20a Smallpox (variola)/Monkeypox

NOTIFIABLE

Key changes

Smallpox vaccine

Recommendations

- Post exposure prophylaxis for contacts

Contents

20a.1 Smallpox
- 20a.1.1 Introduction
- 20a.1.2 Epidemiology
- 20a.1.3 Effects

20a.2 Monkeypox
- 20a.2.1 Introduction
- 20a.2.2 Epidemiology
- 20a.2.3 Effects

20a.3 Smallpox Vaccine

20a.4 Vaccine Recommendations
- 20a.4.1 Pre exposure prophylaxis for healthcare workers (including domestic staff etc.)
- 20a.4.2 Post exposure prophylaxis for contacts
- 20a.4.3 Prioritisation
- 20a.4.4 Prior to vaccination

20a.1 Smallpox

20a.1.1 Introduction

Smallpox is a highly infectious systemic illness caused by the variola virus, a species of Orthopoxvirus. Humans are the only reservoir. There are two strains of the smallpox virus, each with a different clinical course. Variola minor has a case fatality rate of less than 1%; Variola major has a case fatality rate among unvaccinated populations ranging from 15% to 45% or higher. Following a global vaccination campaign led by the WHO, the last naturally occurring case of smallpox was in 1977. It is the only disease to have been eradicated.

20a.1.2 Epidemiology

Smallpox was first described over 3,000 years ago in Egypt. Based on available data, the disease was endemic in a number of European countries from the mid-18th century. In the 20th century alone an estimated 300 million people died of the disease. The last known case of naturally occurring smallpox occurred in Somalia in 1977. In December 1979, the WHO declared that smallpox had been eradicated.

Transmission

Smallpox is spread by respiratory droplets or by direct or indirect contact with the virus shed from skin lesions. Airborne spread is thought to be less frequent, but transmission over significant distances has been documented, including transmission through a hospital stairwell. The virus is stable in dried form for months and has been transmitted by fomites such as bed linen.

Infectivity

Smallpox is infectious from the development of the rash to the disappearance of all scabs - approximately three weeks. Infectivity is highest early in the clinical disease.

20a.1.3 Effects

The incubation period is typically 10 to 14 days (range 7 to 19 days). Prodromal symptoms include sudden onset of high fever, malaise, headache, fatigue and occasional abdominal pain and vomiting. After two to four days the fever subsides and a rash first appears on the face and extremities (centrifugal), including the palms and soles, and subsequently on the trunk. The lesions progress at the same pace through the phases of macules, papules, vesicles, pustules and crusted scabs. The crusted scabs fall off three to four weeks after the appearance of the rash, leaving pitted scars.

The patient remains febrile throughout the evolution of the rash and customarily experiences considerable pain as the pustules grow and expand.

In 5% to 10% of patients, more rapidly progressive, malignant disease develops, which is almost always fatal within 5 to 7 days. In such patients, the lesions are so densely confluent that the skin looks like crinkled rubber; some patients exhibit bleeding into the skin and intestinal tract. Such cases are difficult to diagnose, but they are exceedingly infectious.

Death rates vary depending on the virulence of the circulating strain and the vulnerability of the population it attacks. The case fatality rate is higher in pregnant women and in young children.

During the first 2 to 3 days of rash, the lesions may be confused with varicella (chickenpox). However, all smallpox lesions develop at the same pace and appear identical; they are mainly on the face and extremities (centrifugal) and to a lesser extent on the trunk. Chickenpox lesions develop in crops. With chickenpox, papules, vesicles, pustules and scabs may be seen simultaneously on adjacent areas of skin; they appear mainly on the trunk (centripetal), and almost never on the palms or soles.

20a.2 Monkeypox

20a.2.1 Introduction

Monkeypox is a zoonotic disease caused by an orthopoxvirus that results in a smallpox-like disease in humans. Monkeypox virus belongs to the Orthopoxvirus genus in the family Poxviridae. The Orthopoxvirus genus also includes variola virus (which causes smallpox), vaccinia virus (used in the smallpox vaccine), and cowpox virus. There are two strains of monkeypox, i.e., Central African and West African strain.

Monkeypox was first recognised in 1958 when two outbreaks of a pox-like disease occurred in monkeys kept for research. The first human case was recorded in 1970 in the Democratic Republic of the Congo (DRC), and since then the infection has been reported in a number of central and western African countries. Most cases are reported from the DRC and Nigeria.

