]. The causative agent of MPX—the *Monkeypox virus* (MPXV)—is related to the *Variola virus* responsible for the now-extinct human scourge of smallpox. MPXV is an enveloped, large-sized, double-stranded DNA virus with a genome size of approximately 190 kb that belongs to the *Orthopoxvirus* genus in the Poxviridae family. This genus comprises several species that infect humans, including *Variola virus*, *Vaccinia virus*, *Cowpox virus* and MPXV [5].

Since 1 January 2022, cases of MPX have been reported to WHO from 92 Member States across all six WHO regions. As of 15 August 2022, a total of 35 275 laboratory confirmed cases and 141 probable

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cases, including 12 deaths, have been reported to the WHO. Since 13 May 2022, a high proportion of these cases have been reported from countries without the previously documented MPX transmission. This is the first time that the cases and sustained chains of transmission have been reported in countries without direct or immediate epidemiological links to areas of West or Central Africa [6].

French epidemiological data on the spread of MPXV are evolving and can be accessed on the website of Santé publique France [7]. As of 11 August 2022, 2643 of 2673 (98.8%) confirmed cases were adult men with a median age of 36 years.

To date, the modes of transmission of MPXV, previously documented primarily during epidemics in Africa, consist of direct contact with either body fluids or skin lesions (blisters) of infected animals. Human-to-human transmission may result from close contact with skin lesions (vesicles) or mucous membranes of a sick person (oral, genital, conjunctival or even corneal mucosa). Indirect transmission after contact with objects or materials (bedding, linen and dishes) recently contaminated with biological fluids has been discussed without scientific proof. Mucosal lesions precede skin lesions, which could explain why MPXV is initially transmitted mainly by respiratory droplets after prolonged face-to-face contact, hence the risk of exposure of close contacts to the case [8]. The risk of transmission by direct blood contact appears to be limited, given the brevity of viremia, that occurs within 1–2 days before the appearance of mucosal and then cutaneous lesions [9]. Transmission during pregnancy, via the placenta or during delivery through contact with biological fluids, is possible, but the risk has not been well quantified.

Through the current epidemic, most cases reported to date have occurred in the men having sex with men (MSM) community, although other circumstances have also been reported. Although close physical contact with the mucous membrane of an infected person is a well-established mode of transmission, MPXV can also be transmitted sexually.

Herein, we describe the French guidelines for the management of patients with mild or moderate infection (isolation and monitoring at home) and their contacts in the general population to provide both public and healthcare workers (HCWs) with essential information at this early stage of the MPXV emergence.

Methods

The High Council for Public Health (HCSP) is a national institute mandated to provide guidelines for helping the French Ministry of Health and the Government to monitor sanitary crises. The HCSP was commissioned by the French Government between 20 May 2022, and 7 June 2022, to rapidly establish recommendations for the therapeutic management of severe cases of MPXV infection in hospitals and for the isolation and surveillance of patients with mild or moderate severity infections and their contacts in the general population. To respond urgently, the HCSP set up a working group of specialists (see Acknowledgements section) with expertise in the field (public health, infectiology, virology, vaccination and infection control).

Selection of articles

A literature review from the MEDLINE database was performed that included recent and older articles from January 2000 to June 2022 using a single keyword 'Monkeypox'. Only articles in English over the study period were selected. There was no filter for the type of study. Titles and summaries of all articles were read by the experts to select the articles of interest for drafting of recommendations, including MPXV human-to-human transmission [8,9];

definition of MPXV cases and contacts; clinical forms of this infection (MPXV infection graded as severe, atypical or asymptomatic); risk factors associated with severe forms of the infection [10–16]; and molecules used for the treatment of severe forms [17–26]. Evidence of each article reviewed was summarized to establish recommendations based on expert consensus [27].

Methodology to apply expert panel for clinical practice and strength of recommendations

Through the strength of a recommendation, the working group has indicated the importance of adherence to a particular recommendation. It is based on the quality of the studies supporting the recommendation and the magnitude of the potential benefit and harm. The proposed classification had four levels: strong recommendation, recommendation, optional recommendation and no recommendation [27]. It was made possible by the consensus of experts of the HCSP working group, without grading the level of evidence. The consensus does not mean unanimity or definitive advice but rather a consensual state of the art at the initial stage of the epidemic. To develop and methodologically validate our recommendations, we were inspired by some of the items and criteria of the AGREE-II chart [28].

