CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

June 22, 2001 / Vol. 50 / No. RR-10

MMWR™
MORBIDITY AND MORTALITY
WEEKLY REPORT

Recommendations and Reports

Inside: Continuing Education Examination

Vaccinia (Smallpox) Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention (CDC)
Atlanta, GA 30333

The *MMWR* series of publications is published by the Epidemiology Program Office, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30333.

SUGGESTED CITATION

Centers for Disease Control and Prevention. Vaccinia (smallpox) vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001. MMWR 2001;50(No. RR-10:[inclusive page numbers].

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Vaccinia (Smallpox) Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

Summary

*These revised recommendations regarding vaccinia (smallpox) vaccine update the previous Advisory Committee on Immunization Practices (ACIP) recommendations (*MMWR 1991;40; No. RR-14:1–10*) and include current information regarding the nonemergency use of vaccinia vaccine among laboratory and health-care workers occupationally exposed to vaccinia virus, recombinant vaccinia viruses, and other Orthopoxviruses that can infect humans. In addition, this report contains ACIP's recommendations for the use of vaccinia vaccine if smallpox (variola) virus were used as an agent of biological terrorism or if a smallpox outbreak were to occur for another unforeseen reason.*

INTRODUCTION

Variola virus is the etiological agent of smallpox. During the smallpox era, the only known reservoir for the virus was humans; no known animal or insect reservoirs or vectors existed. The most frequent mode of transmission was person-to-person, spread through direct deposit of infective droplets onto the nasal, oral, or pharyngeal mucosal membranes, or the alveoli of the lungs from close, face-to-face contact with an infectious person. Indirect spread (i.e., not requiring face-to-face contact with an infectious person) through fine-particle aerosols or a fomite containing the virus was less common (*1,2*).

Symptoms of smallpox begin 12–14 days (range: 7–17) after exposure, starting with a 2–3 day prodrome of high fever, malaise, and prostration with severe headache and backache. This preeruptive stage is followed by the appearance of a maculopapular rash (i.e., eruptive stage) that progresses to papules 1–2 days after the rash appears; vesicles appear on the fourth or fifth day; pustules appear by the seventh day; and scab lesions appear on the fourteenth day (Figures 1,2) (*3*). The rash appears first on the oral mucosa, face, and forearms, then spreads to the trunk and legs (*3,4*). Lesions might erupt on the palms and soles as well. Smallpox skin lesions are deeply embedded in the dermis and feel like firm round objects embedded in the skin. As the skin lesions heal, the scabs separate and pitted scarring gradually develops (Figure 2) (*4*). Smallpox patients are most infectious during the first week of the rash when the oral mucosa lesions ulcerate and release substantial amounts of virus into the saliva. A patient is no longer infectious after all scabs have separated (i.e., 3–4 weeks after the onset of the rash).

During the smallpox era, overall mortality rates were approximately 30%. Other less common but more severe forms of smallpox included a) flat-type smallpox with a mortality rate >96% and characterized by severe toxemia and flat, velvety, confluent lesions that did not progress to the pustular stage; and b) hemorrhagic-type smallpox, characterized by severe prodromal symptoms, toxemia, and a hemorrhagic rash that was almost always fatal, with death occurring 5–6 days after rash onset (*4*).

FIGURE 1. Man with smallpox

Source: CDC/Public Health Images Library, identification no. 131. Photographer: Barbara Rice. Available at <http://phil.cdc.gov/Phil/>; accessed on May 16, 2001.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp> (accessed April 20, 2001).

FIGURE 2. Progression of smallpox lesions from, left to right, pustules to scabs to scars

Source: Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and its eradication. Geneva, Switzerland: World Health Organization (WHO), 1988. Reprinted with permission from WHO.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp> (accessed April 20, 2001).

Vaccinia vaccine is a highly effective immunizing agent that enabled the global eradication of smallpox. The last naturally occurring case of smallpox occurred in Somalia in 1977. In May 1980, the World Health Assembly certified that the world was free of naturally occurring smallpox (*5*). By the 1960s, because of vaccination programs and quarantine regulations, the risk for importation of smallpox into the United States had been reduced. As a result, recommendations for routine smallpox vaccination were rescinded in 1971 (*6*). In 1976, the recommendation for routine smallpox vaccination of health-care workers was also discontinued (*7*). In 1982, the only active licensed producer of vaccinia vaccine in the United States discontinued production for general use, and in 1983, distribution to the civilian population was discontinued (*8*). All military personnel continued to be vaccinated, but that practice ceased in 1990. Since January 1982, smallpox vaccination has not been required for international travelers, and International Certificates of Vaccination forms no longer include a space to record smallpox vaccination (*9*).

In 1980, the Advisory Committee on Immunization Practices (ACIP) recommended the use of vaccinia vaccine to protect laboratory workers from possible infection while working with nonvariola Orthopoxviruses (e.g., vaccinia and monkeypox) (*10*). In 1984, those recommendations were included in guidelines for biosafety in microbiological and biomedical laboratories (*11*). The guidelines expanded the recommendations to include persons working in animal-care areas where studies with Orthopoxviruses were being conducted. They further recommended that such workers have documented evidence of satisfactory smallpox vaccination within the preceding 3 years. CDC has provided vaccinia vaccine for these laboratory workers since 1983 (*12*). In 1991, ACIP further expanded smallpox vaccination recommendations to include health-care workers involved in clinical trials using recombinant vaccinia virus vaccines and lengthened the recommendations for revaccination for persons working with vaccinia virus, recombinant vaccinia viruses, or other nonvariola Orthopoxviruses to every 10 years (*13*).

Currently, international concern is heightened regarding the potential use of smallpox (variola) virus as a bioterrorism agent (*14,15*). Because of these concerns, ACIP has developed recommendations for vaccinia (smallpox) vaccine regarding the potential use of smallpox virus as a biological weapon. Additionally, recommendations regarding vaccination of persons working with highly attenuated strains or recombinant vaccines derived from highly attenuated strains of vaccinia virus have been revised.

VACCINIA VACCINE

Dryvax,® the vaccinia (smallpox) vaccine currently licensed in the United States, is a lyophilized, live-virus preparation of infectious vaccinia virus (Wyeth Laboratories, Inc., Marietta, Pennsylvania). Vaccinia vaccine does not contain smallpox (variola) virus. Previously, the vaccine had been prepared from calf lymph with a seed virus derived from the New York City Board of Health (NYCBOH) strain of vaccinia virus and has a minimum concentration of 10^8 pock-forming units (PFU)/ml. Vaccine was administered by using the multiple-puncture technique with a bifurcated needle. A reformulated vaccine, produced by using cell-culture techniques, is now being developed.

Vaccine Efficacy

Neutralizing antibodies induced by vaccinia vaccine are genus-specific and cross-protective for other Orthopoxviruses (e.g., monkeypox, cowpox, and variola viruses) (*16–18*). Although the efficacy of vaccinia vaccine has never been measured precisely during controlled trials, epidemiologic studies demonstrate that an increased level of protection against smallpox persists for ≤5 years after primary vaccination and substantial but waning immunity can persist for ≥10 years (*19,20*). Antibody levels after revaccination can remain high longer, conferring a greater period of immunity than occurs after primary vaccination alone (*3,19*). Administration of vaccinia vaccine within the first days after initial exposure to smallpox virus can reduce symptoms or prevent smallpox disease (*2–4*).

