Clinical Evaluation Tool for Smallpox Vaccine Adverse Reactions
Ophthalmologic Reactions/Inadvertent Innoculation in a Vaccinee (or in a Close Contact)

www.bt.cdc.gov/agent/smallpox/vaccination/clineval **(01-19-2011 Version)**

Legend
Morbidity and Mortality Risk based on clinical presentation.

- Low
- Moderate
- High

Vaccine Recipient or Close Contact? → Yes → History of known risk factors for smallpox vaccine adverse reactions?

Yes → **Consult with state/local health department and CDC to obtain clinical guidance and to report inadvertent exposure to vaccinia virus contained in smallpox vaccine. Management of the adverse reactions discussed in this Tool may be different when risk factor(s) are present. See Consultation and Reporting Information.**

Vaccine recipients or close contacts with risk factor(s) should be reported, whether or not an adverse event develops.

Risk Factor	Adverse Reaction (Potential/ Reported Historically)
Atopic Dermatitis/Eczema (including severe atopic blepharitis	Eczema Vaccinatum
Acute Exfoliative Dermatitis	Inadvertent Inoculation
Immunocompromised including/HIV+	Progressive Vaccinia/Generalized Vaccinia (Severe form)
Pregnancy	Fetal Vaccinia and potential unknown risks to fetus
Topical Ocular Steroid Use	Autoinoculation to the eye

No → New onset red eye and/or lesions suspicious for vaccinia (papules, vesicles, pustules or ulcerations) in or near the eye up to 10 days after the period beginning with initial vaccination through final resolution and scarification of lesions at vaccination site.

Exposure resulted from inadvertent splash in laboratory setting?

- No → **Patient history and physical exam of eye:** Use infection control precautions.
  Consider differential diagnosis (see differential diagnosis box). Conduct ophthalmic evaluation to include:
  - o Presence and severity of corneal and lid involvement
  - o Visual acuity testing
  - o Presence or absence of lesions/Location of lesions
  - o Presence and severity conjunctival inflammation ("red eye")

  Magnified exam of eye surface (slit lamp exam if available) and fluorescein exam for corneal epithelial defects
  Obtain photos of involved eye if possible (or have ophthalmology consultant obtain) **[8]**
- Yes → **Request VIG consultation (See Consultation and Reporting Information). Laboratory vaccinia strains may be of higher concentration and greater virulence.** → Continue with exam

PROBABLE **inadvertent inoculation** in or near the eye.

White non-inflamed eye associated with suspicious lid **[2]** or **periocular [1]** lesions only. No visible lesions in eye.

Lesions on or near lid margin (**blepharitis [2]**)?

- No → **Isolated periocular lesions**: Close observation. Consider ophthalmology consultation to assist in management.
- Yes → **Mild Blepharitis**: Recommend topical antiviral **prophylaxis [5]** especially if lesions are present on lid margin. Recommend ophthalmology consultation to assist in management.
  Moderate/Severe Blepharitis: Begin topical antiviral **prophylaxis [5]**. Ophthalmology consultation in 12-24 hours (or sooner depending on severity) to evaluate and assist in management. Consider VIG consultation.

Red inflamed eye (**conjunctivitis [3]**) with suspicious lesions in or near the eye. Urgent ophthalmology consultation and consider beginning antivirals right away.

Corneal [4] lesions?

- No → **Conjunctival [3], lid [2] or periocular [1] lesions.**
  Mild: Begin prophylaxis [5], urgent ophthalmology consultation. Consider VIG consultation.
  Severe: Begin prophylaxis [5], emergent ophthalmology consultation. Recommend VIG consultation.
- Yes → **Associated conjunctival [3] or lid [2] lesions?**
  - No → **Keratitis only: Begin topical antiviral treatment [6]. Emergent ophthalmology consultation to evaluate and assist with management. VIG not indicated. See additional information at footnote [7]**
  - Yes → **Blepharitis and/or conjunctivitis associated with keratitis: Emergent ophthalmology consultation.**
    Mild: Begin topical antiviral treatment [6].
    Observe for progressive disease
    Severe: Begin topical antiviral treatment [6]. Consider VIG (one dose).

POSSIBLE **inadvertent inoculation** in or near the eye.

Red inflamed eye (**conjunctivitis [3]**) only - no visible lesion in or near the eye.