Definition

- *At-risk person for severe infection*: immunocompromised individuals, pregnant women, and children [13–15].
- *Criteria used to characterize a severe MPXV infection*: fever >38.3 °C and its duration >7 days; the intensity of the rash according to the WHO criteria (>100 lesions); the presence of oral pain with odynophagia and dysphagia; the existence of large cervical adenopathy with a risk of compression of the airways; the presence of digestive disorders, such as nausea, vomiting or the presence of hypertransaminasemia, hypoalbuminemia, hyperleukocytosis and thrombocytopenia [16].
- *At-risk contact*: Any person who had unprotected direct physical contact of any duration with the injured skin or body fluids of a probable or confirmed symptomatic case, under any circumstances, including sexual intercourse, medical or paramedical care, indirect physical contact through sharing of toiletries, textiles (clothing, linens, bedding) or dirty dishes used by the probable or confirmed symptomatic case.

French guidelines about vaccination

Recommendations related to vaccination have been published by the French High Authority for Health (HAS) and are summarized [29]. The HAS recommends smallpox vaccination for adults whose contact with an MPXV-infected person is considered to be at risk of transmission, including healthcare professionals exposed without personal protective measures [29]. The reactive vaccination should take place preferably within 4 days of exposure, and up to 14 days. The vaccine regimen consists of two doses spaced 28 days apart, with those previously vaccinated against smallpox receiving a single dose. The vaccines currently available for these individuals are the Imvanex and Jynneos vaccines, which are interchangeable. The adverse effects of these vaccines are limited compared with those of first- and second-generation smallpox vaccines.

In addition to post-exposure vaccination, the HAS recommends offering pre-exposure vaccination against MPXV to those most exposed to the virus [30]: LGBTQ people (Lesbian, Gay, Bisexual, Transgender, Queer/Questioning) reporting multiple sexual partners; people in prostitution; professionals in sexual consumption

facilities, regardless of the status of these facilities. The HAS does not recommend, at this stage, the pre-exposure vaccination of healthcare professionals caring for sick people because usual hygiene measures and the wearing of personal protective equipment make the risk of transmission very low in practice. Nevertheless, the HAS recommends that this vaccination can be considered on a case-by-case basis, depending on the exposure, the existence of individual risk factors, or at their request.

Clarification of the procedure for cases and contacts

In accordance with the procedure developed by Santé publique France ('Cases of MPXV infection in Europe: definitions and procedures') [10], only symptomatic patients suspected of having MPXV infection with a characteristic vesicular rash should be tested. Diagnosis is based on skin lesion sampling (crusts, dry swab rubbing of several vesicles or even biopsy) or oropharyngeal sampling in case of a rash in the mouth or throat [11]. Asymptomatic patients [1,13] presenting spontaneously for testing or vaccination should be referred to their general practitioner and an emergency helpline number must be provided to these individuals (French Centre 15) for planning a consultation or teleconsultation with an infectious disease specialist, if the contact with a confirmed or probable MPXV case is validated. MPXV infection is a mandatory reportable disease in France. Only patients with severe MPXV infection must be hospitalized [16].

HCSF considerations for recommending specific treatment in a patient with MPXV infection

Therapeutic indications

Not all symptomatic confirmed cases should be treated with an antiviral drug or anti-MPXV immunoglobulin (*recommendation*). Patients with severe MPXV or those at risk of severe infections should be referred to an infectiologist or the practitioner in charge of the patient for the consideration of specific treatment (*recommendation*).

