13a Mpox (Monkeypox)

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Key changes

The chapter has been extensively revised and updated.

13a.1 Mpox (Monkeypox)

13a.1.1 Introduction

Human monkeypox was given its name in 1970 (after the virus that causes the disease was discovered in captive monkeys in 1958). On 28 November 2022 the WHO recommended using a new preferred term "mpox" as a synonym for monkeypox.

Mpox is a zoonotic disease caused by an orthopoxvirus that results in a smallpox-like disease in humans. The orthopoxvirus genus also includes variola virus (which causes smallpox), vaccinia virus and cowpox virus.

The first human mpox infection was observed in 1970 in the Democratic Republic of the Congo (DRC) in a 9-month old baby suspected of having smallpox. The first human mpox case outside of Africa was identified in 2003.

In July 2022, the WHO declared a multi country mpox outbreak as a Public Health Emergency of International Concern (PHEIC). This outbreak was caused by the spread of clade IIb virus. The outbreak was overwhelmingly concentrated in gay and bisexual men who have sex with men (gbMSM), mainly in the 18-44 year age group. Among those with known HIV status 48% were HIV positive (information on HIV status is not available for the majority of cases).

On the 14 August 2024 the WHO determined that an upsurge of cases of mpox clade I infection in the DRC and a growing number of neighboring countries in Africa constituted another PHEIC.

13a.1.2 Epidemiology

In Ireland, there have been no cases to date of clade I mpox infection.

Since 2022, there have been 246 confirmed cases of clade II mpox infection reported in Ireland; 227 in 2022, 13 in 2023 and 6 in 2024. Cases were mostly reported in males (99%) with a median age of 35.5 years (range 16-68 years). In those in which data were available, 99.5% self-identified as gbMSM and 25% of cases occurred in people living with HIV.

Multiple factors have likely contributed to the observed decline in mpox cases, including efforts in risk communication and community engagement, increasing immunity in the most affected population groups due to natural immunity and vaccination, and a decrease in the number of large cultural

and social events frequented by the main risk groups for this outbreak.

From 1 January 2023 to 14 April 2024 there were 19,919 cases of suspected clade I mpox and 975 deaths reported (4.9% case fatality rate) in the DRC. Two thirds (67%) of suspected cases and more than three quarters (78%) of suspected deaths have occurred in persons ≤15 years. To date in 2024 there have been more than 17,800 cases of clade I and >600 deaths in the DRC.

Initially cases were mostly clade Ia, but since December 2023 there has also been an outbreak of clade Ib in DRC linked with extensive human to human transmission amplified by sexual contact especially through commercial sex workers, with evidence of community transmission in Burundi which borders DRC to the East.

DRC and Burundi are both reporting ongoing community transmission with increasing numbers of cases. Uganda, Gabon and Kenya have also reported sporadic cases in adult males, however the specific clades are not yet confirmed. To date there have been two clade I cases confirmed in non-African countries; one each in Sweden and Thailand. Both were cases of clade Ib infection in adult males who had travelled from an African county where mpox is circulating.

Transmission
Mpox infection can spread through direct contact with infected wild animals, through close contact with skin or respiratory secretions (including intimate and sexual contact) of a person with mpox, and through contact with contaminated objects or surfaces.

Airborne transmission is thought to occur primarily through large respiratory droplets that generally cannot travel more than one to two metres. Close household or sexual contact poses the greatest risk of person-to-person spread, particularly direct contact with lesions. Transmission can also occur from mother to fetus. The risk of spread within the community is very low.

Clade I outbreaks historically involved multiple introductions from animal hosts within DRC rather than a single introduction that has then spread by human to human transmission. There is evidence of the transmission of clade I mpox with close household contacts, with many family clusters reported. There has also been an outbreak of clade Ib in DRC linked with extensive human to human transmission amplified by sexual contact especially through commercial sex workers. Transmission in healthcare settings has also been reported, but it is assumed that suitable PPE was not worn.

Incubation period
The incubation period is 6-13 days (range 5–21 days).