Consider differential diagnosis for new onset red eye with high index of suspicion for vaccinia infection. Close observation for development of suspicious lesions.
Recommend ophthalmology consultation as indicated to evaluate for possible vaccinia versus other unrelated causes. Further treatment as indicated by ophthalmic exam

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Footnotes:

1. **Periocular involvement:** (generally above the brow or below the inferior orbital rim)
   Papules, vesicles or pustules not involving the ocular adnexa, lids, lid margins or canthi.
2. **Blepharitis:** (lid involvement)
   Mild - few pustules, mild edema, no fever.
   Severe - pustules, edema, hyperemia, lymphadenopathy (preauricular and/or submandibular), cellulitis, fever.
3. **Conjunctivitis:** (involvement of membrane that lines inner surface of the eyelid and exposed surface of the eyeball; excluding the cornea)
   Mild - mild hyperemia and/or edema, no membranes or focal lesions.
   Severe - marked hyperemia, edema, membranes, focal lesions, lymphadenopathy (preauricular and/or submandibular), fever.
4. **Keratitis:** (corneal involvement)
   Mild - grey epitheliitis, no epithelial defect, no stromal haze or infiltrate (no cloudy cornea).
   Moderate - epithelial defect.
   Severe - ulcer, stromal haze or infiltrate (cloudy cornea).
5. **Prophylaxis:** To prevent extension of vaccinia infection to conjunctiva and cornea: Topical trifluridine - 5 times/day (every four hours while awake) for up to 14 days or until all periocular and/or lid lesions have healed and scabs have fallen off. If no improvement or symptoms worsen after 24-48 hours consider increasing to 9 times/day (see footnote [6]). Hyperemia is an expected consequence of therapy, especially after 14 days of use. Recommend ophthalmology consultation to assist in management anytime trifluridine is used.
6. **Treatment:** To minimize progression and begin resolution of vaccinia infection in cornea and conjunctiva: Topical trifluridine - 9 times/day (every two hours while awake) for up to 14 days or until all lesions have healed. Hyperemia is an expected consequence of therapy, especially after 14 days of use. Recommend ophthalmology consultation to assist in management anytime trifluridine is used.
   Available topical antiviral agents: Trifluridine (Viroptic®) and vidarabine (Vira-A®). Trifluridine and vidarabine are not approved by FDA for treatment of vaccinia disease, although the product labels for trifluridine and vidarabine state that the drugs have *in vitro* and *in vivo* activity against vaccinia virus. Vidarabine is no longer being manufactured, but supplies might be available in certain areas.
7. **Keratitis only:** VIG should not be withheld if a co-morbid condition exists (EV or PV). Consider topical ophthalmic antibacterial prophylaxis in the presence of keratitis. After corneal epithelium has healed consider use of topical steroids (steroids should only be used under supervision of an ophthalmologist).
8. **Photographs:** Recommend obtaining digital photos of involved eye and periocular region. Consult with ophthalmology as needed for photos (Digital photos preferred but 35mm photos or scanned images are welcome).

Differential Diagnosis for smallpox vaccine adverse reactions*

Consider non-smallpox vaccine related conditions, such as:

- Viral conjunctivitis (usually adenovirus)
- Bacterial conjunctivitis
- Allergic conjunctivitis
- Allergic contact dermatitis (e.g. poison ivy, poison oak)
- Contact lens-related infection
- Hordeolum (stye) or chalazion
- Subconjunctival hemorrhage
- Herpes simplex virus (HSV)
- Herpes zoster virus (varicella or shingles)
- Molluscum contagiosum
- Bacterial keratitis
- Preseptal or orbital cellulitis
- Drug reaction
- Insect bite
- Norwegian scabies
- Chemical/toxic exposure

* List should not be regarded as comprehensive.

This clinical tool is intended to guide primary care clinicians (such as ER physician, internist, pediatrician, family practice, optometrist, physician assistant or nurse practitioner) in preliminary evaluation/ treatment. Referral to ophthalmology for suspected cases as indicated is recommended.

Consultation and Reporting Information

Civilian health care providers who need clinical consultation with or without release of vaccinia immune globulin (VIG) (first line agent) or cidofovir (second line agent) for potential smallpox vaccine adverse reactions should contact their state/ local health department or the CDCINFO Line at (800) 232-4636. Military health care providers (or civilian providers treating a DoD healthcare beneficiary) requesting clinical consultation should call (866) 210-6469, and if requesting VIG release should call (888) USA-RIID or (301) 619-2257. Health care providers should report smallpox vaccine adverse events to their state/ local health department and to the Vaccine Adverse Event Reporting System (VAERS) at http://www.vaers.org/ or (800) 822-7967.

Please call (888) 246-2675 (Español (888) 246-2857, TTY (866) 874-2646) or visit http://www.bt.cdc.gov/agent/smallpox/index.asp for general public information about smallpox vaccination. Persons experiencing urgent or life-threatening medical events should seek immediate medical assistance.