Prioritization of specific therapies if their indication is deemed necessary

The use of tecovirimat is recommended as first-line therapy owing to its oral availability, approval in the European market and good safety profile (*recommendation*). As the second-line therapy, brincidofovir can be used, subject to availability, due to its oral administration and its better tolerance than cidofovir (*optional recommendation*). Cidofovir represents only the third-line treatment because of its disadvantages: injectable route, high renal and haematological toxicity, as well as a potential carcinogenic, teratogenic and reprotoxic effect (*optional recommendation*). This product is currently available on a compassionate basis. Anti-MPXV immunoglobulins must be reserved for patients who cannot be treated by antivirals, such as pregnant women and children (*optional recommendation*) [17–26].

General guidelines for controlling the spread of MPXV infection

Isolation of infected patients and surveillance of contacts are the basis of the strategy proposed by the HCSF. After a documented evaluation, home isolation is recommended as a priority for infected patients for whom a specialized medical opinion (referent infectious diseases specialist) has ruled that this measure is clinically appropriate, with the implementation of psychological, socio-economic and medical support if needed [31] (*strong recommendation*).

The risk of environmental contamination should be controlled by regular ventilation of the room where the infected patient is staying, vacuuming of dust and regular washing of floors and surfaces and washing of cloths in contact with the body of the infected patient (if possible, at 60 °C for 30 minutes with a usual detergent). It is advisable to avoid sharing objects or sanitary facilities; their regular and systematic cleaning after each contact with the infected patient is recommended using a usual detergent [32] (*strong recommendations*).

Transportation from home to healthcare facilities should be done by personal transport or by personnel trained in biohazards, taking care to disinfect the vehicle after transportation [33] (*strong recommendation*).

Proactive communication by health authorities on the risks of infection and transmission should be conducted to increase the awareness among both persons at risk of severe disease and the public through the dissemination of regularly updated advice as new data become available (*strong recommendation*). Risk communication messages should emphasize that MPXV is transmitted through close and direct contact between people, especially within the same household, including through sexual contact (which may present as an ano-genital blistering infection) or through shared objects. A balance should be maintained between information to those most at risk (population in which the virus initially circulated) and communication to the public, which should remind that, at present, data on the level of dissemination of the virus among the general population are still very fragmentary.

Specific guidelines for controlling the spread of MPXV infection

The following measures are recommended for all patients with MPXV infection (*strong recommendations*):

- Avoid close contact (direct unprotected physical contact, sexual relations, sharing of textiles or objects, sharing of a room or bed, etc.) with people around them.
- Ensure that people at risk of severe infection are kept away from the place of residence of the patient infected with MPXV infection.
- If possible, cover the skin lesions with a bandage or a cloth depending on their number and location; use single-use coverings such as gauze or bandage or use cloths that can be reused after washing at 60 °C for 30 minutes if possible.
- Wear a surgical mask when a third party is present at home and when leaving the home is deemed necessary.
- Do not scratch the lesions to avoid re-inoculating the virus.

Keep mammal pets away from the infected person's home to prevent the risk of human-animal transmission [34].

Specific guidelines for HCWs in charge of infected patients

The guidelines concerning the infected patients are as follows (*strong recommendations*):

- Isolate the patient in a dedicated room or chamber, if available with negative pressure.
- The patient should wear a surgical mask in the presence of another person in the room or when moving outside the room.
- The patient should perform regular hand hygiene when leaving the room.

The guidelines concerning the HCWs are as follows (*strong recommendations*):

- Wear a respirator and eye protection with goggles when wearing the respirator, single-use non-sterile gloves and single-use

Table 1

Prevention, isolation, and surveillance measures for patients with low or moderate severity of confirmed MPXV infection and their contacts

