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)

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
- Atopic Dermatitis/Eczema (including severe atopic blepharitis)
- Acute Exfoliative Dermatitis
- Immunocompromised including/HIV+
- Pregnancy
- Topical Ocular Steroid Use

Adverse Reaction (Potential/Reported Historically)
- Eczema Vaccinatum
- Inadvertent Inoculation
- Progressive Vaccinia/Generalized Vaccinia (Severe form)
- Fetal Vaccinia and potential unknown risks to fetus
- Autoinoculation to the eye

Patient history and physical exam of eye: Use infection control precautions. Consider differential diagnosis (see differential diagnosis box). Conduct ophthalmic evaluation to include:
- Presence and severity of corneal and lid involvement
- Visual acuity testing
- Presence or absence of lesions/Location of lesions
- Presence and severity conjunctival inflammation (“red eye”)
- Magnified exam of eye surface (slit lamp exam if available) and fluorescein exam for corneal epithelial defects
- Patient history and physical exam of eye:
- Presence of lesions/Location of lesions
- Presence and severity conjunctival inflammation (“red eye”)
- Magnified exam of eye surface (slit lamp exam if available) and fluorescein exam for corneal epithelial defects
- Request VIG consultation (See Consultation and Reporting Information). Laboratory vaccinia strains may be of higher concentration and greater virulence.
- Observation of involved eye if possible (or have ophthalmology consultant obtain) [8]
- 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.


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

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

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]

Blepharitis and/or conjunctivitis associated with keratitis: Emergent ophthalmology consultation.
- Severe: Begin topical antiviral treatment [6]. Consider VIG (one dose).

Disclaimer: The CDC and its partners in the Clinical Immunization Safety Assessment (CISA) network have developed Clinical Evaluation Tools to help health care providers manage patients with potential adverse reactions from smallpox vaccination in the absence of circulating smallpox virus (pre-event setting). These Tools are based on studies conducted before routine US childhood smallpox vaccination was discontinued in 1972 and on expert opinion; they are not entirely evidence-based. The Tools may not apply to all patients with smallpox vaccine adverse reactions and are not intended to substitute for evaluation by a trained clinician. This Tool was last updated on 1-19-11. Please direct feedback on these Tools to spoxtool@cdc.gov.
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: (conveal involvement)
   Mild - grey epitheliitis, no epithelial defect, no stromal haze or infiltrate (no cloudy cornea).
   Moderate - epithelial defect.

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).

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.

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