13a.1.3 Effects

Common symptoms include rash (80% (generalised 50%, genital 45%), fever ≥38.5°C (57%), headache (30%), lymphadenopathy (generalised 20%, local 20%), myalgia (25%), fatigue (20%) and sore throat (13%). The rash appears within 1 to 10 days of development of fever, usually beginning on the face and then spreading to other parts of the body. The lesions are similar to those of chickenpox. Symptoms generally last for 2–4 weeks.

The disease is more severe in young children, pregnant women, older persons and those with severe immunocompromise especially if related to HIV.

Clade I mpox virus has been shown to be more virulent than clade II in animal studies. Case fatality rates (CFR) reported from clade I range from 4.6-17%.

In the current outbreak in DRC the reported case fatality rate (CFR) is 4.9%. CFRs reported for clade II are generally lower ranging between 0.1-3.6%. There is some indication that the mortality associated with clade Ib may be lower than that of Ia, however this is based on early data and should be interpreted with caution. It has been hypothesized that the lower CFR seen with the clade Ib outbreak may be related to the lower proportion of children affected compared with Ia.

The ECDC has assessed the current risk of mpox clade I infection to the general population in the EU/EEA as low. The likelihood of infection for close contacts of imported cases is high, with the risk of severe disease increased in those with underlying conditions, particularly those with immunocompromise.

The likelihood of infection for people with multiple sexual partners who were not previously infected or vaccinated against mpox since 2022 is deemed to be moderate. However, the risk is understandably higher in affected areas in the African continent.

The likelihood of mpox clade I infection for EU/EEA citizens travelling to affected areas if they are in close contact with affected communities is high, while the likelihood of infection is low when contact with affected communities is avoided.

For further information refer to HPSC guidance.
https://www.hpsc.ie/a-z/zoonotic/monkeypox/guidance/

13a.2 Mpox vaccines

Two mpox vaccines are distributed in the EU, both containing Smallpox Modified Vaccinia Ankara –Bavarian Nordic (MVA-BN). Imvanex is authorised by the EMA and Jynneos by the FDA.

Licensed indications

1. Imvanex: active immunisation against smallpox, mpox and disease caused by vaccinia virus in individuals 12 years of age and older.

2. Jynneos: prevention of smallpox and mpox disease in adults 18 years of age and older determined to be at high risk for smallpox or mpox infection.

Jynneos is considered as a suitable vaccine against mpox by the EMA Emergency Task Force together with the CHMP Biologics Working Party and the European Directorate for the Quality of Medicines & HealthCare.

The vaccines contain a non-replicating form of vaccinia virus that does not cause disease in humans as it cannot replicate in human cells.

Vaccine safety

Evidence on the safety of MVA-BN (Imvanex) primary series from clinical trials and post marketing surveillance continues to indicate that the vaccine demonstrates an acceptable safety profile. The most common adverse events reported are injection site pain, redness, swelling and systemic reactions such as fatigue, headache, and myalgia. No cases of severe neurological disease or myocarditis were reported in clinical trials or post marketing surveillance. Generally, the second dose was better tolerated than the first.

In September 2024 the EMA recommended extending the indication of the smallpox and mpox vaccine Imvanex to adolescents from 12 to 17 years of age. This was based on interim results from a Phase 2 randomised, open label, multisite trial (DMID 22 -0020) in which two doses of MVA-BN were administered to adolescents and assessed for safety and immunogenicity. The safety profile of Imvanex in adolescents was comparable to that seen in adults and no additional risk was identified.

Vaccine efficacy and effectiveness

There are several recent studies examining effectiveness of MVA-BN (Imvanex) as a primary series vaccination against mpox.

Observational studies from the USA, UK, Spain, Israel and Canada estimated vaccine effectiveness (VE) against mpox clade II infection of 36-81% for a one dose regimen with most studies reporting VE of 65%-81%. Four of the studies, all from the USA, reported VE against infection for a two dose vaccination regimen of 66-89%.

One of the studies, a small case-control study from Canada reported an effectiveness of 82% (95% CI, 50-98) from the one dose regimen against severe disease (hospitalisation, having a complication or receiving tecovirimat treatment).

