Risk Assessment Group

MONKEYPOX MULTI-COUNTRY OUTBREAK, 2022

Date of the signal	Date of the PRA	Signal provider	Experts consulted	Method
07/05/2022: first case UK (imported) **17/05/2022: cases in second country**	**17/05/2022**	UK/ECDC/ Portugal	Pierre-Louis Deudon (Collège de Médecine Générale), Wouter Dhaeze (AZG), Niel Hens (UHasselt/UAntwerpen), Oriane Lambricht (AVIQ), Kris Keersmaekers (Violett Antwerpen), Amaryl Lecompte (Sciensano), Nicolas Ledent (COCOM), Agnes Libois (CHU-St Pierre), Christelle Meuris (ULiège), Maud Mittler (Violett Antwerpen), Mark Sergeant (Sensoa), Patrick Soentjens (ITG), Pierre Van Damme (UA), Wim Vanden Berghe (Sciensano), Stefaan Van der Borght (FOD/SPF), Marjan Van Esbroeck (ITG), Steven Van Gucht (Sciensano), Johan Van Laethem (UZ Brussel), Yves Van Laethem (CSS-HGR), Marc Van Ranst (UZ Leuven), Koen Vercauteren (ITG), Jean Cyr Yombi (UCLouvain)	**E-mail** consultation 17/05/2022 **Meetings** 20/05/2022 24/05/2022 31/05/2022 08/06/2022 19/07/2022, 26/07/2022 & 29/07/2022 23/08/2022
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20/05/2022 **24/05/2022** **31/05/2022** **08/06/2022** **29/07/2022** **23/08/2022**				

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Signal	Since 13 May 2022, cases of monkeypox have been reported in different countries worldwide, without travel link to endemic areas. Cases have mainly but not exclusively been identified amongst men who have sex with men (MSM).

UPDATE 23/08/2022

Epidemiological situation

As of August 22, a total of 671 confirmed cases of Monkeypox have been identified in Belgium, of which 360 (54%) persons were living in Flanders, 236 (35%) in Brussels and 75 (11%) in Wallonia. The characteristics of the cases and transmission mode did not change. The main route of transmission remains sexual contact, but person to person transmission (e.g. skin to skin contact) has also been described. Thus, the occurrence of an infection in a woman and a young child is not unexpected. Overall, the number of new infections seems to have reached a plateau. For more information, see the weekly epidemiological bulletin.

In the WHO European Region[1], a total of 19,429 cases of monkeypox have been identified up to August 16, in 43 countries. The number of new cases seems to decrease, but a delay in diagnosis and reporting cannot be excluded. Of the 18960 cases reported in TESSy, a large majority are male (98.9%). About 6% of the cases were hospitalised. Three cases were admitted to ICU, among whom one was admitted to ICU for reasons unrelated to monkeypox infection. The two other cases admitted to ICU were reported to have died of monkeypox. Some (57) cases were reported to be health workers, however no occupational exposure has been reported.

The number of infections in children remains very low. In Europe, 29 out of the 18 960 cases (7 female-22 male) were 0-17 years old (0,15%). And in the United States (based in info in the media), three cases were reported (in a minor, a toddler and an infant), out of 14 050 (0,02%).

Elements of discussion

- Both in Belgium and in Europe, the number of new infections seems to slow down, but the decreasing trend still needs to be confirmed the coming weeks. Cases are still in majority adult men, infected through sexual relationships. As expected, spill over to the general population sporadically occurs, but the risk assessment remains unchanged at this stage.
- In the context of possible infections in children and teachers, a protocol is needed for measures in schools and crèches. A proposal will be prepared (based on previous discussions in the RAG), to be finalised electronically. Based on the limited available information (see Background) on the severity of infections in children, it is currently not possible to define an age cut-off for risk of severe disease. Regarding risk of transmission, prolonged skin to skin contact between children is expected to occur more often in younger children (crèche and kindergarten).
- The past weeks, a huge work was done in the HIV reference centres and by associations to identify, invite and vaccinate eligible persons, according to the criteria decided by the RMG end of July. Up to the 22nd of August, 1,001 persons were vaccinated as PrEV and 282

[1] https://monkeypoxreport.ecdc.europa.eu/

persons in the context of PEV. In addition, 384 persons will be vaccinated the coming days. This means there are about 1,500 doses left. In addition, another 1,500 doses will be received from the Netherlands (to be returned once the larger stock of vaccines in Belgium will be delivered). In total, about 3,000 doses will thus be available the coming weeks, of which a small stock needs to be kept for PEV.