Although the level of antibody that protects against smallpox infection is unknown, after percutaneous administration of a standard dose of vaccinia vaccine, >95% of primary vaccinees (i.e., persons receiving their first dose of vaccine) will experience neutralizing or hemagglutination inhibition antibody at a titer of ≥1:10 (*21*). Neutralizing antibody titers of ≥1:10 persist among 75% of persons for 10 years after receiving second doses and ≤30 years after receiving three doses of vaccine (*22,23*). The level of antibody required for protection against vaccinia virus infection is unknown also. However, when lack of local skin response to revaccination with an appropriately administered and potent vaccine dose is used as an indication of immunity, <10% of persons with neutralizing titers of ≥1:10 exhibit a primary-type response at revaccination, compared with >30% of persons with titers <1:10 (*24*). Lack of major or primary-type reaction can indicate the presence of neutralizing antibody levels sufficient to prevent viral replication, although it can also indicate unsuccessful vaccination because of improper administration or less potent vaccine.

Recombinant Vaccinia Viruses

Vaccinia virus is the prototype of the genus Orthopoxvirus. It is a double-stranded DNA (deoxyribonucleic acid) virus that has a broad host range under experimental conditions but is rarely isolated from animals outside the laboratory (*25,26*). Multiple strains of vaccinia virus exist that have different levels of virulence for humans and animals. For example, the Temple of Heaven and Copenhagen vaccinia strains are highly pathogenic among animals, whereas the NYCBOH strain, from which the Wyeth vaccine strain was derived, had relatively low pathogenicity (*3*).

Vaccinia virus can be genetically engineered to contain and express foreign DNA with or without impairing the ability of the virus to replicate. Such foreign DNA can encode protein antigens that induce protection against one or more infectious agents. Recombinant vaccinia viruses have been engineered to express immunizing antigens of herpesvirus, hepatitis B, rabies, influenza, human immunodeficiency virus (HIV), and other viruses (*27–32*).

Recombinant vaccinia viruses have been created from different strains of vaccinia virus. In the United States, recombinants have been made from a nonattenuated NYCBOH strain, or a mouse neuroadapted derivative, the WR strain. Recombinants have also been made by using the Copenhagen and Lister vaccinia strains, which are more pathogenic among animals than the NYCBOH strain. Additionally, certain highly attenuated, host-restricted, non- or poorly replicating poxvirus strains have been developed for use as substrates in recombinant vaccine development. These strains include the

Orthopoxviruses, modified vaccinia Ankara (MVA) and NYVAC (derived from the Copenhagen vaccinia strain), and the Avipoxviruses, ALVAC and TROVAC (derived from canarypox and fowlpox viruses, respectively) (*33–36*) (Table 1).

TABLE 1. Highly attenuated poxvirus strains used for recombinant vaccine development

Strain	Parent virus strain	Biosafety level
MVA	Vaccinia virus (Ankara)	2
NYVAC	Vaccinia virus (Copenhagen)	1
TROVAC	Fowlpox virus	1
ALVAC	Canarypox virus	1

Animal studies indicate that recombinants are less pathogenic than the parent strain of vaccinia virus (*37*). Laboratory-acquired infections with nonhighly attenuated vaccinia and recombinant viruses derived from nonhighly attenuated vaccinia strains have been reported (*38–41*). However, highly attenuated poxvirus strains (MVA, NYVAC, ALVAC, and TROVAC) are unable to replicate (MVA, ALVAC, and TROVAC) or replicate poorly (NYVAC) in mammalian host cells; therefore, highly attenuated poxvirus strains do not create productive infections (*36*).

These highly attenuated strains have also been reported to be avirulent among normal and immunosuppressed animals (MVA, NYVAC, ALVAC, or TROVAC) and safe among humans (MVA) (*33,35,42,43*). Although no formal surveillance system has been established to monitor laboratory workers, no laboratory-acquired infections resulting from exposure to these highly attenuated strains or recombinant vaccines derived from these strains have been reported in the scientific literature or to CDC. Because of the biological properties and accumulated attenuation data for NYVAC, ALVAC, and TROVAC, the Recombinant DNA Advisory Committee of the National Institutes of Health (NIH) reduced the biosafety level for these viruses to biosafety level 1 (*44*). The Occupational Safety and Health Board of NIH no longer requires vaccinia (smallpox) vaccination for personnel manipulating MVA or NYVAC in a laboratory where no other vaccinia viruses are being manipulated (*45*).

During human trials of recombinant vaccines, physicians, nurses, and other health-care personnel who provide clinical care to recipients of these vaccines could be exposed to both vaccinia and recombinant viruses. This exposure could occur from contact with dressings contaminated with the virus or through exposure to the vaccine. Although the risk for transmission of recombinant vaccinia viruses to exposed health-care workers is unknown, no reports of transmission to health-care personnel from vaccine recipients have been published. If appropriate infection-control precautions are observed (*46,47*), health-care workers are at less risk for infection than laboratory workers because of the smaller volume and lower titer of virus in clinical specimens compared with laboratory material. However, the potential does exist of nonhighly attenuated vaccinia viruses or recombinant viruses derived from these strains being transmitted to health-care personnel. Therefore, those workers who have direct contact with contaminated dressings or other infectious material from volunteers in clinical studies where such strains are used can be offered vaccination. Vaccination is not indicated for health-care personnel who are exposed to clinical materials contaminated with highly attenuated poxvirus strains used to develop vaccine recombinants.

Laboratory and other health-care personnel who work with highly attenuated strains of vaccinia virus (e.g., MVA and NYVAC) do not require routine vaccinia vaccination. Laboratory and other health-care personnel who work with the Avipoxvirus strains ALVAC and TROVAC also do not require routine vaccinia vaccination because these viruses do not grow in mammalian cells and, therefore, do not produce clinical infections among humans. In addition, antibodies induced by vaccinia vaccine are genus-specific (*16*) and would probably not inhibit the expression of genes incorporated into recombinant vaccines derived from ALVAC and TROVAC. Therefore, vaccination would provide no theoretical benefit in preventing seroconversion to the foreign antigen expressed by a recombinant virus if an inadvertent exposure occurred. Laboratory and other health-care personnel who work with viral cultures or other infective materials should always observe appropriate biosafety guidelines and adhere to published infection-control procedures (*46–48*).

Routine Nonemergency Vaccine Use

Vaccinia vaccine is recommended for laboratory workers who directly handle a) cultures or b) animals contaminated or infected with, nonhighly attenuated vaccinia virus, recombinant vaccinia viruses derived from nonhighly attenuated vaccinia strains, or other Orthopoxviruses that infect humans (e.g., monkeypox, cowpox, vaccinia, and variola). Other health-care workers (e.g., physicians and nurses) whose contact with nonhighly attenuated vaccinia viruses is limited to contaminated materials (e.g., dressings) but who adhere to appropriate infection control measures are at lower risk for inadvertent infection than laboratory workers. However, because a theoretical risk for infection exists, vaccination can be offered to this group. Vaccination is not recommended for persons who do not directly handle nonhighly attenuated virus cultures or materials or who do not work with animals contaminated or infected with these viruses.

Vaccination with vaccinia vaccine results in high seroconversion rates and only infrequent adverse events (see Side Effects and Adverse Reactions). Recipients of standard potency vaccinia vaccine (Dryvax) receive controlled percutaneous doses (approximately 2.5×10^5 PFU [*3*]) of relatively low pathogenicity vaccinia virus. The resulting immunity should provide protection to recipients against infections resulting from uncontrolled, inadvertent inoculation by unusual routes (e.g., the eye) with a substantial dose of virus of higher or unknown pathogenicity. In addition, persons with preexisting immunity to vaccinia might be protected against seroconversion to the foreign antigen expressed by a recombinant virus if inadvertently exposed (*41*). However, persons with preexisting immunity to vaccinia might not receive the full benefit of recombinant vaccinia vaccines developed for immunization against other infections (*31,49*).

