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PART 4

SMALLPOX VACCINE

KEY INFORMATION (refer to text for details)

What	• Smallpox is a systemic viral illness with a characteristic rash that can have a 15% to 45% or higher mortality rate in an unimmunized population. • Naturally occurring smallpox disease was eradicated by 1977 through a worldwide vaccination program. • Smallpox vaccine provides cross-protection against all orthopox viruses and is used to protect laboratory workers against these viruses. • Remaining variola (smallpox) virus stocks are kept in two World Health Organization (WHO) reference laboratories. There is a lingering concern that variola virus stocks may be held outside of the two official laboratories which could result in an accidental release or use for terrorist purposes.
Who	• Routine immunization of the general Canadian population with smallpox (vaccinia virus) vaccine is not recommended. • Vaccination is recommended for laboratory workers who handle vaccinia or other orthopox viruses (including recombinant vaccinia products) in specialized reference or research facilities. • In the event of a suspect case of smallpox, vaccination of public health and health care personnel involved in the case investigation and clinical management is indicated. • Once a case is confirmed, vaccination of contacts of cases and those living in the immediate vicinity (ring vaccination) is indicated. Vaccination of public health staff and health care workers, as well as first responders, such as police officers, firefighters, ambulance attendants, the military and others may also be indicated. • Because of the relatively long incubation period for smallpox, historical data collected during the smallpox eradication program using the first generation vaccine showed that vaccination within 2 to 3 days of exposure may protect against clinical disease, and if given within 4 to 5 days, may decrease the risk of death.
How	• Should a smallpox case be suspected, immediate telephone communication with local or provincial/territorial public health officials is required; the Public Health Agency of Canada (PHAC) should then be notified. • Smallpox vaccine can be obtained by contacting PHAC's Centre for Emergency Preparedness and Response

Why	• To protect laboratory workers from orthopox virus infections (e.g., smallpox [variola virus]) • To prevent the re-emergence of smallpox, a severe and frequently fatal disease that has been eradicated by vaccination. • A case of smallpox anywhere in the world constitutes a global health emergency. • Under the International Health Regulations, it is the responsibility of PHAC to notify the WHO if a case of smallpox is suspected.

Since the publication of the *2006 Canadian Immunization Guide:*

- Recommendations for smallpox vaccination of laboratory personnel who handle vaccinia or other orthopox viruses have been updated.
- A new recommendation has been made about the reporting of secondary or tertiary cases of vaccinia from smallpox vaccine.
- Frozen, liquid smallpox vaccine has been stockpiled in addition to the licensed lyophilized vaccine.

The *Canadian Smallpox Contingency Plan* provides recommendations for actions to be taken if smallpox occurs in Canada or elsewhere in the world. For additional information, refer to the National Advisory Committee on Immunization (NACI) Statement on smallpox vaccination. (http://www.collectionscanada.gc.ca/webarchives/20071116035239/http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/02vol28/28sup/acs1.html)

EPIDEMIOLOGY

DISEASE DESCRIPTION

Infectious agent

Smallpox is a systemic viral disease caused by the variola virus, a species of the *Orthopoxvirus*.

Reservoir

Humans. There are no animal reservoirs of variola virus and the last human case occurred in 1978. Currently the virus is maintained in two designated laboratories.

Transmission

Smallpox is spread by droplets from the respiratory tract 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. In addition, the virus is stable in dried form for months and has been transmitted by fomites such as bed linen.

The incubation period is from 7 to 19 days, typically 10 to 14 days to the onset of illness and 2 to 4 more days to the onset of the rash. Infectivity can occur at any time from the development of the rash to the disappearance of all scabs – approximately 3 weeks. Infectivity is highest early in the clinical disease.

Risk factors

Canadians born in 1972 or later have not been routinely immunized against smallpox (unless immunized for travel to other countries); therefore, most are fully susceptible. Discontinuation of vaccination for travel was recommended by the WHO in 1980 and was no longer required by any country by 1982. Individuals who have been vaccinated in the past may have partial immunity.