Monkeypox cases have occurred outside of Africa, generally related to international travel. In 2003, monkeypox was recorded in the US when an outbreak occurred in humans and pet prairie dogs following importation of rodents from Africa. The human infections followed contact with an infected pet and all patients recovered.

On 7 May 2022, monkeypox was identified in the UK in a person with recent travel to Nigeria. Since then, hundreds of cases have been reported in non-endemic countries without a history of travel to Africa. Subsequently the majority of cases in the UK have been mainly but not exclusively in those who have self-identified as gay, bisexual or other men who have sex with men (gbMSM). It is likely that cases will become more widespread and involve more countries.

These recommendations are made in anticipation that there may be individuals in Ireland who have contracted or been exposed to the virus and health care workers at risk of occupational exposure.

20a.2.2 Epidemiology

Monkeypox is indigenous to the rainforests of Central and West Africa. The number of human monkeypox cases has been increasing since the 1970s, with the most dramatic increases occurring in the DRC. This is possibly due to the cessation of smallpox vaccination with subsequent waning of immunity and other factors including deforestation, disruption of animal habitats, increase in population mobility and possible genetic evolution of the virus.

There are two clades (strains) of monkeypox, i.e., Central African and West African strains. A recent systematic review reported a case fatality rate of 10.6% for the Central African strain and 3.6% for the West African strain in a Nigerian population. The West African lineage is generally associated with milder disease and is responsible for the 2022 outbreak.

Males are more commonly affected and the median age at presentation had increased from 4 (1970s) to 21 years (2010–2019). Commonly reported occupations included traders, students, artisans, healthcare professionals, farmers, hunters and transport workers. Eating inadequately cooked meat and other animal products of infected animals is a possible risk factor.

The natural reservoir of monkeypox has not yet been identified, though rodents are the most likely hosts.

Transmission

Transmission can occur through contact with the virus from an animal human or other source, e.g., preparation or ingestion of bush meat or contact with bedding contaminated with the virus. The virus enters the body through broken skin, respiratory tract, or mucous membranes (eyes, nose, or mouth). It usually takes close physical contact with a symptomatic individual for transmission to occur.

Person-to-person 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.

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

20a.2.3 Effects

Initial symptoms include fever (38.5-40.5°C), malaise, intense headache, lymph node enlargement, back pain, myalgia and intense weakness. 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 seen in monkeypox are similar to those of chickenpox. The whole process can 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.

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

20a.3 Smallpox vaccine

Imvanex is the only smallpox vaccine authorised by the European Medicines Agency. No previous smallpox vaccines are authorised for use.

Licensed indications
Imvanex is authorised by the EMA for active immunisation against smallpox in adults.

This vaccine is authorised in the US (as JYNNEOS) and in Canada (as Imvamune) for the **prevention of smallpox and monkeypox disease in adults aged 18 years and older determined to be at high risk for smallpox or monkeypox infection.**

The vaccine contains a live non-replicating form of vaccinia called Modified Vaccinia Ankara- Bavarian Nordic. It does not cause disease in humans as it cannot replicate in human cells.

Vaccine efficacy and effectiveness
The protective efficacy or effectiveness of the vaccine against smallpox has not been studied.

Efficacy in animals: Non-human primate (NHP) studies have demonstrated that vaccination with the vaccine induced a comparable immune response and protective efficacy to traditional smallpox vaccines, and protected NHP from severe disease associated with a lethal challenge of monkeypox virus. As seen with traditional smallpox vaccines, a significant reduction in both mortality and morbidity compared to non-vaccinated controls was demonstrated.

Immunogenicity
Clinical studies of seroconversion rates (ELISA GMT) included vaccinia-naïve healthy individuals as well as individuals with HIV infection and atopic dermatitis who received two doses of Imvanex four weeks apart. Conversion rates ranged from 96 to 99% two weeks after the second dose. Rates were lower in those with HIV. Limited data on immunogenicity at 24 months showed seropositivity had fallen to 23%.

Because monkeypox virus is closely related to smallpox virus, the vaccine can protect people from monkeypox. Previous smallpox vaccines have been shown to be 85% effective in preventing monkeypox in close contacts. Data from animal models shows high efficacy of the vaccine against monkeypox and high immunogenicity in humans compared to another smallpox vaccine. Vaccination with the vaccine after monkeypox exposure may help prevent the disease or make it less severe.

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.

Dose, route and schedule
1. *Unvaccinated:* The dose is 0.5ml **subcutaneously** in the deltoid region. The course is two doses 28 days apart.
2. *Previous smallpox vaccination:* the course is one 0.5ml dose **subcutaneously** in the deltoid region.