Routine Nonemergency Revaccination

According to data regarding the persistence of neutralizing antibody after vaccination, persons working with nonhighly attenuated vaccinia viruses, recombinant viruses developed from nonhighly attenuated vaccinia viruses, or other nonvariola Orthopoxviruses should be revaccinated at least every 10 years (*13*). To ensure an increased level of protection against more virulent nonvariola Orthopoxviruses (e.g., monkeypox), empiric revaccination every 3 years can be considered (*17*).

Side Effects and Adverse Reactions

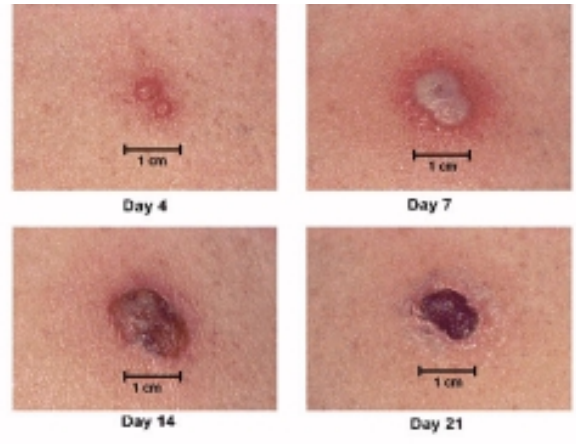
Vaccine Recipients

Side Effects and Less Severe Adverse Reactions. In a nonimmune person who is not immunosuppressed, the expected response to primary vaccination is the development of a papule at the site of vaccination 2–5 days after percutaneous administration of vaccinia vaccine. The papule becomes vesicular, then pustular, and reaches its maximum size in 8–10 days. The pustule dries and forms a scab, which separates within 14–21 days after vaccination, leaving a scar (Figure 3). Primary vaccination can produce swelling and tenderness of regional lymph nodes, beginning 3–10 days after vaccination and persisting for 2–4 weeks after the skin lesion has healed. Maximum viral shedding from the vaccination site occurs 4–14 days after vaccination, but vaccinia can be recovered from the site until the scab separates from the skin (*50*).

A fever is also common after the vaccine is administered. Approximately 70% of children experience ≥1 days of temperatures ≥100 F for 4–14 days after primary vaccination (*21*), and 15%–20% of children experience temperatures ≥102 F. After revaccination, 35% of children experience temperatures ≥100 F, and 5% experience temperatures of ≥102 F (*24*). Fever is less common among adults after vaccination or revaccination (CDC, unpublished data, undated).

Inadvertent inoculation at other sites is the most frequent complication of vaccinia vaccination and accounts for approximately half of all complications of primary vaccination and revaccination (Tables 2,3). Inadvertent inoculation usually results from autoinoculation of vaccinia virus transferred from the site of vaccination. The most common sites involved are the face, eyelid, nose, mouth, genitalia, and rectum (Figure 4). Most lesions heal without specific therapy, but vaccinia immunoglobulin (VIG) can be useful for cases of ocular implantation (see Treatment for Vaccinia Vaccine Complications). However, if vaccinial keratitis is present, VIG is contraindicated because it might increase corneal scarring (*51*).

FIGURE 3. Vaccine site major reaction and progression after primary smallpox vaccination or revaccination after a prolonged period between vaccinations, using multiple-puncture technique



Source: CDC

* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp> (accessed April 20, 2001).

TABLE 2. Vaccine adverse reactions and vaccinia immunoglobulin (VIG) indications

Adverse reactions	VIG treatment
Mild to moderate	
Inadvertent inoculation	Usually not required; might be indicated for ocular implantation*
Erythematous or urticarial rashes	Not indicated†
Bullous erythema multiforme (Stevens-Johnson syndrome)	Not indicated†
Moderate to severe	
Eczema vaccinatum	Indicated in severe cases
Generalized vaccinia	Usually not required but might be indicated if patient is severely ill or has serious underlying illness
Progressive vaccinia (vaccinia necrosum)	Might be effective, depending on immune defect
Postvaccinial encephalitits	Not indicated†
Vaccinial keratitis	Contraindicated*

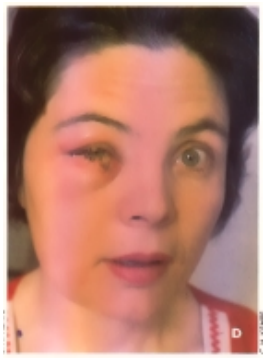
* VIG contraindicated if vaccinial keratitis present because increased scarring can occur.
† VIG is not effective in treatment of these adverse reactions.

TABLE 3. Rates of reported complications* associated with vaccinia vaccinations† (cases/million vaccinations)

Age (yrs) and status	Inadvertent inoculation§	Generalized vaccinia	Eczema vaccinatum	Progressive vaccinia¶	Postvaccinial encephalitis	Total**
Primary vaccination						
<1	507.0	394.4	14.1	—††	42.3	**1549.3**
1–4	577.3	233.4	44.2	3.2	9.5	**1261.8**
5–19	371.2	139.7	34.9	—††	8.7	**855.9**
≥20	606.1	212.1	30.3	—††	—††	**1515.2**
Overall rates††	**529.2**	**241.5**	**38.5**	**1.5**	**12.3**	**1253.8**
Revaccination						
<1	—††	—††	—††	—††	—††	**—††**
1–4	109.1	—††	—††	—††	—††	**200.0**
5–19	47.7	9.9	2.0	—††	—††	**85.5**
>20	25.0	9.1	4.5	6.8	4.5	**113.6**
Overall rates§§	**42.1**	**9.0**	**3.0**	**3.0**	**2.0**	**108.2**

* See text for descriptions of complications.
† Adapted from Lane JM, Ruben FL, Neff JM, Millar JD. Complications of smallpox vaccination, 1968: results of ten statewide surveys. J Infect Dis 1970;122:303–9.
§ Referenced as accidental implantation.
¶ Referenced as vaccinia necrosum.
** Rates of overall complications by age group include complications not provided in this table, including severe local reactions, bacterial superinfection of the vaccination site, and erythema multiforme.
†† No instances of this complication were identified during the 1968 10-state survey.
§§ Overall rates for each complication include persons of unknown age.

FIGURE 4. Inadvertent autoinoculation of lower eyelid with vaccinia virus



Source: Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and its eradication. Geneva, Switzerland: World Health Organization (WHO), 1988. Reprinted with permission from WHO.

* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

Erythematous or urticarial rashes can occur approximately 10 days after primary vaccination and can be confused with generalized vaccinia. However, the vaccinee is usually afebrile with this reaction, and the rash resolves spontaneously within 2–4 days. Rarely, bullous erythema multiforme (i.e., Stevens-Johnson syndrome) occurs (*52*).

Moderate to Severe Adverse Reactions. Moderate and severe complications of vaccinia vaccination include eczema vaccinatum, generalized vaccinia, progressive vaccinia, and postvaccinial encephalitis (Table 2). These complications are rare but occur ≥10 times more often among primary vaccinees than among revaccinees and are more frequent among infants than among older children and adults (*53–55*) (Table 3). A study of Israeli military recruits aged ≥18 years, who were vaccinated during 1991–1996, reported rates of the severe complications progressive vaccinia (i.e., vaccinia necrosum rate: 0/10,000 vaccinees) and postvaccinial encephalitis (rate: 0/10,000 vaccinees) similar to those reported in previous studies (*56*).

Eczema vaccinatum is a localized or systemic dissemination of vaccinia virus among persons who have eczema or a history of eczema or other chronic or exfoliative skin conditions (e.g., atopic dermatitis) (Figure 5). Usually, illness is mild and self-limited but can be severe or fatal. The most serious cases among vaccine recipients occur among

FIGURE 5. Eczema vaccinatum

Source: John M. Leedom, M.D.

* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

primary vaccinees and are independent of the activity of the underlying eczema (*57*). Severe cases have been observed also after contact of recently vaccinated persons with persons who have active eczema or a history of eczema (see Contacts of Vaccinees) (Figure 6).

FIGURE 6. Eczema vaccinatum resulting from contact with recently vaccinated child; patient recovered without sequelae or permanent ocular damage

Photographer: John M. Leedom, M.D.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

Generalized vaccinia is characterized by a vesicular rash of varying extent that can occur among persons without underlying illnesses (Figure 7). The rash is generally self-limited and requires minor or no therapy except among patients whose conditions might be toxic or who have serious underlying immunosuppressive illnesses (e.g., acquired immunodeficiency syndrome [AIDS]) (*58*).

FIGURE 7. Generalized vaccinia in an otherwise healthy child; the child recovered without sequelae

Photographer: John M. Leedom, M.D.
* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

FIGURE 8. Progressive vaccinia (vaccinia necrosum), which was fatal, in a child with an immunodeficiency

Source: Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and its eradication. Geneva, Switzerland: World Health Organization (WHO), 1988. Reprinted with permission from WHO.

* Additional smallpox images are available at <http://www.bt.cdc.gov/Agent/Smallpox/Smallpox.asp.> (accessed April 20, 2001).

Progressive vaccinia (vaccinia necrosum) is a severe, potentially fatal illness characterized by progressive necrosis in the area of vaccination, often with metastatic lesions (Figure 8). It has occurred almost exclusively among persons with cellular immunodeficiency. The most serious complication is postvaccinial encephalitis. In the majority of cases, it affects primary vaccinees aged <1 year or adolescents and adults receiving a primary vaccination (*3*). Occurrence of this complication was influenced by the strain of vaccine virus and was higher in Europe than in the United States. The principle strain of vaccinia virus used in the United States, NYCBOH, was associated with the lowest incidence of postvaccinial encephalitis (*3*). Approximately 15%–25% of affected vaccinees with this complication die, and 25% have permanent neurological sequelae (*52–54*). Fatal complications caused by vaccinia vaccination are rare, with approximately 1 death/million primary vaccinations and 0.25 deaths/million revaccinations (*54*). Death is most often the result of postvaccinial encephalitis or progressive vaccinia.

Contacts of Vaccinees

Transmission of vaccinia virus can occur when a recently vaccinated person has contact with a susceptible person. In a 1968 10-state survey of complications of vaccinia vaccination, the risk for transmission to contacts was 27 infections/million total vaccinations; 44% of those contact cases occurred among children aged ≤5 years (*53*). Before the U.S. military discontinued routine smallpox vaccination in 1990, occurrences of contact transmission of vaccinia virus from recently vaccinated military recruits had been reported, including six cases resulting from transmission from one vaccine recipient (*59–61*).

Approximately 60% of contact transmissions reported in the 1968 10-state survey resulted in inadvertent inoculation of otherwise healthy persons. Approximately 30% of the eczema vaccinatum cases reported in that study were a result of contact transmission (*53*). Eczema vaccinatum might be more severe among contacts than among vaccinated persons, possibly because of simultaneous multiple inoculations at several sites (*54,62*). Contact transmission rarely results in postvaccinial encephalitis or vaccinia necrosum.

Precautions and Contraindications

Routine Nonemergency Laboratory and Health-Care Worker Contraindications

The following contraindications to vaccination apply to routine nonemergency use of vaccinia vaccine (see Smallpox Vaccine for Bioterrorism Preparedness for information regarding precautions and contraindications to vaccination during a smallpox outbreak emergency) (Table 4). Before administering vaccinia vaccine, the physician should complete a thorough patient history to document the absence of vaccination contraindications among both vaccinees and their household contacts. Efforts should be made to identify vaccinees and their household contacts who have eczema, a history of eczema, or immunodeficiencies. Vaccinia vaccine should not be administered for routine nonemergency indications if these conditions are present among either recipients or their household contacts.

TABLE 4. Vaccination contraindications and precautions for nonemergency and emergency use contraindications*

Contraindications for nonemergency vaccine use	Contraindications during smallpox emergency
History or presence of eczema†	Exposure to smallpox virus — no contraindications
Other acute, chronic, or exfoliative skin conditions†§	No virus exposure — same contraindications as nonemergency use
Immunosuppression†¶	—
Pregnancy†	—
Aged <18 yrs	—
Vaccine component allergy	—

* See text for explanation.

† Vaccination also not recommended for persons who live in household with others who have these conditions.

§ Vaccination may be administered after condition resolves.

¶ Conditions include human immunodeficiency virus, acquired immunodeficinecy syndrome, leukemia, lymphoma, generalized malignancy, solid organ transplantation, cellular or humoral immunodeficiencies, or therapy with alkylating agents, antimetabolites, radiation, or high-dose corticosteroids.

History or Presence of Eczema or Other Skin Conditions

Because of the increased risk for eczema vaccinatum, vaccinia vaccine should not be administered to persons with eczema of any degree, those with a past history of eczema, those whose household contacts have active eczema, or whose household contacts have a history of eczema. Persons with other acute, chronic, or exfoliative skin conditions (e.g., atopic dermatitis, burns, impetigo, or varicella zoster) might also be at higher risk for eczema vaccinatum and should not be vaccinated until the condition resolves.

Pregnancy

Live-viral vaccines are contraindicated during pregnancy; therefore, vaccinia vaccine should not be administered to pregnant women for routine nonemergency indications. However, vaccinia vaccine is not known to cause congenital malformations (*63*). Although <50 cases of fetal vaccinia infection have been reported, vaccinia virus has been reported to cause fetal infection on rare occasions, almost always after primary vaccination of the mother (*64*). Cases have been reported as recently as 1978 (*55,65*). When fetal vaccinia does occur, it usually results in stillbirth or death of the infant soon after delivery.

Altered Immunocompetence

Replication of vaccinia virus can be enhanced among persons with immunodeficiency diseases and among those with immunosuppression (e.g., as occurs with leukemia, lymphoma, generalized malignancy, solid organ transplantation, cellular or humoral immunity disorders, or therapy with alkylating agents, antimetabolites, radiation, or high-dose corticosteroid therapy [i.e., ≥2 mg/kg body weight or 20 mg/day of prednisone for ≥2 weeks] [*66*]). Persons with immunosuppression also include hematopoietic stem cell transplant recipients who are <24 months posttransplant, and hematopoietic stem cell transplant recipients who are ≥24 months posttransplant but who have graft-versus-host disease or disease relapse. Persons with such conditions or whose household contacts have such conditions should not be administered vaccinia vaccine.

Persons Infected with HIV

Risk for severe complications after vaccinia vaccination for persons infected with HIV is unknown. One case of severe generalized vaccinia has been reported involving an asymptomatic HIV-infected military recruit after the administration of multiple vaccines that included vaccinia vaccine (*58*). Additionally, a 1991 report indicated that two HIV-infected persons might have died of a progressive vaccinia-like illness after treatment with inactivated autologous lymphocytes infected with a recombinant HIV-vaccinia virus (*67*). No evidence exists that smallpox vaccination accelerates the progression of HIV-related disease. However, the degree of immunosuppression that would place an HIV-infected person at greater risk for adverse events is unknown. Because of this uncertainty, until additional information becomes available, not vaccinating persons (under routine nonemergency conditions) who have HIV infection is advisable.

Infants and Children

Before the eradication of smallpox, vaccinia vaccination was administered routinely during childhood. However, smallpox vaccination is no longer indicated for infants or children for routine nonemergency indications.