Spectrum of clinical illness

Early symptoms of smallpox are initially similar to influenza: sudden onset of high fever, malaise, headache, fatigue and occasional abdominal pain and vomiting. After 2 to 4 days the fever subsides

and there is a characteristic "centrifugal rash" first appearing on the face and extremities, including the palms and soles, and subsequently on the trunk. The rash progresses through all the phases of macules, papules, vesicles, pustules and then crusted scabs that fall off 3 to 4 weeks after the appearance of the rash. 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. Rates may vary depending up the virulence of the specific variola virus strain that circulates, and the vulnerability of the population it attacks. The case fatality rate is higher in pregnant women and in young children.

DISEASE DISTRIBUTION

Incidence/prevalence

Global

The last known case of naturally occurring smallpox occurred in Somalia in 1977; two cases of smallpox occurred in England in 1978 as a result of a laboratory accident. In December 1979, the WHO officially declared that smallpox had been eradicated globally and in 1980 the World Health Assembly recommended all countries cease routine smallpox immunization programs. Remaining variola virus stocks are kept in two WHO reference laboratories in the United States (US) and Russia for research purposes.

With the breakup of the Soviet Union and the subsequent loss of safety and security controls over their biological weapon stockpiles, there has been a concern that there could be an accidental release of variola virus. Weapon-grade variola virus could also have been sold covertly by former Soviet laboratory personnel to other governments or terrorist groups. In the US, a smallpox vaccination program was initiated in the military in December 2002. Subsequent smallpox vaccination programs were conducted in some health care workers in the US and the United Kingdom.

Due to its current eradication yet potential use as a biological weapon, the occurrence of a single case of smallpox anywhere in the world constitutes a global health emergency.

National

Concerted vaccination campaigns were successful in eliminating endemic smallpox from Canada by 1946. Nova Scotia had a suspected case in 1949; with rigid quarantine the disease did not spread. The final laboratory-confirmed case in Canada in 1962 involved an adolescent who returned to Toronto from Brazil.

PREPARATIONS AVAILABLE FOR USE IN CANADA

PHAC has a stock of two types of smallpox (vaccinia virus) vaccine (Sma):

- lyophilized (freeze-dried) vaccine - Smallpox Vaccine (Dried) (sanofi pasteur Ltd.)
- frozen liquid formulation vaccine - Smallpox Vaccine (Frozen-Liquid) (sanofi pasteur Ltd).

The lyophilized vaccine is an authorized product and is currently used to vaccinate laboratory workers working with orthopox viruses. The frozen liquid vaccine would be released in emergency situations (e.g., in response to a smallpox case) through Health Canada's Special Access Programme. Both vaccines are prepared from live, vaccinia virus. Vaccinia virus is a member of the *Orthopoxvirus* family and confers immunity against variola (smallpox) and other orthopox viruses through cross-reactivity. A third generation vaccine is currently under development.

PHAC provides smallpox vaccine to laboratory staff working with vaccinia virus or other orthopox viruses and would also provide vaccine to provinces/territories in the event of a smallpox case. For non-emergency situations, contact the Centre of Emergency Preparedness and Response, PHAC by telephone: (613) 960-1830 or email: vaccine.info@phac-aspc.gc.ca to obtain additional information.

For emergency situations (suspected or confirmed smallpox case), contact the PHAC Operations Centre by telephone: 1-800-545-7661 or 613-952-7940 or e-mail: hpoc_cops@phac-aspc.gc.ca

VACCINIA IMMUNE GLOBULIN

Vaccinia Immune Globulin Intravenous (Human) (VIG) is a solution of gamma globulin from the serum of individuals recently immunized with smallpox vaccine. It is used to treat severe smallpox vaccine-associated adverse events. The *Canadian Smallpox Contingency Plan* indicates that VIG would be sent to the provinces/territories at the same time as smallpox vaccine and related supplies if smallpox occurs in Canada.

EFFICACY, EFFECTIVENESS, AND IMMUNOGENICITY

In the early 1970s before smallpox was eradicated, a retrospective study conducted in West Pakistan showed a mortality rate of 52% among those who had never been vaccinated, 1.7% among those who had been vaccinated within 10 years, and 11% among those who had been vaccinated 20 or more years earlier.

The specific mechanisms that result in immunity to smallpox following vaccination have not been well characterized. Studies conducted in the 1970s suggest that both antibody and cell-mediated immunity are stimulated by smallpox vaccination. A more recent study showed that more than 95% of primary vaccinees had detectable neutralizing antibody within 1 to 2 weeks after immunization and strong increases in vaccinia-specific CD8+ cytotoxic T lymphocytes and interferon-gamma-producing T cells.