- On the 9th of August, the FDA issued an emergency use authorization for the JYNNEOS vaccine to allow the use of the vaccine by intradermal injection for individuals 18 years of age and older, and increase thus the total number of doses available for use by up to five-fold. The Belgian NITAG has been requested to give an advice on the matter. While waiting for this advice, the RAG experts consider that the epidemiological situation cannot be controlled with the current limited stock of vaccines and that an increase of the number of doses by intradermal injection is therefore an interesting option. All steps should therefore be taken to prepare the possibility of intradermal vaccination, in all vaccination centres.
- Considering that severely immunocompromised patients still need to be vaccinated SC (full dose) and need two doses, that ID administration should follow the regular vaccination schedule (2 doses with 4 weeks interval), and that a stock needs to be kept for PEV, the total number of people that can be vaccinated for PrEV will in practice be about twice as high, i.e. about 6,000 persons. Of note is that ID vaccination is expected to cause more side-effects, which might have a negative impact on the willingness of the persons to be vaccinated, especially for the second dose.
- With a possible stock for 6,000 persons for PrEV, and since the eligible people based on the current criteria have now had several weeks the opportunity to be vaccinated, the indications can be extended to the following target groups:
    - all MSM with at least 1 STI in the last year. The exact size of this group is unknown. However, within the population of MSM on PrEP or HIV+, about 2,000 to 3,000 people are estimated to have had at least 1 STI the past year, and part of them were already included in the current indication (at least 2 STIs). Also, not all eligible persons will accept the vaccination. Since identification of MSM who are non PrEP users and/or HIV- with one STI in the past year might be complex, a first possible approach could be to propose vaccination to MSM consulting with an STI in a clinic or at a GP (transfer to a vaccination centre);
    - female PrEP users, if risk behaviour (e.g. having sexual contact with bisexual men). This target group is very small (a few persons by vaccination centre). With the availability of vaccines at this stage, vaccination of female sex workers is not possible, but overall the risk for infection in women in the current context is much lower (only one women infected in Belgium so far).
- The vaccination centres report that following the indications for PEV, with contact of the regional health authorities for consultation (except for the known regular sexual partner), is very time consuming and difficult in practice. The strict criteria were decided by the RMG, because it was suspected that not all persons presenting as a very-high-risk contact had actually a contact with a confirmed case. If the target group for PrEV is extended, there might be less ‘possible abuse’, because a larger group will have access to vaccination. This will be followed-up the coming weeks (once that the vaccination has actually been extended). For now, the procedure is not changed yet.

- Discussions are ongoing with RIZIV/INAMI for the reimbursement of MPX diagnostics tests. In this context, the recommended number and type of sampling has been discussed. In general, and especially if there is a strong clinical suspicion of MPX (such as multiple typical skin lesions) or an epidemiological link with a case, one sample would allow to have a correct diagnosis. Studies on MPX patients showed that 97 to 99% of skin lesion swabs were positive with PCR. However more and more atypical presentations have been described, and the quality of sampling might be doubtful (e.g. not enough material for swabbing). Therefore, the possibility must be given to reimburse more than one sample. Pooling of samples is technically possible, but not recommended, especially in case of possible low viral load (further dilution possible).
- In line with the 21 days isolation period for asymptomatic persons, the same duration has to be applied for symptomatic people but without skin lesions. It is noted that 21 days (especially in absence of skin lesions) is a very long period for isolation and difficult to adhere to. Based on scientific evidence, there are no elements to allow to reduce the isolation period. However, of most importance is harm reduction and certainly avoidance of close contacts. If wearing a mask and covering possible skin lesions, exceptions to leave the isolation can be accepted (e.g for grocery shopping in case no one else can help).
- The RAG agrees that cancelling organized gatherings or closing places considered at risk, is likely to be counterproductive and that liaising with the organizers or owners to spread preventive messages is more efficient (see background).

Recommendations

1) Risk Assessment

The risk evaluation for human to human transmission remains unchanged: there is a very high risk of transmission in people having multiple sex partners, including some MSM groups, and a very low risk for the broader general population.

2) Sampling

- In general, one sample (with swabbing of multiple lesions) would be sufficient for diagnosis of MPX with a typical clinical presentation. Reimbursement of a second sample should however be foreseen for atypical presentations and in case of suspicion of low viral load. If the outbreak lasts, a possibility of several possible episodes (e.g. at least two) in one year should also be foreseen.
- The most appropriate swab(s) to be taken depends on the clinical presentation: multiple swabbing of lesions (skin or anorectal, or oropharyngeal) if present; anorectal swab if anal symptoms; saliva or throat swab in the prodromal stage or in case of tonsillitis; and a urethral swab in case of urethritis. EDTA whole blood or serum/plasma sample may also be useful in the prodromal stage.
- The guideline document for sampling on the website will be updated, taking into account also updated information on regulations for transport of sample (and waste), see background document.