Those who are immunocompromised require two doses 28 days apart **regardless of whether they have had previous smallpox vaccination.**

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

20a.4 Recommendations

20a.4.1 Pre exposure prophylaxis for healthcare workers (including domestic staff etc.)

All healthcare workers (including domestic staff etc.) should follow recommended infection protection control (IPC) measures. Where possible, healthcare workers (including domestic staff etc.) who are immunocompromised or pregnant should not directly care for suspected or confirmed monkeypox cases.

While the priority is to ensure appropriate IPC measures are followed, the vaccine may provide additional protection depending on the nature and timing of exposure risk. Designated healthcare and laboratory staff (including domestic staff etc.) who will be involved in the management of monkeypox cases or their samples should be offered two doses 28 days apart. Those who have had previous smallpox vaccination only require one 0.5ml dose.

20a.4.2 Post exposure prophylaxis for contacts

High and intermediate risk contacts within four days of last exposure to a laboratory confirmed case should be offered one 0.5 ml dose of the vaccine. This may include healthcare workers (including domestic staff, etc.) caring for the case, and other contacts who have not previously been vaccinated.

The vaccine can prevent the onset of symptoms if given within four days of last exposure. If given within five to 14 days after the date of last exposure, it may reduce the symptoms but may not prevent the disease.

If there is a likelihood of ongoing exposure, those who have not had smallpox vaccination require a second dose given at least 28 days after the first.

20a.4.3 Prioritisation

If vaccine supplies permit, pre and post exposure prophylaxis should be offered as above.

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

i. High risk contacts within 4 days of last exposure
ii. Intermediate risk contacts within 4 days of last exposure
iii. High and intermediate risk contacts from 5 and up to 14 days of last exposure
iv. Pre-exposure prophylaxis following individual risk assessment

20a.4.4 Prior to vaccination

Vaccine recipients should be informed that the vaccine is being used off label and given comprehensive information about the disease, the risks of contracting it, and the benefits and risks of the vaccine. They should also be informed that they may develop adverse reactions similar to the prodromal symptoms of monkeypox 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).

Precautions

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

Immunocompromised

The vaccine can be used for vaccination of people aged 18 years and older with certain immune deficiencies or conditions, such as HIV or atopic dermatitis although the immune response may be lower.

Pregnancy

There are limited data on the use of the vaccine in pregnancy. However, animal studies do not indicate harmful effects regarding reproductive toxicity. There is no theoretical reason for concerns in pregnancy and the adverse events profile would be expected to be similar to that in non-pregnant vaccinees.

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

Breastfeeding

The use of the vaccine during breastfeeding is not contraindicated. Consideration may be given to using the vaccine, a non replicating vaccine, for those at increased risk who are breastfeeding following individual benefit risk assessment.

Children

The vaccine is not authorised for use in those under 18 years of age and safety and effectiveness have not been established. Based on clinical trials of vaccines using similar platforms, adverse events would be expected to be similar to those in adults. As monkeypox may cause severe disease in children, the vaccine may be considered for use in children at increased risk following an individual risk assessment.

Adverse reactions

Local	*Very common*: injection site erythema, induration, pain, pruritus and swelling
	Common: injection site discolouration, haematoma, nodule, warmth
	Uncommon: injection site haemorrhage, irritation *Rare*: injection site anaesthesia, dryness, exfoliation, inflammation, movement impairment, paraesthesia, peripheral oedema, rash, vesicles
General	*Very common*: fatigue, headache, myalgia and nausea
	Common: appetite disorder, arthralgia, fever, pain in extremity, pyrexia, rigors/chills
	Uncommon: chest pain, cough, dermatitis, diarrhoea, dizziness, flushing, hepatic enzyme increased, lymphadenopathy, malaise, mean platelet volume decreased, musculoskeletal stiffness, nasopharyngitis, paraesthesia, pharyngolaryngeal pain, pruritus, rash, rhinitis, sleep disorder, troponin increased, underarm swelling, upper respiratory tract infection, vomiting, white blood cell count decreased
	Rare: asthenia, angioedema, axillary pain, back pain, conjunctivitis, contusion, dry mouth, ecchymosis, influenza, influenza like illness, hyperhidrosis, migraine, muscle spasms, muscular weakness, musculoskeletal pain, neck pain, night sweats, oropharyngeal pain, peripheral sensory neuropathy, sinusitis, skin discolouration, somnolence, subcutaneous nodule, tachycardia, vertigo, white blood cell count increased.

Similar rates of side effects are seen after either dose.

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.

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