RECOMMENDATIONS FOR USE

Given that naturally occurring smallpox has been eradicated worldwide and smallpox vaccination is associated with the risk of significant morbidity and even mortality, the overall risk benefit analysis supports the recommendation to not routinely immunize the general Canadian population against smallpox. As a result, smallpox vaccination is highly restricted.

WORKERS

Smallpox vaccine may be indicated for certain workers at high risk of exposure, such as laboratory workers who handle vaccinia or other orthopox viruses (including recombinant vaccinia vaccine products) in specialized reference or research facilities.

In the event of a suspect case of smallpox, vaccination of public health and health care personnel involved in the case investigation and clinical management is indicated. Once a case is confirmed, vaccination of public health staff and health care workers, as well as first responders such as police officers, firefighters, ambulance attendants, the military and others may also be indicated.

Laboratory workers may be hesitant to receive smallpox vaccine. Vaccine providers should explain that the lyophilized smallpox vaccine is authorized by Health Canada and that vaccination is important in light of the highly contagious nature of orthopox viruses and the implications of even a single case.

OUTBREAK CONTROL

The *Canadian Smallpox Contingency Plan* includes actions to be taken if a case of smallpox occurs in Canada or elsewhere. A single case of smallpox is considered an outbreak. In general terms, cases should be isolated immediately, preferably at home. If hospitalisation is required, cases should be admitted to rooms under negative pressure equipped with high efficiency particulate air-filtration (HEPA) filters (airborne infection isolation rooms). Contacts and those living in the immediate vicinity of the identified case should be immunized immediately (ring vaccination) and placed under observation in quarantine. Vaccination is indicated for face-to-face contacts (less than 6.5 feet or 2 meters), household contacts, personnel involved in the medical care, public health evaluation or transportation of confirmed or suspected smallpox cases, laboratory personnel involved in the collection or processing of clinical

specimens from confirmed or suspected smallpox cases, and persons who have a high likelihood of exposure to infectious materials (e.g., those responsible for medical waste disposal, linen disposal or disinfection) of smallpox cases.

Vaccine can be given after exposure with beneficial effect as smallpox has a relatively long incubation period. Historical data collected during the smallpox eradication program using first generation vaccine showed that vaccination within 2 to 3 days of exposure may protect against clinical disease, and if given within 4 to 5 days, may decrease the risk of death.

VACCINIA IMMUNE GLOBULIN

PHAC's Centre for Emergency Preparedness and Response has a supply of VIG based on a requirement of 1 dose of VIG for every 10,000 doses of smallpox vaccine. VIG is indicated to treat severe smallpox vaccine-associated adverse events: eczema vaccinatum, progressive vaccinia, severe or recurrent generalized vaccinia, and extensive lesions resulting from accidental implantation (transfer of vaccinia virus from the primary vaccination site to other parts of the body). VIG is ineffective in the treatment of post-vaccinial encephalitis and has no role in the treatment or prevention of smallpox.

VACCINE ADMINISTRATION

DOSE, ROUTE OF ADMINISTRATION, AND SCHEDULE

Smallpox vaccine is administered by scarification into the epidermis, usually in the deltoid area of the non-dominant arm, by using the multiple-puncture technique with a bifurcated needle, packaged with the vaccine and diluent. According to the product labelling, 15 punctures are recommended for vaccination. A trace of blood should appear at the vaccination site after 15 to 20 seconds; if no trace of blood is visible, additional insertions should be made by using the same bifurcated needle without reinserting the needle into the vaccine vial. If alcohol is used to cleanse the skin before immunization, the skin must be allowed to dry thoroughly before the vaccine is administered, to prevent inactivation of the vaccine by alcohol.

Other methods of administration, such as multiple pressure method are possible in case bifurcated needles are not readily available. Refer to the product label for detailed instructions.