A further cohort study from the USA estimated a 0.20 (95% CI, 0.01-0.90) odds ratio of hospitalisation with mpox for patients vaccinated with the two dose regimen versus unvaccinated patients. The same study further analysed results in a subpopulation of patients who were HIV positive. The estimated odds ratio for hospitalisation in this study was 0.28 (95% CI, 0.05-0.91) with the one dose regimen. Follow-up periods (time since vaccination) of effectiveness studies ranged from 14 days to 12 months.

The above effectiveness studies were conducted in regions in which the circulating virus was mpox clade II. There is limited evidence which specifically relates to the efficacy or effectiveness offered by MVA-BA against clade I although cross-protection is expected. The vaccine has been shown to offer protection specifically against mpox clade I in a small number of preclinical studies.

The duration of protection of MVA-BA against mpox is unknown but may be between 2 and 10 years based on the duration of protection of first generation smallpox vaccines. Duration of protection of MVA-BA against severe mpox infection in non-human primates has been demonstrated up to 2.7 years. Immunogenicity studies show that, after an initial early waning of protection at approximately five months from vaccination, IgG titers remain detectable at two years post vaccination (final dose), however it is not known if these levels of antibodies will provide protection against mpox disease as a minimum threshold of immunogenicity for mpox has not yet been established. Longer term MVA-BA mpox effectiveness studies are needed.

There are, as yet, no effectiveness studies specifically focused on the use of MVA-BN vaccine as a booster following receipt of either a one or two dose primary series. Immunogenicity studies show that a booster dose two years post primary series MVA-BN vaccination increases neutralising antibodies (nAb) geometric mean titers (GMT) two weeks post booster exceeding primary vaccination peak responses. Four weeks post booster, nAb GMTs decreased by nearly half and declined further after six months although levels remained elevated and higher than those observed six months following primary series.

Vaccine storage

The vaccine should be stored in a freezer at -20°C +/-5°C or -50°C +/-10°C or -80°C +/-10°C. After thawing, the vaccine should be used immediately or if previously stored at -20°C +/-5°C, the vaccine can be stored for up to eight weeks at +2°C to +8°C prior to use. Once thawed, the vaccine cannot be refrozen.

If the vial is punctured and all the contents are not used, the vial should be stored at +2°C to +8°C and used within eight hours of the first puncture.

Dose, route of administration and schedule

1. Unvaccinated:

The dose is 0.5ml subcutaneously (SC) in the deltoid area. The course is two doses no less than four weeks apart.

The SC route is preferred, as the technique is familiar and adverse reactions are significantly less

If vaccine supplies are limited, mpox vaccine may be administered **intradermally (ID)** in the volar (palmar) side of the forearm **for those aged 18 years and older**. If the volar (palmar) side of the forearm is not an option (e.g., scarring or patient preference), the vaccine may be administered ID into the deltoid area. Two 0.1ml doses no less than four weeks apart are required.

Available data regarding ID administration are based on two doses of vaccine no less than four weeks apart so it is important that the vaccine course is completed.

ID administration should be performed by health professionals appropriately trained in the correct administration of ID vaccines.

A person who has received their first vaccine dose SC may receive the second dose ID. Those whose 18th birthday occurs between their first and second dose may complete the series with the alternative ID dosing.

Those who received their first vaccine dose ID may receive the second dose SC.

Directions for intradermal administration

When possible, low dead volume syringes and/or needles should be used to extract up to five doses (0.1 ml each) from a single vial. If standard syringes and needles are used, there may not be sufficient volume to obtain five doses from a single vial.

- The vaccine should be allowed to reach room temperature before use.
- Hold the vaccine vial upright and swirl gently for at least 30 seconds before each use.
- The suspension should be visually inspected for particulate matter and discoloration before each use. In the event of any damage to the vial, foreign particulate matter and/or variation of physical aspect being observed, discard the vaccine.
- Clean the vaccine vial stopper with a single-use antiseptic swab before each use.
- Using a 1ml syringe and a 25-27G, 10-16mm needle carefully withdraw 0.1 ml of vaccine.
- Do NOT combine residual vaccine from multiple vials.
- Administer the vaccine by ID injection into the volar (palmar) side of the forearm or in the deltoid area.
- Using the finger and thumb of the non dominant hand, stretch the skin at the mid point of the volar (palmar) side of the forearm or in the deltoid area.
- Insert the needle into the dermis with the bevel facing upwards, at an angle of 5-10 degrees, to a distance of 2-3 mm. The bevel should be covered by skin and visible through the epidermis.
- Slowly inject 0.1ml. When given correctly, an ID injection should raise a blanched bleb or wheal. If no resistance is felt when the needle is inserted, the needle may be in SC tissue. In this case, withdraw the needle and repeat the injection at a new site.

