

Smallpox Vaccination

Vaccination Method & Reactions

Because routine smallpox vaccination ceased 30 years ago, many clinicians are unacquainted with the vaccinia (smallpox) vaccine.

This pocket guide provides health care personnel with concise information on the vaccine, method of vaccination and the nature of the expected responses to vaccination. Additional in-depth information is available by visiting:

www.bt.cdc.gov/training/smallpoxvaccine/reactions

The guide also includes images and text to help differentiate the more common, self-limiting adverse reactions of vaccination from those that are serious and may require intervention.



About the Vaccine

The vaccinia (smallpox) vaccine is a live virus that multiplies in the superficial layers of the skin. It does not contain variola virus, the virus that causes smallpox. A successful vaccination is often referred to as a "take."

Two vaccine types will be used in the coming years:

1. Calf-lymph vaccine: Dryvax (Wyeth and Aventis)
2. Tissue culture cell vaccine (Acambis/Baxter)

Immunity

Primary vaccination	Fades after 5 years, after 20 years probably negligible
Revaccination	Found to persist 30+ years (1)
Vaccination after exposure to smallpox	Within 2-3 days, can protect against smallpox Within 4-5 days, may protect against a fatal outcome

(1) May protect against a fatal outcome, but not against developing a milder form of smallpox

Contraindications for Vaccinees & Potential Contacts

- Pregnancy
- Immunodeficiencies
- Extensive skin diseases (1)
- Immunosuppressive therapies (2)
- Inflammatory eye diseases (3)
- Eczema; present, past or "healed" (atopic dermatitis)
- Vaccine component allergy (4)

- (1) E.g., acne, burns, wounds, recent incisions, impetigo, contact dermatitis
- (2) E.g., cancer Rx, organ transplants, other conditions with Rx
- (3) Implantation by rubbing of eye; no immune defect present
- (4) Dryvax contains: polymyxin B sulfate, streptomycin sulfate, chlortetracycline hydrochloride and neomycin sulfate

Smallpox Outbreak

In the event of a smallpox outbreak, those who normally would have a contraindication for vaccination, but who are at risk of exposure to smallpox, would be offered the vaccination.

Recommended vaccination method:

Multiple puncture vaccination on the deltoid area of the upper arm, using an individually wrapped, sterile, bifurcated needle.



Bifurcated Needle

Step-by-Step Instructions

1. NO alcohol: vaccination will be inhibited. No skin preparation is required prior to vaccination.
2. Dip needle into vaccine vial; a minute drop of vaccine is retained.
3. Make 15 perpendicular insertions within a 5-mm diameter area. NOTE: Strokes should be vigorous enough to evoke a trace of blood after 15-30 seconds.
4. Absorb excess vaccine with sterile gauze and discard gauze in a biohazard waste receptacle.
5. Cover site with sterile gauze (loosely taped).
6. Prevent contact transmission.

Unlike other immunizations, smallpox vaccination is characterized by a virus that propagates in the skin and can potentially contaminate the vaccinee's hands or the skin and mucosa of others with whom the vaccinee comes into contact.

Caution vaccinee and/or guardian (until a scab has formed) to:

- Keep the vaccination site covered
- Do not touch, scratch or rub the site, even though it is itchy
- Avoid person-to-person contact with susceptible individuals (see contraindications)
- Avoid touching, rubbing or any other maneuvers that might transfer vaccinia virus to the eye or surrounding skin
- Discard used gauze safely in a sealed plastic bag
- After handling used gauze, thoroughly wash hands

Health care worker caution: Treat contaminated materials as infectious waste (e.g., towels, gowns, instruments, etc.). These materials should be placed in an appropriate biohazard container.



Dip Needle

Retained Vaccine



Proper Position

15 Insertions



Post-insertion

Absorb Excess



Discard Properly

Sterile Cover

Normal Reaction Timeline

Day	Description
0	Vaccination
3-4	Papule
5-6	Vesicle with surrounding erythema -> vesicle with depressed center
8-9	Well-formed pustule
12+	Pustule crusts over -> scab
17-21	Scab detaches revealing scar

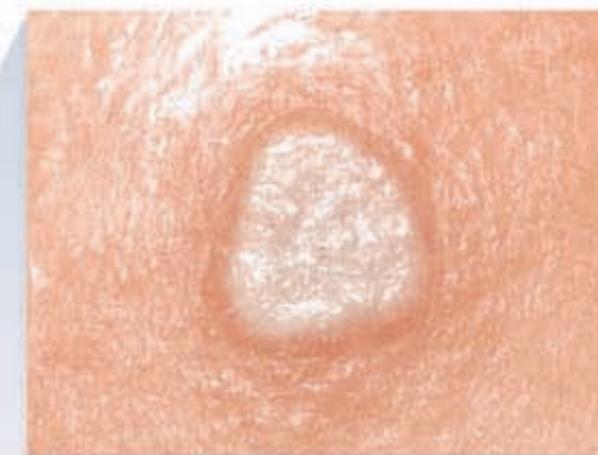
No Reaction

A non-reaction means no immunity and vaccination must be repeated.