When vaccinia virus is inoculated into the epidermis the virus induces an immune reaction that is termed "a take". There is often no visible reaction for the first few days. On day 3 to 4 a papule appears and progresses to a vesicle with surrounding erythema. Typically, one week or so after vaccination, the centre of the vesicle umbilicates and pustulates. After about 2 weeks, the pustule crusts and a dark brown or black scab forms. After 3 weeks, the scab detaches leaving a scar. The vaccination site should be inspected 6 to 8 days after vaccination to ensure that a take has occurred. If there is no evidence of papules or vesicles and erythema, the person should be vaccinated again.

Optimal infection-control practices and appropriate vaccination site care should be used. Gloves should be worn by the vaccine provider when administering smallpox vaccine due to the increased risk of autoinoculation from the use of a bifurcated needle. Each vaccinee and anyone caring for the vaccination site should wash their hands thoroughly after touching the site or handling bandages used to cover the site. Contaminated bandages and scabs should be placed in sealed plastic bags before disposal in the garbage. The vaccinee should avoid rubbing or scratching the site.

A sterile piece of porous bandage (e.g., gauze) should be used to loosely cover the vaccination site until the scab falls off in order to deter the vaccinee from touching the scab, to prevent inadvertent self-inoculation or inoculation of others, and to contain the scab so it is not lost. Preferably, a semi-permeable dressing should be placed over the gauze and not directly on the site; occlusive dressings should not be used. Dressings used to cover the site should be changed frequently to prevent accumulation of exudates and consequent maceration. Frequent dressing changes are particularly important for vaccinees who have close contact with children or people at high risk for vaccinia complications.

Health care workers providing direct patient care should keep their vaccination sites covered with gauze in combination with a semipermeable membrane dressing to absorb exudates and to provide a barrier for containment of vaccinia virus to minimize the risk of transmission; the dressing should also be covered by a layer of clothing. Similar precautions should be used for vaccinated persons in close contact with children or other persons at high risk of serious complications of vaccinia.

BOOSTER DOSES AND RE-IMMUNIZATION

Booster doses should be given every 10 years for laboratory workers with ongoing risk of exposure.

VACCINIA IMMUNE GLOBULIN

VIG should be given intravenously through a dedicated infusion line at a rate of 2 mL/min; VIG is compatible with sodium chloride 0.9%. Parenteral products should be inspected visually for particulate matter and discoloration prior to administration; it should not be used if the solution is turbid. The vial should not be shaken as it may cause foaming.

VIG should be administered at a dose of 6,000 units/kg as soon as symptoms appear and are judged to be due to a severe vaccinia-related complication. Two exceptions to this are vaccinia keratitis and encephalitis. VIG should not be given for vaccinia keratitis due to the potential of increased corneal scarring, and should not be given for encephalitis due to lack of efficacy. For other VIG-treated complications, consideration may be given to repeat dosing, depending on the severity of the symptoms and response to treatment; however, clinical data on repeat doses are lacking. The administration of an additional dose of 9,000 units/kg may be considered in the event that the person does not respond to the initial 6,000 units/kg dose.

SEROLOGICAL TESTING

Serologic testing is not recommended before or after receiving smallpox vaccine.

STORAGE REQUIREMENTS

Lyophilized smallpox vaccine should be stored in a refrigerator at +2°C to +8°C and reconstituted before use. The frozen liquid smallpox vaccine is frozen for long-term storage and thawed for shipping; the thawed vaccine should be maintained between +2°C and +8°C. Open vaccine vials should be used within 24 hours.

Refer to Storage and Handling of Immunizing Agents in Part 1 for additional general information.

SIMULTANEOUS ADMINISTRATION WITH OTHER VACCINES

In non-emergency situations (i.e., non-outbreaks), smallpox vaccine can be administered simultaneously with any inactivated vaccine. To avoid confusion in ascertaining which vaccine might have caused post-vaccination skin lesions or other adverse events, varicella (chickenpox) vaccine or herpes zoster (shingles) vaccine should not be administered concomitantly with smallpox vaccine; there must be an interval of at least 4 weeks between administration of varicella or herpes zoster vaccines and smallpox vaccine. Smallpox vaccine can be administered simultaneously with other live parenteral vaccines; if not administered simultaneously, there must be an interval of at least 4 weeks between smallpox vaccine and other live parenteral vaccines.

VACCINE AND IMMUNE GLOBULIN SAFETY AND ADVERSE EVENTS

Refer to Vaccine Safety Part 2 for additional general information.