Patients with MPXV infection	Contact people
<ul style="list-style-type: none"> • Avoid contact with other people, especially those at risk of severe disease • Avoid close contact with mammal pets • Isolate the patient at home until he/she is cured (complete removal of skin lesions) if conditions allow the patient to remain at home and if he/she is well informed and able to follow the measures to be taken with respect to potential contacts and to correctly perform the clinical surveillance adapted to his/her status. <p>Patients without risk factors for severe disease: self-monitoring (passive surveillance) of clinical signs with a minimum weekly call to the Agence Régionale de santé (regional health agency-ARS). A telephone number will be given to the patient by the ARS, to be contacted in case of aggravation of symptoms.</p> <p>Patients with risk factors for severe disease: active monitoring of clinical signs through systematic multi-weekly calls to the ARS-designated referring medical team.</p> <ul style="list-style-type: none"> • Avoid, whenever possible, keeping any person at risk for severe form at home. • If conditions for isolation and home care cannot be adequately provided: <ul style="list-style-type: none"> - give preference to isolation in a dedicated ad hoc facility; - discuss the possibility of temporary hospitalization for clinical monitoring and ensure, especially in patients with risk factors for severe disease, the absence of complications and a favourable short-term evolution with, in these cases, a satisfactory return to the home or to an ad hoc structure. 	<ul style="list-style-type: none"> • Organize under the coordination of the regional health agency (and the infectious control team for hospitalized cases): <ul style="list-style-type: none"> - the identification of contacts and evaluation of the risk (negligible or not) of being infected; - the assessment of the risk of developing a severe form of the disease, taking into account a proven history of vaccination against smallpox (persons born before 1977, vaccination record or characteristic embossed scar); - the logistics for performing confirmatory virological diagnostic tests if the contact person becomes symptomatic. • Do not place contacts under eviction. • Ask contacts to watch for clinical signs (fever, blistering rash, etc.) for 21 d after the last contact with the infected person. • Remove contacts at risk for severe disease from the infected person's home. • In case clinical signs appear, warn contacts of the need to get isolated immediately and to contact very soon the emergency centre or their general practitioner.

MPXV, *Monkeypox virus*.

gown in case of contact with the skin or mucous membrane lesions skin or mucous membranes.

- Perform hand hygiene at each opportunity during care and before entering and leaving the patient's room.
- Cover the patient's skin lesions with a bandage or gauze.
- Apply additional hygiene rules according to the healthcare facility's recommendations such as disinfecting the patient's environment (floors, surfaces) with an updated and validated protocol using standardized detergents and disinfectants; use proper containment and disposal of contaminated waste; do not

handle soiled linen. Potentially infected articles of clothing or linen should be placed in a water-soluble bag, sealed or tied, and placed inside a waterproof bag for transport to the laundry.

Specific guidelines for MPXV-infected children

- The same isolation and prevention measures should be used for infected children as for adults (*recommendation*).
- Personal contact and social relationship between parents and their infected children must be maintained, while direct

Table 2

Hygiene measures for patients with low or moderate severity MPXV infection, contacts, and home healthcare workers

Control measures	Patient with MPXV infection	Contact person	Healthcare workers at home (and other person providing cares)
Hand hygiene	Yes, frequently	Yes regularly, especially after contact with the case's environment	Yes, at every opportunity of care, when entering and leaving the home
Surgical mask	Yes, when other persons are present in the house	Yes, for one-time visits No for contacts living in the same household	No, unless Filtering Face Piece type 2 (FFP2) respirator is not available
FFP2 respirator	No	No	Yes, on entry to the home, with removal after leaving the home
Personal protective equipment	No	No	In case of contact with the patient: wearing of non-sterile gloves; wearing of a protective gown; wearing of an apron in case of care with exposure to biological liquids or injured mucous membrane or skin; wearing of protective goggles, depending on the type of care with or without exposure
Covering skin lesion	Yes	Not applicable	Not applicable
Healthcare waste	Not applicable	Not applicable	Disposal in a double-wrapped garbage bag and deposited in public garbage cans after 24–48 h of storage in a dedicated area of the home (closet, cellar, etc.) due to the environmental resistance of MPXV Disposal of waste by the caregiver using specific bags for waste from care at infectious risk
Linens and clothing that have been in contact with the lesions	Washing of cloths in contact with the body of the infected person (if possible, at 60 °C for 30 minutes with a usual detergent)		
Home ventilation	It is difficult to establish the level of ventilation quality in a home. Airing the rooms through the natural openings (door, windows) for approximately 10 min every hour allows a renewal of air that reduces the risk of airborne infection, in addition to the level of the ventilation system in the home		

MPXV, *Monkeypox virus*.

contacts must be avoided, especially among pregnant women (*strong recommendation*).