Persons with Allergies to Vaccine Components

The currently available vaccinia vaccine (i.e., Dryvax) contains trace amounts of polymyxin B sulfate, streptomycin sulfate, chlortetracycline hydrochloride, and neomycin sulfate. Persons who experience anaphylactic reactions (i.e., hives, swelling of the mouth and throat, difficulty breathing, hypotension, and shock) to any of these antibiotics should not be vaccinated. Vaccinia vaccine does not contain penicillin. Future supplies of vaccinia vaccine will be reformulated and might contain other preservatives or stabilizers. Refer to the manufacturer's package insert for additional information.

Treatment for Vaccinia Vaccine Complications

Using VIG

The only product currently available for treatment of complications of vaccinia vaccination is VIG, which is an isotonic sterile solution of the immunoglobulin fraction of plasma from persons vaccinated with vaccinia vaccine. It is effective for treatment of eczema vaccinatum and certain cases of progressive vaccinia; it might be useful also in the

treatment of ocular vaccinia resulting from inadvertent implantation (*68,69*). However, VIG is contraindicated for the treatment of vaccinial keratitis (*51,54*). VIG is recommended for severe generalized vaccinia if the patient is extremely ill or has a serious underlying disease. VIG provides no benefit in the treatment of postvaccinial encephalitis and has no role in the treatment of smallpox. Current supplies of VIG are limited, and its use should be reserved for treatment of vaccine complications with serious clinical manifestations (e.g., eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, and severe ocular viral implantation) (Table 2).

The recommended dosage of the currently available VIG for treatment of complications is 0.6 ml/kg of body weight. VIG must be administered intramuscularly and should be administered as early as possible after the onset of symptoms. Because therapeutic doses of VIG might be substantial (e.g., 42 ml for a person weighing 70 kg), the product should be administered in divided doses over a 24- to 36-hour period. Doses can be repeated, usually at intervals of 2–3 days, until recovery begins (e.g., no new lesions appear). Future reformulations of VIG might require intravenous administration, and health-care providers should refer to the manufacturer's package insert for correct dosages and route of administration. CDC is currently the only source of VIG for civilians (see Vaccinia Vaccine Availability for contact information).

Other Treatment Options for Vaccinia Vaccine Complications

The Food and Drug Administration has not approved the use of any antiviral compound for the treatment of vaccinia virus infections or other Orthopoxvirus infections, including smallpox. Certain antiviral compounds have been reported to be active against vaccinia virus or other Orthopoxviruses in vitro and among test animals (*70–75*). However, the safety and effectiveness of these compounds for treating vaccinia vaccination complications or other Orthopoxvirus infections among humans is unknown. Questions also remain regarding the effective dose and the timing and length of administration of these antiviral compounds. Insufficient information exists on which to base recommendations for any antiviral compound to treat postvaccination complications or Orthopoxvirus infections, including smallpox. However, additional information could become available, and health-care providers should consult CDC to obtain up-dated information regarding treatment options for smallpox vaccination complications (see Consultation Regarding Complications of Vaccinia Vaccine).

Consultation Regarding Complications of Vaccinia Vaccine

CDC can assist physicians in the diagnosis and management of patients with suspected complications of vaccinia vaccination. VIG is available when indicated. Physicians should telephone CDC at (404) 639-3670 during Mondays–Fridays, except holidays, or (404) 639-3311 during evenings, weekends, and holidays. Health-care workers are requested to report complications of vaccinia vaccination to the Vaccine Adverse Event Reporting System at (800) 822-7967, or to their state or local health department.

PREVENTING CONTACT TRANSMISSION OF VACCINIA VIRUS

Vaccinia virus can be cultured from the site of primary vaccination beginning at the time of development of a papule (i.e., 2–5 days after vaccination) until the scab separates from the skin lesion (i.e., 14–21 days after vaccination). During that time, care must be

taken to prevent spread of the virus to another area of the body or to another person by inadvertent contact. Thorough hand-hygiene with soap and water or disinfecting agents should be performed after direct contact with the site or materials that have come into contact with the site to remove virus from the hands and prevent accidental inoculation to other areas of the body (*76*). In addition, care should be taken to prevent contact of the site or contaminated materials from the site by unvaccinated persons. The vaccination site can be left uncovered, or it can be loosely covered with a porous bandage (e.g., gauze) until the scab has separated on its own to provide additional barrier protection against inadvertent inoculation. An occlusive bandage should not be routinely used because maceration of the site might occur. Bandages used to cover the vaccination site should be changed frequently (i.e., every 1–2 days) to prevent maceration of the vaccination site secondary to fluid buildup. Hypoallergenic tape should be used for persons who experience tape hypersensitivity. The vaccination site should be kept dry, although normal bathing can continue. No salves or ointments should be placed on the vaccination site. Contaminated bandages and, if possible, the vaccination site scab, after it has fallen off, should be placed in sealed plastic bags before disposal in the trash to further decrease the potential for inadvertent transmission of the live virus contained in the materials. Clothing or other cloth materials that have had contact with the site can be decontaminated with routine laundering in hot water with bleach (*2,4*).

Recently vaccinated health-care workers should avoid contact with unvaccinated patients, particularly those with immunodeficiencies, until the scab has separated from the skin at the vaccination site. However, if continued contact with unvaccinated patients is unavoidable, health-care workers can continue to have contact with patients, including those with immunodeficiencies, as long as the vaccination site is well-covered and thorough hand-hygiene is maintained. In this setting, a more occlusive dressing might be required. Semipermeable polyurethane dressings (e.g., Opsite®) are effective barriers to vaccinia and recombinant vaccinia viruses (*31*). However, exudates can accumulate beneath the dressing, and care must be taken to prevent viral contamination when the dressing is removed. In addition, accumulation of fluid beneath the dressing can increase the maceration of the vaccination site. Accumulation of exudates can be decreased by first covering the vaccination site with dry gauze, then applying the dressing over the gauze. The dressing should also be changed at least once a day. To date, experience with this type of containment dressing has been limited to research protocols. The most critical measure in preventing inadvertent implantation and contact transmission from vaccinia vaccination is thorough hand-hygiene after changing the bandage or after any other contact with the vaccination site.

VACCINATION METHOD

The skin over the insertion of the deltoid muscle or the posterior aspect of the arm over the triceps muscle are the preferred sites for smallpox vaccination. Alcohol or other chemical agents are not required for skin preparation for vaccination unless the area is grossly contaminated. If alcohol is used, the skin must be allowed to dry thoroughly to prevent inactivation of the vaccine by the alcohol. The multiple-puncture technique uses a presterilized bifurcated needle that is inserted vertically into the vaccine vial, causing a droplet of vaccine to adhere between the prongs of the needle. The droplet contains the recommended dosage of vaccine, and its presence within the prongs of the bifurcated needle should be confirmed visually. Holding the bifurcated needle perpendicular to the

skin, 15 punctures are rapidly made with strokes vigorous enough to allow a trace of blood to appear after 15–20 seconds (*3*). Any remaining vaccine should be wiped off with dry sterile gauze and the gauze disposed of in a biohazard waste container.

EVIDENCE OF IMMUNITY AND VACCINATION-RESPONSE INTERPRETATION

Appearance of neutralizing antibodies after vaccination with live vaccinia virus indicates an active immune response that includes the development of antibodies to all viral antigens and increased vaccinia-specific cell-mediated immunity. In a person with normal immune function, neutralizing antibodies appear approximately 10 days after primary vaccination and 7 days after revaccination (*3*). Clinically, persons are considered fully protected after a successful response is demonstrated at the site of vaccination.