3) Vaccination

- Modelling studies in Belgium and elsewhere indicate that pre-exposure vaccination of high risk MSM was more effective than post-exposure vaccination, especially if not all risk contacts can be identified. Therefore, the RAG reiterates that the vaccination strategy should focus on PrEV rather than PEV. However, PEV should still be possible, especially to protect

people at risk of severe disease. A stock of at least 500 vaccine doses should be kept for PEV the coming 2 months.

- Using (temporarily) intradermal administration of the available doses (except for PrEV in immunocompromised will allow to extend the indications for vaccinations to 1) all MSM with at least 1 STI in the last year and 2) female PrEP users, with risk behaviour.
- This change in strategy will need some preparation and training of staff (through a webinar or online guidance). While pending the advice from the NITAG, preparation for ID vaccination should already start. All vaccination centres (HIV reference centres and associations) should apply the same strategy for the same populations, to avoid that people “chose” where to be vaccinated.

4) Others

- The duration period of isolation for symptomatic people without skin lesions is 21 days, starting from the day of the first symptoms.
- Cancelling of events or closure of places considered at risk for infection is not recommended.
- Guidance on handling the body of a deceased person in Belgium will be based on WHO recommendations.

Background information

Severity of disease in children

There is still no evidence if the severity of MPX is different in children than in adults in the current outbreak. Only few cases have been reported in children. According the latest WHO global update, age was available of 17,422 cases (out of 26,556 cases that had been reported until August 7, 2022), and of these 97 (0.6%) were aged 0-17, out of which 25 (0.1%) were aged 0-4 (1). However, the majority (65 of the 97 children, and 21 of the 25 children aged 0-4) had been reported from West- and Central Africa. Western countries reporting cases in young children include the US (2 cases, one toddler and one infant) (2), the Netherlands (1 case, <10 years) (3) and Luxemburg (one case) (4). All these children were in good health and did not develop severe disease.

The concern that a MPX infection might be more severe in young children comes from earlier data from the DRC. During the 70-80s all reported deaths were among children in the DRC younger than 10 years. A clinical evaluation of 338 MPX cases in DRC between 1981 and 1986, of which 86% were children <10 years, reported no deaths among the 23 adults and 24 children 10-14 years old, and 33 deaths among the 291 children <10 years (5). The CFR was higher among children 0-4 years old (14.5%) than among children 5-9 years old (7.5%).

However, the context of the current MPX outbreak is very different than that of the DRC in the 70-80s. During that period few cases were reported and the majority (about 85%) were children, living in a different context (general health and nutrition status and access to health) (6). The number of infections was too low to accurately measure the CFR in adults. All deaths were caused by the Congo-Basin clade, known to be more severe than the clade causing the current outbreak, and happened in settings with poor health care. At that time, children were also the only population that had not been vaccinated against smallpox, and all children who died had not been vaccinated.

In the 2003 US outbreak, 24 out of 34 cases were pediatric cases (<=18 years old). Pediatric patients were significantly more likely to be admitted to the intensive care unit, although this was out of precaution and they were not significantly more likely to develop severe illness (7). None died.

In the 2017-2018 Nigerian outbreak, only 12 out of 122 evaluated cases (10%) were children <10 years old. Of the seven cases that died, one was a child <10 years (8). It was a neonate whose mother had died from suspected monkeypox, and who could thus have been infected in-utero.

There is concern that with the start of the school year MPX might spread among young children in schools and daycare centers. Reassuring is that in the US MPX was confirmed in an adult working at a daycare center, and that no other cases were reported from the center (9).

Sampling for diagnosis

In its interim guidance on laboratory testing for the monkeypox virus, WHO stipulates that the recommended specimen type for diagnostic confirmation of MPX in suspected cases is skin lesion material, including swabs of lesion exudate, roofs from more than one lesion, or lesion crusts (10). However, because the current outbreak is still under investigation, collection of additional specimen types can be considered. These may include urine, semen, rectal and/or genital swabs, based on location of lesions, and nasopharyngeal or oropharyngeal swabs in the absence of lesions. EDTA blood may support detection of MPXV but may not contain the high