- If the vial is punctured and all the contents are not used, the vial should be stored at +2°C to +8°C and used within eight hours of the first puncture.
- A person who still has erythema or induration at the site of the first ID dose may have the second ID dose in the other forearm or in the deltoid area.

It may be helpful to view the CDC video 'How to administer a JYNNEOS vaccine intradermally'

2. Previous smallpox vaccination
The course is one 0.5ml dose SC in the deltoid area or 0.1ml ID in the volar (palmar) side of the forearm or in the deltoid area.

Those who are immunocompromised require two doses no less than four weeks apart **regardless of whether they have had previous smallpox vaccination**.

A person is fully immunised two weeks after the completion of a course.

13a.3 Vaccine recommendations

13a.3.1 Pre exposure prophylaxis for those at high risk of infection

Mpox vaccination should be offered as soon as practicable **to those at high risk of infection** who are unvaccinated or partially vaccinated, e.g., gay, bisexual and men who have sex with men (gbMSM), commercial sex workers and others at high risk of mpox exposure.

13a.3.2 Pre exposure prophylaxis for healthcare workers (including domestic staff etc.)

Mpox vaccination should be considered for designated **healthcare and laboratory staff** (including domestic staff etc.) who will be involved in the management of mpox cases or their samples based on a health and safety risk assessment. While the priority is to ensure appropriate infection prevention and control (IPC) measures are followed, the mpox vaccine may provide additional protection depending on the nature and timing of exposure risk. When wearing suitable PPE and applying correct precautions, the risk of acquiring clade IIb (B.1 lineage) infection is low. There is less certainty about the transmissibility of clade I. Transmission of clade I infection in healthcare settings has been reported but in settings where it is assumed that suitable PPE has not been worn.

13a.3.3 Pre exposure prophylaxis for persons who are planning to travel to areas currently affected by clade 1 mpox outbreaks

Mpox vaccination is recommended for persons who are planning to **travel** to areas currently affected by clade I mpox outbreaks, following discussion with a healthcare provider, if the likelihood of close contact with affected local communities within these areas is high (e.g. aid workers, and those living or working with affected communities). Where feasible, this discussion should occur 4-6 weeks prior to travel to allow time to complete the two-dose schedule.

The decision to offer the vaccine prior to travel should also consider an individuals' risk of severe disease. Children, pregnant women, and those who are immunocompromised are at increased risk for complications and/or death from mpox.

All those at risk of infection as outlined above who are **incompletely vaccinated** with only one dose should receive a second dose as soon as practicable.

NIAC does not currently recommend booster mpox vaccination for pre exposure prophylaxis in those who have completed the two-dose primary course.

Mpox vaccine should be made available to all who are at risk of infection as outlined above as soon as is practicable.

13a.3.4 Postexposure prophylaxis for contacts

Persons with a high/intermediate exposure to mpox who are unvaccinated should be offered one dose of the vaccine within four days of exposure. If there is likelihood of ongoing exposure, those who have not had smallpox vaccination require a second dose given four weeks after the first.

In persons with a high/intermediate exposure to mpox who were vaccinated against mpox more than two years prior to the exposure, a booster dose should be considered within four days of exposure as post exposure prophylaxis.

The vaccine may prevent the onset of symptoms if given within four days of last exposure. If given within 5 to 14 days after the date of last exposure, it may reduce the symptoms but may not prevent the disease. There is no evidence that vaccination beyond 14 days from exposure confers any benefit however vaccination beyond 14 days could be considered in those who are severely immunocompromised in consultation with their treating specialist.