Systemic Symptoms

Approximately one week after vaccination:

- Fever
- Malaise
- Myalgia
- Soreness at the vaccination site
- Local lymphadenopathy
- Intense erythema ringing the vaccination



Day 8

Most vaccinees experience only a mild fever and local discomfort with localized redness and swelling.



Day 6

Day 8

Day 10

Day 14



Day 6

Day 8

Day 10

Day 14



Satellite Lesions

Lymphangitis

Edema

Normal Variants

Normal variants (rate: 2.4% - 6.6%) are NOT adverse events and require no specific treatment.

They include:

- Satellite lesions
- Lymphangitis from the site to regional nodes
- Regional lymphadenopathy
- Considerable local edema at the site
- Intense erythema (viral cellulitis)

Revaccination

Potential revaccination responses:

Response	Description
Typical primary reaction	Clear-cut pustule 6-8 days after vaccination
Major reaction	Area of definite induration or congestion surrounding a central lesion that may be a scab or ulcer 6-8 days after vaccination. The evolution of the lesion is more rapid than following a primary reaction.
Equivocal reaction	Any other reaction or response; e.g., an "allergic" reaction (revaccination is indicated) or no reaction (revaccination is indicated)

If a patient has never had a successful take, the patient should be informed that he/she is almost certainly NOT immune.

Vaccinia Immune Globulin (VIG) was produced in the 1960's from plasma obtained from recently vaccinated donors and was administered intramuscularly.

Vials of intramuscular VIG (IM-VIG) are stored at the CDC and are available only under IND protocols. An effort is underway to produce new lots that will meet the standards for intravenous VIG (IV-VIG).

VIG Administration

Indicated

- Accidental implantation (extensive lesions)
- Eczema vaccinatum
- Generalized vaccinia (if severe or recurrent)
- Progressive vaccinia

Not Recommended

- Accidental implantation (mild instances)
- Generalized vaccinia (mild or limited - most instances)
- Erythema multiforme
- Post-vaccinial encephalitis

Contraindicated

- Vaccinia keratitis (may produce severe corneal opacities)

Dosage

The usual dose of IM-VIG is 0.6 ml/kg body weight. As much as 1-10 ml/kg body weight has been used in serious, life-threatening complications.

The exact dose of IV-VIG has not been determined but most likely will be administered at a lower dose than the intramuscular preparation.

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ADVERSE REACTIONS

Adverse Reactions: **Accidental Implantation**

Adverse Reactions: **Bacterial Infections**

Adverse Reactions: **Eczema Vaccinatum**

Adverse Reactions: **Erythema Multiforme**

Adverse Reactions: **Generalized Vaccinia**

Adverse Reactions: **Progressive Vaccinia**

Adverse Reactions: **Vaccinia Keratitis**

Smallpox (vaccinia) vaccination is a generally safe, effective preventative against smallpox. Some individuals may experience an adverse event; many are harmless, a few are mild to moderate and require specific treatment, and rarely, more serious adverse events occur in susceptible individuals.

Reporting Adverse Events
To report adverse events or request consultation about an adverse event, please call your state or local public health authorities.

Accidental Administration
Occasionally, an individual may ingest vaccine accidentally or may be injected inadvertently by the intramuscular or subcutaneous route. These are not recommended routes of administration. It is prudent to follow the individual clinically and to examine the administration site for a vaccination lesion. **Severity:** Benign **Frequency:** Rare

Post-Vaccinial Encephalitis
Post-vaccinial encephalitis is a rare complication of primary vaccination (15/million). Encephalitis occurs 10-14 days after vaccination with headache, vomiting, drowsiness and fever as the first symptoms. In severe cases life-threatening complications can develop. **Severity:** Severe - hospitalize **Frequency:** Rare

Accidental Implantation
Accidental implantation by autoinoculation or contact is one of the most common adverse events. Although no age group is spared, infants and children are most susceptible to more extensive inoculations because of their tendency to scratch an itching vaccination site.

This surface virus is easily transferred to the hands and to fomites. Either may be the source of inoculation elsewhere, but most implantations occur as a result of transfer from hand to skin or to mucosa.

Lesions follow the same course as the primary vaccination, except in patients with cell-mediated immune dysfunction where each lesion progresses without an inflammatory response, does not heal, and expands.

If there are only one or a few lesions, no specific treatment is required. Multiple lesions, especially if they are confluent and cover large portions of the body warrant treatment with Vaccinia Immune Globulin (VIG).

Severity: Mild to severe - hospitalize severe
Frequency: Common
VIG: Indicated with extensive lesions
Not recommended for mild instances

Bacterial Infections
Bacterial infections of the vaccination site are not common. Children are at greater risk as they may manipulate the site more often and contaminate the vaccination. Occlusive dressings may lead to maceration and increased risk of infection.