- In case of home isolation, the child must be kept isolated in a single room if possible; alternatively, the number of people present at home must be reduced, for example by entrusting the siblings to relatives, while continuing to monitor family contacts (*strong recommendation*).
- Parents must wear protective equipment in case of close contact with an infected child (respirator or at least a surgical mask if possible), particularly if they are at risk of severe infection (*strong recommendation*).

Specific guidelines in case of occurrence of an MPXV infection in a school or in a children community

The medical and social workers in these communities (school doctors, nursery doctors, school nurses and psychologists) must be involved in the management of the situation under the coordination of the regional health agency (*strong recommendation*). It is necessary to rapidly inform all parents of children in the community, reassuring them about the possibility of transmission (low risk of transmission in the absence of direct close physical contact with a confirmed case) and proposing self-surveillance (*strong recommendation*). If nurses or other personnel in schools will be looking at the lesions, they should examine the patients using personal protective equipment (*strong recommendation*).

High-risk contacts (close peers, same section or class, sharing of clothing) and contacts at highest risk of severe disease (immunocompromised children) must be identified (*strong recommendation*). Surveillance by parents and regular medical contact should be provided (*strong recommendation*).

Routine cleaning and ventilation of the building need to be reinforced to control the possible risk of contact and respiratory contamination (*strong recommendation*).

The occurrence of clustered cases must be identified, and infection control measures must be adapted (*strong recommendation*). School classroom should not be closed unless several cases are identified (*recommendation*).

Isolation guidelines for patients with low or moderate severity MPXV infection and their contacts are described in [Table 1](#). Personal infection control measures recommended for patients, contacts, and home HCWs are described in [Table 2](#).

Conclusive considerations

Although MPX is mostly a mild disease, patients with severe forms of MPX should be hospitalized and receive specific antiviral treatment. Pre- and post-exposure individuals should receive at least one dose of vaccine based on their history of smallpox vaccination. People at risk of severe disease should be given priority for vaccine availability and should strictly adhere to hygiene measures to protect themselves. Infected persons should follow isolation measures until clinical recovery to protect their environment. Prevention measures are all the more important as contact tracing operations run into difficulties (impossibility of identifying the person who transmitted the virus, under-reporting of contact cases, especially around anonymous sexual relations). Contacts are not subject to isolation measures or eviction from social and professional places.

The recommendations presented in this article and related to the treatment of patients with severe infection and isolation measures for outpatients with low or moderate severity MPXV infection at home have the aim to inform the public and healthcare workers. The capacity to perform contact tracing is also a big

challenge, particularly among people at risk of severe infection. The messages recall the modes of transmission, the symptoms, and what to do in case of symptoms. They are currently being disseminated digitally on the Sexosafe website (<https://www.sexosafe.fr/Mon-coeur>) dedicated to MSM and via social networks. At the same time, posters, flyers and advice sheets have been distributed in the field thanks to associations, regional health agency and Sexosafe teams present in the field. The U.S. Centers for Disease Control and Prevention have also published information 'Safer Sex, Social Gatherings, and Monkeypox' available online (<https://www.cdc.gov/poxvirus/monkeypox/sexualhealth/index.html>). Preventive actions will be adapted as the situation evolves. Moreover, WHO has estimated that the current situation is unlikely to escalate into a full-blown pandemic. The infection control measures reported herein rise unknowns and challenges, including vaccination of contacts [35] due to many uncertainties regarding its availability, efficiency, tolerance and acceptance. As discussed in this report, the recommended strategies must be able to evolve according to the progression of knowledge on the ability of MPXV to become endemic in non-endemic areas.

Ethics approval and consent to participate

This manuscript has met the ethical approval of the French official institution 'Haut Conseil de la santé publique' (High Council for Public Health), and all authors have given their approval to participate in this work.

Transparency declaration

The authors declare that they have no conflicts of interest.

Author contributions

D.L., B.P., and C.C. designed the study. D.L., B.P., and C.C. screened the literature for relevancy. D.L., B.P., F.C., and C.C. performed the quality appraisal. All the co-authors revised the manuscript for intellectual content. All authors have given their consent for the publication of the manuscript.

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