13a.3.5 Children and pregnant women

Currently available mpox vaccines are not licensed in children less than 12 years of age or in pregnant women but they may be considered as pre or post exposure prophylaxis following an individual benefit-risk assessment.

13a.3.6 Prioritisation

In the event of limited vaccine supplies, priority should be given to the groups in the following order:

i. High risk contacts within four days of last exposure.

ii. Intermediate risk contacts within four days of last exposure.

iii. High and intermediate risk contacts within 5 to 14 days of last exposure.

iv. Pre exposure prophylaxis following individual risk assessment.

13a.3.7 Prior to vaccination

Vaccine recipients should be given comprehensive information about the disease, the risks of contracting it, and the benefits and risks of the vaccine. They should be informed that they may develop adverse reactions similar to the prodromal symptoms of mpox infection during the first 48 hours after vaccination.

Contraindications

Anaphylaxis to any of the vaccine constituents (these include benzonase, chicken protein, ciprofloxacin, gentamicin and trometamol). People with a known severe allergy to egg protein who are recommended to receive mpox vaccine should discuss this with an immunologist.

Intradermal administration is not recommended for those with a history of keloid scar formation. They should receive subcutaneous vaccination.

Precautions

Acute severe febrile illness - defer until recovery **unless the risks of deferral outweigh the low risks of vaccination**.

No interval is required between a COVID-19 or influenza vaccine and a mpox vaccine. The vaccines should be given in different arms.

There should be an interval of four weeks between mpox vaccine and a subsequent COVID-19 vaccine because of the unknown risk of myocarditis.

Immunocompromised
The vaccine can be administered SC or ID in those with immunocompromise aged 18 years and older, although the immune response may be lower than in those who are immunocompetent.

Pregnancy
Data on the use of MVA-BN in pregnant women are limited with fewer than 300 reported pregnancy outcomes. Animal studies have not shown direct or indirect harmful effects with respect to reproductive toxicity. As it is a non-replicating vaccine, there is no theoretical reason for concerns in pregnancy, and the expected adverse events profile should be similar to that observed in non-pregnant individuals.

Consideration may be given to using the vaccine in pregnancy for those at increased risk following individual benefit risk assessment.

Breastfeeding
Consideration may be given to using the vaccine for those at increased risk who are breastfeeding, following individual benefit risk assessment.

Children
While the MVA-BN vaccine is not currently licensed in children under 12 years of age, several paediatric studies of other vaccines using MVA as a vector - often at a considerably higher dose than used in MVA-BN- have shown a reassuring side effect profile. The adverse event profile of MVA-BN is expected to be similar to that of the TB and malaria candidate vaccines which use MVA, providing some reassurance of its use in children.

In a recent study from the UK including 87 children who received a single dose of MVA-BN as part of an outbreak response, none developed serious adverse events. Seven of the children provided blood for serology testing post vaccination, all of whom mounted adequate IgG antibody response well above the assay cut off.

Adverse reactions
The most common adverse reactions observed in clinical trials were injection site reactions and common systemic reactions typical for vaccines which were mild to moderate in intensity and resolved without intervention within seven days following vaccination. Adverse reaction rates reported after either vaccination dose were similar.

Subcutaneous (SC) administration

Local: Very common: injection site erythema, induration, pain, pruritus and swelling.
Common: injection site discolouration, haematoma, nodule, warmth.

General: Very common: fatigue, headache, myalgia and nausea.
Common: appetite disorder, arthralgia, fever, pain in extremity, pyrexia, rigors/chills.

Those with atopic dermatitis may have higher rates of local and general adverse reactions following vaccination. In clinical trials of those with atopic dermatitis, 7% experienced exacerbation of their condition after vaccination.

Intradermal (ID) administration

A 2015 clinical study of Jynneos evaluated the safety of a two-dose series of 0.1ml given ID compared to 0.5ml given SC.

The proportion of those with erythema, induration or itching was significantly higher after ID vaccination compared to SC and the reactions lasted longer in the ID group. Over a third had mild injection site skin discoloration lasting six or more months.

Pain at the injection site was less commonly reported and systemic reactions were similar to those after SC administration.

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