The vaccination site should be inspected 6–8 days after vaccination and the response interpreted at that time. Two types of responses have been defined by the World Health Organization (WHO) Expert Committee on Smallpox. The responses include a) major reaction, which indicates that virus replication has taken place and vaccination was successful; or b) equivocal reaction, which indicates a possible consequence of immunity adequate to suppress viral multiplication or allergic reactions to an inactive vaccine without production of immunity.

Major Reaction

Major (i.e., primary) reaction is defined as a vesicular or pustular lesion or an area of definite palpable induration or congestion surrounding a central lesion that might be a crust or an ulcer. The usual progression of the vaccination site after primary vaccination is as follows:

- The inoculation site becomes reddened and pruritic 3–4 days after vaccination.
- A vesicle surrounded by a red areola then forms, which becomes umbilicated and then pustular by days 7–11 after vaccination.
- The pustule begins to dry; the redness subsides; and the lesion becomes crusted between the second and third week. By the end of approximately the third week, the scab falls off, leaving a permanent scar that at first is pink in color but eventually becomes flesh-colored (*77*).

Skin reactions after revaccination might be less pronounced with more rapid progression and healing than those after primary vaccinations. Revaccination is considered successful if a pustular lesion is present or an area of definite induration or congestion surrounding a central lesion (i.e., scab or ulcer) is visible upon examination 6–8 days after revaccination (*3*).

Equivocal Reaction

Equivocal reaction, including accelerated, modified, vaccinoid, immediate, early, or immune reactions, are defined as all responses other than major reactions. If an equivocal reaction is observed, vaccination procedures should be checked and the vaccination repeated by using vaccine from another vial or vaccine lot, if available. Difficulty in determining if the reaction was blunted could be caused by immunity, insufficiently po-

tent vaccine, or vaccination technique failure. If the repeat vaccination by using vaccine from another vial or vaccine lot fails to elicit a major reaction, health-care providers should consult CDC or their state or local health department before attempting another vaccination.

MISUSE OF VACCINIA VACCINE

Vaccinia vaccine should not be used therapeutically for any reason. No evidence exists that vaccinia vaccine has any value in treating or preventing recurrent herpes simplex infection, warts, or any disease other than those caused by human Orthopoxviruses (*78*). Misuse of vaccinia vaccine to treat herpes infections has been associated with severe complications, including death (*54,79,80*).

VACCINIA VACCINE AVAILABILITY

CDC is the only source of vaccinia vaccine and VIG for civilians. CDC will provide vaccinia vaccine to protect laboratory and other health-care personnel whose occupations place them at risk for exposure to vaccinia and other closely related Orthopoxviruses, including vaccinia recombinants. Vaccine should be administered under the supervision of a physician selected by the institution. Vaccine will be shipped to the responsible physician. Requests for vaccine and VIG, including the reason for the request, should be referred to

Centers for Disease Control and Prevention
Drug Services, National Center for Infectious Diseases
Mailstop D-09
Atlanta, GA 30333
Telephone: (404) 639-3670
Facsimile: (404) 639-3717

SMALLPOX VACCINE FOR BIOTERRORISM PREPAREDNESS

Although use of biological agents is an increasing threat, use of conventional weapons (e.g., explosives) is still considered more likely in terrorism scenarios (*81*). Moreover, use of smallpox virus as a biological weapon might be less likely than other biological agents because of its restricted availability; however, its use would have substantial public health consequences. Therefore, in support of current public health bioterrorism preparedness efforts, ACIP has developed the following recommendations if this unlikely event occurs.

Surveillance

A suspected case of smallpox is a public health emergency. Smallpox surveillance in the United States includes detecting a suspected case or cases, making a definitive diagnosis with rapid laboratory confirmation at CDC, and preventing further smallpox transmission. A suspected smallpox case should be reported immediately by telephone to state or local health officials and advice obtained regarding isolation and laboratory specimen collection. State or local health officials should notify CDC immediately at (404) 639-2184, (404) 639-0385, or (770) 488-7100 if a suspected case of smallpox is reported.

Because of the problems encountered previously in Europe with health-care–associated smallpox transmission from imported cases present in a hospital setting (*82,83*), health officials should be diligent regarding use of adequate isolation facilities and precautions (see Infection Control Measures). Currently, specific therapies with proven treatment effectiveness for clinical smallpox are unavailable. Medical care of more seriously ill smallpox patients would include supportive measures only. If the patient's condition allows, medical and public health authorities should consider isolation and observation outside a hospital setting to prevent health-care–associated smallpox transmission and overtaxing of medical resources. Clinical consultation and a preliminary laboratory diagnosis can be completed within 8–24 hours. Surveillance activities, including notification procedures and laboratory confirmation of cases, might change if smallpox is confirmed.

Prerelease Vaccination

The risk for smallpox occurring as a result of a deliberate release by terrorists is considered low, and the population at risk for such an exposure cannot be determined. Therefore, preexposure vaccination is not recommended for any group other than laboratory or medical personnel working with nonhighly attenuated Orthopoxviruses (see Routine Nonemergency Vaccine Use).

Recommendations regarding preexposure vaccination should be on the basis of a calculable risk assessment that considers the risk for disease and the benefits and risks regarding vaccination. Because the current risk for exposure is considered low, benefits of vaccination do not outweigh the risk regarding vaccine complications. If the potential for an intentional release of smallpox virus increases later, preexposure vaccination might become indicated for selected groups (e.g., medical and public health personnel or laboratorians) who would have an identified higher risk for exposure because of work-related contact with smallpox patients or infectious materials.

Postrelease Vaccination

If an intentional release of smallpox (variola) virus does occur, vaccinia vaccine will be recommended for certain groups. Groups for whom vaccination would be indicated include

- persons who were exposed to the initial release of the virus;
- persons who had face-to-face, household, or close-proximity contact (<6.5 feet or 2 meters) (*84*) with a confirmed or suspected smallpox patient at any time from the onset of the patient's fever until all scabs have separated;
- personnel involved in the direct medical or public health evaluation, care, or transportation of confirmed or suspected smallpox patients;
- laboratory personnel involved in the collection or processing of clinical specimens from confirmed or suspected smallpox patients; and
- other persons who have an increased likelihood of contact with infectious materials from a smallpox patient (e.g., personnel responsible for medical waste disposal, linen disposal or disinfection, and room disinfection in a facility where smallpox patients are present).

Using recently vaccinated personnel (i.e., <3 years) for patient care activities would be the best practice. However, because recommendations for routine smallpox vaccination in the United States were rescinded in 1971 and smallpox vaccination is currently recommended only for specific groups (see Routine Nonemergency Vaccine Use), having recently vaccinated personnel available in the early stages of a smallpox emergency would be unlikely. Smallpox vaccine can prevent or decrease the severity of clinical disease, even when administered 3–4 days after exposure to the smallpox virus (*2,4,85*). Preferably, healthy persons with no contraindications to vaccination, who can be vaccinated immediately before patient contact or very soon after patient contact (i.e., ≤3 days), should be selected for patient care activities or activities involving potentially infectious materials. Persons who have received a previous vaccination (i.e., childhood vaccination or vaccination >3 years before) against smallpox might demonstrate a more accelerated immune response after revaccination than those receiving a primary vaccination (*3*). If possible, these persons should be revaccinated and assigned to patient care activities in the early stages of a smallpox outbreak until additional personnel can be successfully vaccinated.