level of virus found in lesion samples, as any viremia occurs early in the course of infection, usually in the prodromal period, and before skin lesions become manifest.
In a case study in Italy, positive PCR results were obtained from four different samples: oropharyngeal swab, perianal lesion, anal swab and foot lesion (11). In Spain, saliva, rectal swabs, nasopharyngeal swabs, semen, urine and fecal samples were collected from 12 male cases (12). DNA was detected in swabs of skin lesions and in several follow-up samples taken between 4 and 16 days post-symptom onset in all 12 cases (rectal swab (11/12 cases), nasopharyngeal swab (10/12 cases), semen (7/9 cases), urine (9/12) and feces (8/12)). High viral loads (Cq values ≤ 21) were observed in some saliva, rectal swab, semen, urine and fecal samples. Intermittent shedding (negative PCR results that became positive in the following time point collected) was also observed in samples such as urine or saliva.
An analysis of 181 MPX patients in Spain showed that 178/180 (99%) of skin lesion swabs were positive with PCR, 82/117 (70%) of throat swabs and 43/55 (78%) of anal swabs (13). The mean Ct value of positive lesion swabs was significantly lower than from positive pharyngeal swabs (23 *vs* 32) and this was true regardless of where the skin lesions were found. The mean Ct value of anal swabs was 27. When participants with oral lesions or tonsillitis were excluded, 38 (63%) of 60 oropharyngeal specimens were positive, with a mean Ct value of 34. Similarly, when participants with anal lesions or proctitis were excluded, 14 (58%) of 24 anal swabs were positive, with a mean Ct value of 30.
Another study in Spain collected from 37 suspected MPX cases systematically samples from skin lesions and plasma specimens (14). Anal and oropharyngeal swabs were also collected, depending on the reported type of sexual intercourse or the patient's symptoms (sore throat or anal pain). Of the 140 collected samples, 10 were negative for MPXV (four oropharyngeal, three plasma, two anal and one skin lesion sample). One patient had a negative MPXV result in skin lesions but was positive in oropharyngeal, anal and plasma samples with Cq values of 25, 33 and 36, respectively, on day 5 after symptom onset. The highest positivity rate (97%) and viral loads (Cq range: 14–33) were in samples taken from skin lesions of any part of the body. Plasma specimens achieved a positivity rate of 91.9% with the lowest viral load (Cq range: 28–40). The positivity rate of oropharyngeal swabs was 88% in (Cq range: 19–37) and of anal swabs 94% (Cq range: 14–37).

Efficacy of PrEV vs. PEV

Modelling by ECDC of different vaccination strategies, in addition to the isolation of cases and contact tracing, suggests that pre-exposure vaccination would be most efficient at less effective tracing, as it would result in a relatively larger increase in the probability of outbreak control per vaccinated individual (15). Post-exposure vaccination of contacts would offer a marginally more efficient approach, if there are both higher uptake levels and more effective tracing, although the absolute probability of outbreak control per vaccinated individual is lower with post-exposure vaccination than with pre-exposure vaccination. In addition, for pre-exposure vaccination, a higher efficiency can also be achieved by targeting a smaller group of individuals.
Similar results were found by modelling by the Belgian Institute of Tropical Medicine, UAntwerpen and UHasselt (16). Pre-exposure vaccination of high risk MSM was more effective than post-exposure vaccination. Post-exposure vaccination of contacts in last 7 days led to 5-10% additional reduction in number of cases and an unchanged epidemic duration. Pre-exposure vaccination, in addition to 10% contact isolation, led to a similarly proportionate reduction of cases if less than~ 5% were vaccinated. If≥ 5% was vaccinated there was a substantial additional benefit, in particular if 50% of cases are undiagnosed.

Closing of venues/ cancelation of events where MPX transmission is suspected

No agency or country was identified that recommends this. On the contrary, in its interim advice for public health authorities on summer events during the monkeypox outbreak in Europe, 2022, ECDC states that lessons from outbreaks spread through social and sexual networks have shown that cancelling organized gatherings is likely to be counterproductive to disease control efforts (17). Venue closure or event cancellation does not reduce sexual contacts but rather shifts the activities to other settings, including private parties, which are less accessible to community outreach or public health interventions. Liaising with commercial venues and events is more feasible and efficient than mapping private parties (18). Engaging with populations through the organized events represents a powerful opportunity to develop responses that are accepted and promoted by the members of these population groups.

Transport of waste

The statement in the previous RAG that "*In response to a previous recommendation of the RAG, a multilateral agreement was signed in July between the Belgian competent authorities to allow a derogation for transport of substances containing monkeypox virus (except for cultures), where samples can be carried under UN3373 or UN3291, as appropriate, instead of UN2814. This means that transport through a carrier with ADR licence is not requested anymore*." appears not to be entirely correct. It is correct that specimens collected for diagnosis can be transported under UN3373, which does not require transportation through a carrier with ADR licence if they are packaged and the packages being marked according to packing instruction P650. However, waste from patients infected with MPX are carried under UN3291, which still requires transportation through a carrier with ADR licence. In addition, there are still other conditions of the ADR agreement that need to be fulfilled for transports under UN3373 or UN3291 (see for the agreement: About the ADR | UNECE).

Handling deceased bodies

The only available official recommendations on measures for handling the body of a deceased persons is a document from WHO (file:///C:/Users/GiSt2761/Downloads/WHO-MPX-Clinical and IPC-2022.1-eng%20(1).pdf):

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

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.

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