

3.20 SMALLPOX

Virology

The smallpox or variola virus is one of the poxviruses, a group characterised by large brick-shaped virus particles, which includes the agents vaccinia, monkeypox, mousepox and cowpox. The virus is inhaled into the respiratory tract, multiplies in local lymph nodes and then seeds to the reticuloendothelial system. During the clinical prodrome the virus then circulates to the skin and mucous membranes where the cell destruction produces the characteristic vesicular lesions.¹

Clinical features

An incubation period of about 12 days is abruptly followed by the prodrome, a 2 to 5 day period of high fever, malaise and severe headache. Then follows the pharyngeal enanthem and, a day later, the skin rash begins as small red macules before progressing to papules, vesicles and finally pustules over the next 4 to 7 days.¹ Death follows in about 20% of cases. The diagnosis is made by collecting vesicular fluid for examination by electron microscopy, or for detection of viral nucleic acids by amplification techniques. Diseases that are most likely to mimic smallpox in Australian populations are varicella and drug eruptions.

Epidemiology

Smallpox, a disease only of humans, was declared eradicated in 1979 after an intense international campaign of detection and vaccination. The disease would now be of only historical interest if not for concerns that illicit laboratory stocks of the virus may exist and may be used as biological weapons.² In the days of endemic disease in rural areas, each case of smallpox would generate several more cases among family and friends attending the victim, who was usually bed-bound from the onset of the prodromal illness. The epidemiology of disease spread by bioterrorists may be quite different. Patients hospitalised in the prodromal period may widely transmit the virus during coughing, as demonstrated in an outbreak in a German hospital after admission of one patient with unrecognised smallpox.³

Vaccines

Little is known of the origin of vaccinia virus, the poxvirus used to immunise humans against smallpox. Despite its name, which has been given generally to compounds (vaccines) which induce artificial immunity, it is not cowpox.⁴⁻⁶

Australia has stocks of smallpox vaccine for use in an emergency situation only.⁴⁻⁶

The USA smallpox vaccine Dryvax, has been used to vaccinate Australian laboratory personnel working with poxviruses. This vaccine contains vaccinia which produces cross-immunity against variola. Dryvax is a freeze-dried formulation.

The duration of immunity is uncertain. A recent review, examining the frequency of adverse events after vaccination with different vaccinia strains, reported that the Lister strain vaccine is associated with a higher risk of severe adverse events, in particular postvaccinal encephalopathy.⁷

Transport, storage and handling

Transport according to *Guidelines for smallpox outbreak, preparedness, response and management*.⁴ Smallpox vaccine should be kept frozen at -30°C . The shelf life of the vaccine is 24 hours once thawed and, once thawed, the vaccine should be stored at $+2^{\circ}\text{C}$ to $+8^{\circ}\text{C}$.

Dosage and administration

Only trained healthcare workers should perform smallpox vaccination. One of several techniques can be used to place a tiny volume of the reconstituted vaccine on the skin of the lateral surface of the upper arm. Most commonly, a bifurcated needle is dipped into a multidose container and then positioned vertically over the skin, which is then punctured repeatedly with sufficient vigour to produce no more than a trace of blood at the site.^{4,6,8}

Personal protective equipment must be used while performing smallpox vaccination.

Smallpox vaccines *must not* be injected subcutaneously, intramuscularly or intravenously.

Intradermal inoculation with smallpox vaccine results in the formation of an erythematous papule within 3 to 5 days. It becomes a vesicle, then a pustule reaching a maximum size of 1 to 2 cm in 8 to 12 days, then scabs and separates by 14 to 21 days. When the procedure results in this circumscribed infection, vaccination provides long-term protection against fatal disease. Furthermore, vaccination very soon after exposure to smallpox markedly attenuates or prevents clinical disease.^{4,6}

Recommendations

The only current indication for vaccination in Australia is for workers using live pox virus in recombinant gene research, in order to prevent infection at sites of accidental inoculation. Currently, no vaccine is licensed for use in Australia; however, information about sources of vaccines and their use should be obtained from the Therapeutic Goods Administration, Canberra.⁴

Australian guidelines for smallpox outbreak, preparedness, response and management may be found at <http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pubhlth-publicat-others.htm>.⁴