Personnel involved with direct smallpox patient care activities should observe strict contact and airborne precautions (*47*) (i.e., gowns, gloves, eye shields, and correctly fitted N-95 masks) for additional protection until postvaccination immunity has been demonstrated (i.e., 6–8 days after vaccination). Shoe covers should be used in addition to standard contact isolation protective clothing to prevent transportation of the virus outside the isolation area. After postvaccination immunity has occurred, contact precautions with shoe covers should still be observed to prevent the spread of infectious agents (see Infection Control Measures). If possible, the number of personnel selected for direct contact with confirmed or suspected smallpox patients or infectious materials should be limited to reduce the number of vaccinations and to prevent unnecessary vaccination complications.

Children who have had a definite risk regarding exposure to smallpox (i.e., face-to-face, household, or close-proximity contact with a smallpox patient) should be vaccinated regardless of age (*20,52*). Pregnant women who have had a definite exposure to smallpox virus (i.e., face-to-face, household, or close-proximity contact with a smallpox patient) and are, therefore, at high risk for contracting the disease, should also be vaccinated (*52*). Smallpox infection among pregnant women has been reported to result in a more severe infection than among nonpregnant women (*3*). Therefore, the risks to the mother and fetus from experiencing clinical smallpox substantially outweigh any potential risks regarding vaccination. In addition, vaccinia virus has not been documented to be teratogenic, and the incidence of fetal vaccinia is low (*52,63,86,87*). When the level of exposure risk is undetermined, the decision to vaccinate should be made after assessment by the clinician and patient of the potential risks versus the benefits of smallpox vaccination.

In a postrelease setting, vaccination might be initiated also for other groups whose unhindered function is deemed essential to the support of response activities (e.g., selected law enforcement, emergency response, or military personnel) and who are not otherwise engaged in patient care activities but who have a reasonable probability of contact with smallpox patients or infectious materials. If vaccination of these groups is initiated by public health authorities, only personnel with no contraindications to vaccination should be vaccinated before initiating activities that could lead to contact with suspected smallpox patients or infectious materials. Steps should be taken (e.g.,

reassignment of duties) to prevent contact of any unvaccinated personnel with infectious smallpox patients or materials.

Because of increased transmission rates that have been described in previous outbreaks of smallpox involving aerosol transmission in hospital settings (*1,82,83*), potential vaccination of nondirect hospital contacts should be evaluated by public health officials. Because hospitalized patients might have other contraindications to vaccination (e.g., immunosuppression), vaccination of these nondirect hospital contacts should occur after prudent evaluation of the hospital setting with determination of the exposure potential through the less-common aerosol transmission route.

Contraindications to Vaccination During a Smallpox Emergency

No absolute contraindications exist regarding vaccination of a person with a high-risk exposure to smallpox. Persons at greatest risk for experiencing serious vaccination complications are also at greatest risk for death from smallpox (*20,52*). If a relative contraindication to vaccination exists, the risk for experiencing serious vaccination complications must be weighed against the risk for experiencing a potentially fatal smallpox infection. When the level of exposure risk is undetermined, the decision to vaccinate should be made after prudent assessment by the clinician and the patient of the potential risks versus the benefits of smallpox vaccination.

Infection Control Measures

Isolation of confirmed or suspected smallpox patients will be necessary to limit the potential exposure of nonvaccinated and, therefore, nonimmune persons. Although droplet spread is the major mode of person-to-person smallpox transmission, airborne transmission through fine-particle aerosol can occur. Therefore, airborne precautions using correct ventilation (e.g., negative air-pressure rooms with high-efficiency particulate air filtration) should be initiated for hospitalized confirmed or suspected smallpox patients, unless the entire facility has been restricted to smallpox patients and recently vaccinated persons (*88,89*). Although personnel who have been vaccinated recently and who have a demonstrated immune response should be fully protected against infection with variola virus (see Evidence of Immunity and Vaccination-Response Interpretation), they should continue to observe standard and contact precautions (i.e., using protective clothing and shoe covers) when in contact with smallpox patients or contaminated materials to prevent inadvertent spread of variola virus to susceptible persons and potential self-contact with other infectious agents. Personnel should remove and correctly dispose of all protective clothing before contact with nonvaccinated persons. Reuseable bedding and clothing can be autoclaved or laundered in hot water with bleach to inactivate the virus (*2,4*). Laundry handlers should be vaccinated before handling contaminated materials.

Nonhospital isolation of confirmed or suspected smallpox patients should be of a sufficient degree to prevent the spread of disease to nonimmune persons during the time the patient is considered potentially infectious (i.e., from the onset of symptoms until all scabs have separated). Private residences or other nonhospital facilities that are used to isolate confirmed or suspected smallpox patients should have nonshared ventilation, heating, and air-conditioning systems. Access to those facilities should be limited to recently vaccinated persons with a demonstrated immune response. If suspected small-

pox patients are placed in the same isolation facility, they should be vaccinated to guard against accidental exposure caused by misclassification as someone with smallpox.

In addition to isolation of infectious smallpox patients, careful surveillance of contacts during their potential incubation period is required. Transmission of smallpox virus rarely occurs before the appearance of the rash that develops 2–4 days after the prodromal fever (*3*). If a vaccinated or unvaccinated contact experiences a fever >101 F (38 C) during the 17-day period after his or her last exposure to a smallpox patient, the contact should be isolated immediately to prevent contact with nonvaccinated or nonimmune persons until smallpox can be ruled out by clinical or laboratory examination.

VIG for Prophylaxis and Treatment of Adverse Reactions During a Smallpox Emergency

If vaccination of persons with contraindications is required because of exposure to smallpox virus after an intentional release as a bioterrorism agent, current stores of VIG are insufficient to allow its prophylactic use with vaccination. Because of the limited stores of VIG, its use in such a scenario should be reserved for severe, life-threatening complications (e.g., progressive vaccinia, eczema vaccinatum, or severe, toxic generalized vaccinia). If additional VIG becomes available in sufficient quantities to allow its prophylactic use, VIG should be administered intramuscularly as a dose of 0.3 mg/kg along with vaccinia vaccine to persons with contraindications who require vaccination.

RESEARCH PRIORITIES

Development and Evaluation of New Vaccinia Vaccine

Current supplies of vaccinia vaccine are limited to remaining stores of vaccine that were produced before the discontinuation of production by Wyeth Laboratories, Inc., in 1981. Although viral titer evaluations have indicated that the vaccine has remained potent, additional quantities of vaccine are needed to augment the current stores and replace expired vaccine. Previous methods of vaccine production that used calf lymph are no longer available; therefore, virus produced for use in a new vaccine must be grown by using a Food and Drug Administration-approved cell-culture substrate. Any new cell-culture vaccine should be evaluated for safety and efficacy by direct comparison with Dryvax by using appropriate animal models, serologic and cell-mediated immunity methods, and cutaneous indicators of successful vaccination (major reaction).

Treatment and Prevention Alternatives for Vaccine Adverse Reactions

Regarding alternatives to VIG for potential treatment and prevention of vaccine adverse reactions, research priorities include a) evaluating antivirals for activity against vaccinia virus by using in vitro assays and test animals that demonstrate vaccinia virus pathogenicity, and b) developing and evaluating monoclonal antibodies against vaccinia virus. Antivirals or monoclonal antibodies that demonstrate activity against vaccinia virus in vitro and efficacy in protecting against dissemination of vaccinia virus among test animals without compromising vaccine effectiveness could provide medical personnel with alternatives to VIG.

Acknowledgements

The members of the Advisory Committee on Immunization Practices, Smallpox Working Group, are grateful for the contributions of Carlton K. Meschievitz, M.D., M.P.H., Aventis Pasteur, Swiftwater, Pennsylvania; Donald A. Henderson, M.D., M.P.H., John Hopkins Center for Civilian Biodefense, Baltimore, Maryland; and John W. Huggins, Ph.D., U.S. Department of Defense, Ft. Detrick, Maryland, during the preparation of these recommendations.