The most common organisms are Staphylococcus aureus and Group A Beta Hemolytic Streptococci. Anaerobic organisms occasionally infect the site. Impetiginous vesiculo-pustular lesions are seen in staph infection and piled-up eschar formation is common in streptococcal infections, although lesions identical to the staph infections also occur. Mixed infections may be encountered.

Bacterial cultures should be obtained from the site by swabbing or aspiration.

Treatment is with antibiotics specific to the agent. Initial treatment should anticipate staphylococcal and streptococcal etiology.

Severity: Mild
Frequency: Unknown
VIG: Not recommended

Eczema Vaccinatum
Individuals with eczema (i.e., atopic dermatitis), active or healed, are at special risk from implantation of vaccinia virus into the diseased skin, sometimes with a fatal outcome.

Transfer of vaccinia virus can occur from autoinoculation or from contact with a vaccinee whose lesion is in the florid stages. Because most individuals have large contiguous patches of skin in the affected areas, confluent lesions are the rule (on the face and limbs primarily).

Diagnosis may be more difficult in contact cases, because history of contact with a vaccinee may be unknown or unappreciated as to risk.

With early recognition and prompt treatment with Vaccinia Immune Globulin (VIG), mortality can be reduced to zero, and morbidity alleviated. Scarring may be extensive.

Severity: Severe, especially if untreated
Frequency: Somewhat common
VIG: Indicated

Erythema Multiforme
Toxic and/or hypersensitivity rashes are common 1-2 weeks after vaccination. The rash varies from erythematous macular lesions, to vesicles, urticaria, pustules and typical bulls-eye lesions, all under the rubric "erythema multiforme". These are benign lesions that do not progress. Itching may accompany the rash. The most serious reaction, Stevens-Johnson Syndrome (SJS) is rare.

Diagnosis is by typical rash seen in temporal association with primary vaccination. In the vesicular and pustular forms it is necessary to distinguish these from generalized vaccinia or inoculation vaccinia. The vesicles and pustules in erythema multiforme do not progress into typical vaccinations and usually can be distinguished on this basis.

Treatment is symptomatic, usually employing an anti-histamine and measures to counteract itching, if present. Mucosal involvement and evolution into SJS requires hospitalization and supportive care.

Severity: Benign
(exception: Stevens-Johnson Syndrome (SJS) - severe)
Frequency: Most common (exception: SJS- rare)
VIG: Not recommended

Generalized Vaccinia
Generalized vaccinia is rare, usually benign, and the result of viremia. Within a week, lesions appear on any part of the body (most often on the trunk and abdomen, less commonly on the face, limbs, palms and soles). Lesions undergo rapid evolution to scarring. Rarely, lesions may recur at 4-6 week intervals for as long as one year.

Subtle minor immunologic abnormalities, particularly of the immunoglobulin B-cell system, are suspected to be present. Differentiate from erythema multiforme, eczema vaccinatum, progressive vaccinia, severe chickenpox and smallpox. Consultation with an immunologist is strongly recommended.

Most instances of generalized vaccinia, particularly if the lesions are few, require no specific therapy. In some cases, with extensive lesions, or in recurrent disease, Vaccinia Immune Globulin (VIG) should be administered.

Severity: Benign, avoid hospitalization
(exception: recurrent generalized vaccinia - hospitalize)
Frequency: Rare
(exception: recurrent generalized vaccinia - very rare)
VIG: Indicated if severe or recurrent
Not recommended if mild or limited (most instances)

Progressive Vaccinia
Progressive vaccinia is a rare complication occurring primarily in T-cell deficient persons. Congenital T-cell deficient children, those with T-cell deficient diseases (cancer, immunosuppressive therapy, HIV/AIDS) are at risk.

The primary vaccination fails to heal and spreads locally and by viremia to other parts of the body; each lesion spreads without inflammatory response. Untreated patients succumb to viral effect or to secondary fungal, parasitic or bacterial infections.

Complications include septic shock, disseminated intravascular coagulation, and superimposed microbial infections. If viable lymphocytes are administered, the patient may experience graft-versus-host disease.

Viral and immunologic laboratory investigation is mandatory. Therapy consists of intensive administration of antibody, usually in the form of Vaccinia Immune Globulin (VIG).

Severity: Severe - hospitalize
Frequency: Rare
VIG: Indicated

Vaccinia Keratitis
Although a rare occurrence, vaccinia virus can be implanted into diseased or injured conjunctiva and cornea resulting initially in viral replication with ulceration and ultimately in an antigen-antibody interaction leading to corneal cloudiness.

Ten days after transfer the clinical signs of infection (a central, grayish, disciform corneal lesion) can be seen. VIG is contraindicated for use in vaccinia keratitis. Topical antiviral agents are the treatment of choice in consultation with an experienced ophthalmologist.

Severity: Severe if untreated
Frequency: Rare
VIG: Contraindicated

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