Contraindications

The vaccine is contraindicated in:^{4,5}

- people with diseases that cause impaired immunity such as human immunodeficiency virus (HIV) infection, acquired immune deficiency syndrome (AIDS), leukaemia, lymphoma, generalised malignancy, agammaglobulinaemia,
- those undergoing therapy with alkylating agents, antimetabolites, radiation or large doses of steroids,
- those who have ever been diagnosed with eczema, even if the condition is mild or not presently active,
- those with a history of neurological disorder,
- women who are either pregnant or trying to become pregnant,
- women who are breastfeeding,
- children aged <1 year,
- anyone living in a household with a member who has any of the conditions listed above,
- people with serious, life-threatening allergies to the antibiotics polymyxin B, streptomycin, tetracycline or neomycin (this may depend on brand of vaccine used),
- those vaccinated in the past 30 days with a live vaccine,
- those with a history of cardiac disease, including:
 - previous myocardial infarction,
 - angina,
 - congestive heart failure,
 - cardiomyopathy,
 - valvular disease, including rheumatic heart disease,
 - stroke or transient ischaemic attack,
 - chest pain or shortness of breath with activity,
 - other heart conditions under the care of a doctor.

Precautions⁴⁻⁶

Individuals with acute or chronic skin conditions, such as atopic dermatitis, impetigo and varicella-zoster (chickenpox and shingles), should not be vaccinated until the condition resolves.

Individuals with eczema should live apart from recently vaccinated family members who may have skin lesions.

Women should be advised to avoid pregnancy for 3 months after smallpox vaccination.

Anyone who receives a smallpox vaccination should not receive another live vaccine for 1 month afterwards.

Adverse events^{4-6,8}

Smallpox vaccines have well described adverse events, which vary in frequency according to the virus present in the seed stock. They include:

- postvaccinal encephalitis (PVE) or encephalomyelitis (PVEM), a demyelinating disease which occurs at a rate of 1 per 300 000 vaccinations; PVE is generally seen in those aged <1 year and PVEM in those aged >2 years;
- progressive vaccinia (vaccinia gangrenosa) at the site of inoculation, in vaccinees with immune impairment;
- eczema vaccinatum, being vaccinia skin disease at sites of previous or current eczema; occurs at a rate of about 1 in 26 000 vaccinations;
- generalised vaccinia, a self-limiting condition resulting from blood-borne dissemination of the virus to other skin sites; more serious in people with impaired immunity; occurs at a rate of 1 in 5000 vaccinations;
- inadvertent inoculation of either the vaccinee or vaccinator in sites such as the face, eyes or hands; occurs at a rate of 1 in 20 000 primary vaccinations;
- various skin rashes, usually self-limiting but can progress to Stevens-Johnson Syndrome;
- fetal vaccinia is rare (<50 reported cases), greatest risk occurs during the third trimester;
- cardiac adverse events including myocarditis, pericarditis and, possibly, dilated cardiomyopathy.

Use in pregnancy

Smallpox vaccine is contraindicated in women who are either pregnant or trying to become pregnant. Women should be advised to avoid pregnancy for 3 months after vaccination.

Vaccinia immune globulin^{4,5}

Vaccinia immune globulin (VIG) is a sterile solution of the immunoglobulin fraction of plasma containing antibodies to the vaccinia virus, from individuals who were previously vaccinated with smallpox vaccine. VIG and the nucleoside analogue active against poxviruses, cidofovir, may be used to treat vaccine complications such as inadvertent inoculation of the eye or eyelid without vaccinal keratitis, severe generalised vaccinia if patient is toxic, eczema

vaccinatum and progressive vaccinia. VIG is not indicated for treatment of vaccinal keratitis or postvaccinal encephalitis.

VIG is contraindicated in those with a history of anaphylactic sensitivity to thiomersal or to other humanised monoclonal antibodies.

There are currently limited stocks of VIG and cidofovir available in Australia. Contact the Australian Government Department of Health and Ageing or your State/Territory Health Department for further information regarding these products (see Appendix 1, *Contact details for Australian, State and Territory Government health authorities and communicable disease control*).

References

Full reference list available on the electronic *Handbook* or website <http://immunise.health.gov.au>.