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MMWR™
MORBIDITY AND MORTALITY
WEEKLY REPORT

June 22, 2001 / Vol. 50 / No. RR-10

Recommendations and Reports

Continuing Education Activity Sponsored by CDC

Vaccinia (Smallpox) Vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

EXPIRATION — June 22, 2004

You must complete and return the response form electronically or by mail by **June 22, 2004**, to receive continuing education credit. If you answer all of the questions, you will receive an award letter for 1.25 hours Continuing Medical Education (CME) credit, 0.1 Continuing Education Unit (CEUs), or 1.4 contact hours Continuing Nursing Education (CNE) credit. If you return the form electronically, you will receive educational credit immediately. If you mail the form, you will receive educational credit in approximately 30 days. No fees are charged for participating in this continuing education activity.

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1. Read this *MMWR* (Vol. 50, RR-10), which contains the correct answers to the questions beginning on the next page.
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7. Immediately print your Certificate of Completion for your records.

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GOAL AND OBJECTIVES

This *MMWR*\t provides recommendations regarding vaccinia (smallpox) vaccine. These recommendations were developed by CDC staff and the Smallpox Vaccine Working Group of the Advisory Committee on Immunization Practices (ACIP). The goal of this report is to provide guidance for the use of vaccinia (smallpox) vaccine in the United States. Upon completion of this educational activity, the reader should be able to a) describe the characteristics of the currently licensed vaccinia (smallpox) vaccine; b) identify groups recommended for routine, nonemergency vaccination with vaccinia vaccine; c) list precautions and contraindications for the use of vaccinia vaccine under routine, nonemergency conditions; and d) describe recommended infection control measures for a suspected or confirmed case of smallpox.

To receive continuing education credit, please answer all of the following questions.

1. What is the primary reason that routine vaccinia (smallpox) vaccination is not recommended for the general public?

A. The frequency of adverse events following vaccination is unacceptably high.

B. The cost of vaccination programs prohibits routine vaccination.

C. The supply of vaccine is insufficient to meet demand.

D. Smallpox disease has been eradicated.

E. All the above are reasons that routine vaccinia vaccination is not recommended for the general public.

2. Which of the following groups is recommended to receive vaccinia (smallpox) vaccine under routine, nonemergency conditions?

A. All health-care providers.

B. Military personnel.

C. Laboratory workers who handle cultures containing a nonhighly attenuated strain of vaccinia virus.

D. Emergency medical personnel (e.g., paramedics).

E. All the above groups are recommended to receive vaccinia vaccine under routine, nonemergency conditions.

3. What is the most common adverse reaction or complication after vaccinia (smallpox) vaccination?

A. Generalized vaccinia.

B. Eczema vaccinatum.

C. Progressive vaccinia.

D. Severe allergic reaction.

E. Inadvertent inoculation.

4. Which of the following conditions is a precaution or contraindication for the use of vaccinia (smallpox) vaccine under routine, nonemergency conditions?

A. Immunosuppression.

B. Severe allergy to a component of the vaccine.

C. Household contact with a person with eczema.

D. Pregnancy.

E. All of the above are precautions or contraindications to the use of vaccinia vaccine.

5. Which of the following best describes the currently licensed vaccinia (smallpox) vaccine?

A. Live attenuated smallpox virus.
B. Inactivated smallpox virus.
C. Live vaccinia virus.
D. Inactivated vaccinia virus.
E. Reassortant vaccine containing both vaccinia and smallpox viruses.

6. What is a critical measure in preventing contact transmission of vaccinia virus?

A. Thorough hand washing after contact with the vaccination site.
B. Isolation of the vaccinated person.
C. Use of a porous bandage to cover the vaccination site.
D. Antibacterial ointment applied to the vaccination site.
E. Application of the vaccine at an anatomic site normally covered by clothing.

7. For which of the following conditions is treatment with vaccinia immunoglobulin (VIG) of no benefit?

A. Severe generalized vaccinia.
B. Progressive vaccinia.
C. Postvaccinal encephalitis.
D. Eczema vaccinatum.
E. Ocular vaccinia.

8. What infection control measures are recommended for a person with suspected or confirmed smallpox?

A. Isolation of the person in a negative-air pressure room.
B. Protective clothing for health-care workers in contact with that patient.
C. Vaccination of persons involved in direct medical care of suspected cases.
D. Monitoring contacts of suspected smallpox cases for febrile illness.
E. All the above infection control measures are recommended for a person with suspected or confirmed smallpox.

9. At what point is a vaccinated person considered to be fully protected from smallpox?

A. Ten days after the first dose of vaccine, regardless of the response at the site of administration.
B. Ten days after the second dose of vaccine, regardless of the response at the site of administration.
C. After the appearance of any reaction at the site of administration.
D. After the appearance of a vesicular or pustular lesion at the site of administration.
E. After the appearance of a generalized rash in the vaccinated person.

10. Indicate your work setting.

A. State/local health department.
B. Other public health setting.
C. Hospital clinic/private practice.
D. Managed care organization.
E. Academic institution.
F. Other work setting.

11. Which best describes your professional activities?

A. Patient care — emergency or urgent care.
B. Patient care — inpatient.
C. Patient care — primary-care clinic or office.
D. Laboratory or pharmacy.
E. Public health.
F. Other.

12. I plan to use these recommendations as the basis for . . . (*Indicate all that apply.*)

A. health education materials.
B. insurance reimbursement policies.
C. local practice guidelines.
D. public policy.
E. other uses.

13. Have you administered one or more doses of vaccinia (smallpox) vaccine during the past 12 months?

A. Yes.
B. No.

14. How much time did you spend reading this report and completing the exam and evaluation?

A. <1 hour.
B. 1–1.5 hours.
C. 1.5–2 hours.
D. >2 hours.

15. After reading this report, I am confident I can describe the characteristics of the currently licensed vaccinia (smallpox) vaccine.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

16. After reading this report, I am confident I can identify groups recommended for routine, nonemergency vaccination with vaccinia vaccine.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

17. After reading this report, I am confident I can list precautions and contraindications for the use of vaccinia vaccine under routine, nonemergency conditions.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

18. After reading this report, I am confident I can describe recommended infection control measures for a suspected or confirmed case of smallpox.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

19. The objectives are relevant to the goal of this report.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

20. The tables are useful.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree
E. Strongly disagree.

21. The figures are useful.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree
E. Strongly disagree.

22. Overall, the presentation of the report enhanced my ability to understand the material.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

23. These recommendations will affect my practice.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

24. The availability of continuing education credit influenced my decision to read this report.

A. Strongly agree.
B. Agree.
C. Neither agree nor disagree.
D. Disagree.
E. Strongly disagree.

25. How did you learn about this continuing education activity?

A. Internet.
B. Advertisement (e.g., fact sheet *MMWR* cover, newsletter, or journal).
C. Coworker/supervisor.
D. Conference presentation.
E. *MMWR* subscription.
F. Other.

Correct answers for questions 1–9

1. D; 2. C; 3. E; 4. E; 5. C; 6. A; 7. C; 8. E; 9. D.

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June 22, 2001/Vol. 50/No. RR-10

Vaccinia (Smallpox) Vaccine:
Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001

To receive continuing education credit, you must
1. provide your contact information;
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Fill in the appropriate blocks to indicate your answers. Remember, you must answer <u>all</u> of the questions to receive continuing education credit!

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2. [ ] A [ ] B [ ] C [ ] D [ ] E
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24. [ ] A [ ] B [ ] C [ ] D [ ] E
25. [ ] A [ ] B [ ] C [ ] D [ ] E

Signature ***Date I Completed Exam***

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