Post-Vaccinial Encephalitis
Diagnostic and Management

- None for specific diagnosis of PVE
- Diagnosis of exclusion – Consider other infectious or toxic etiologies
- 15-25% mortality rate
- 25% varying neurological deficits
- VIG not recommended
Fetal Vaccinia
Fetal Vaccinia
Associating the Condition with the Vaccine

- Know Chronology of immunization and adverse event
- Corresponds to those previously associated
- Biologic plausibility
- Lab result confirms association
- Recurs on re-administration
- Controlled clinical or epi trial shows association

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Revaccination of Those with History of AE

- In absence of smallpox, do NOT revaccinate
- Defer those not vaccinated from response teams
Prophylaxis of High-Risk Groups Accidentally Exposed

- VIG NOT recommended
- Vigilant clinical follow-up
- Do NOT administer VIG with smallpox vaccine
- Exclude those with contraindications
Laboratory Diagnosis
Laboratory Diagnosis
Rule Out Testing

- Varicella
- Herpes Zoster
- Herpes Simplex
- Enteroviruses
Laboratory Diagnosis
Tests Available

- Electron Microscopy (EM) - Orthopoxvirus
- PCR – Gene Amplification
- Viral Culture – Identify vaccinia

- May be available through LRN
- Consult with CDC for testing advice
Specimen Collection

- Contact state health department
- CDC Interim Smallpox Response Plan, Guide D
  www.cdc.gov/smallpox
Treatments
Vaccinia Immune Globulin

- Immunoglobulin fraction of plasma
- Antibodies to vaccinia from vaccinated donors
- Previously-licensed IM product (Baxter)
  - Contains 0.01% thimerosal
- New IV products in production
- Obtain as IND product through CDC and DoD
VIG Indications

Indications

- Eczema vaccinatum
- Progressive vaccinia
- Vaccinia necrosum
- Generalized vaccinia – severe cases
<table>
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<tr>
<th>Vaccinia Immune Globulin</th>
<th>Indications</th>
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| **Recommended**          | Inadvertent Inoculation - severe  
                         | Eczema vaccinatum  
                         | Generalized vaccinia – severe or underlying illness  
                         | Progressive vaccinia |
| **Not Recommended**      | Inadvertent Inoculation – Not severe  
                         | Generalized vaccinia – mild or limited  
                         | Non-specific rashes, EM, SJS  
                         | Post-vaccinial encephalitis |
| **Consider**             | Ocular complications |
Vaccinia Immune Globulin
Side Effects - Mild

- Local Pain
- Tenderness
- Swelling
- Erythema
- From few hours to 1 or 2 days
Vaccinia Immune Globulin Side Effects - Moderate

- Joint Pain
- Diarrhea
- Dizziness
- Hyperkinesis
- Drowsiness
- Pruritis
- Rash
- Perspiration
- Vasodilation
Vaccinia Immune Globulin
Side Effects - Serious

- Hypotension
- Anaphylaxis
- Renal Dysfunction
- Aseptic Meningitis Syndrome (AMS)
Vaccinia Immune Globulin

Contraindications

- Allergic reaction to thimerosal
- History of severe reaction with IG preparations
- IgA Deficiency
- Vaccinia keratitis, except in some cases
- Pregnancy
- Theoretical risks as with all human plasma
VIG Administration

- VIG-IM 0.6ml/kg
- IM, preferably in buttock or anterolateral aspect of thigh
- Divide doses > 5ml
- Refer to package insert
Cidofovir

- Nucleotide analogue of cytosine
- Some antiviral activity against orthopoxviruses
- Administer under IND protocol, only
- Released by CDC and DoD if:
  - No response to VIG
  - Patient near death
  - All inventories of VIG exhausted

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Cidofovir Side Effects

- Renal toxicity
- Neutropenia
- Proteinuria
- Decreased intraocular pressure
- Anterior uveitis/iritis
- Metabolic acidosis
Cidofovir Admin

- 5 mg/kg IV over 60 minute period
- Consider 2\textsuperscript{nd} dose one week later if no response
- Adjust dose for renal function
- Assess baseline and post-admin renal function
- IV hydration (1L of 0.9% saline IV)
- 3 doses oral probenicid (25 mg/kg per dose)
Obtaining VIG and Cidofovir

- Civilian Medical Facilities
  - CDC Smallpox Vaccinee Adverse Events Clinical Team

- Military Facilities
  - USAMRIID (301) 619-2257 or 888-USA-RIID
Consultation
Consultation

- State and Territories establish program
- Hospitals assign physicians with expertise
- Provide 24/7 access to vaccinees and affected contacts
- CDC Provider Information Line
Consultation Information to Have

- Thorough vaccination history
- Physical Examination of patient
- High-resolution digital photographs of dermatologic manifestations
- Contact state health department, first
Smallpox Adverse Event Reporting
VAERS Reporting

- Secure web-based reporting
  https://secure.vaers.org/VaersDateEntryintro.htm

- Downloadable form

  Fax to:
  1-877-721-0366
Additional Information

CDC Smallpox Website
www.cdc.gov/smallpox

Adverse Events Training Module
www.bt.cdc.gov/training/smallpoxvaccine/reactions
Infection Control

- Documented rarely in healthcare settings
- Primarily after direct contact with site
- May occur with other infected body sites
- Indirect transmission possible, but never documented
Ocular Vaccinial Infections and Therapy
Treatment of Ocular Infections

- Previous experience with older antivirals
- Not done by today’s standards
- Currently available topical ophthalmic antivirals not studied with vaccinia
- Animal studies
Treatment of Ocular Infections
Topical Ophthalmic Anti-Virals

- Animal studies, rabbit model of vaccinial keratitis
- Topical vidarabine or trifluridine
- Virologic and clinical improvement
- Early use might reduce complications
- Not approved by FDA for vaccinia disease
Treatment of Ocular Infections
Vaccinia Immune Globulin

- No evidence effective
- Might increase scarring after vaccinial keratitis
- Rabbit studies used increased doses
Manage in consult with ophthalmologist
Consider off-label use of topical ophthalmic trifluridine or vidarabine
Balance with risk of drug toxicity
Continue until periocular and/or lid lesions heal and scabs fall off
Treatment of Ocular Infections
Guidance for Clinicians

- Consider VIG when keratitis NOT present
- Useful with severe blepharitis or blepharoconjunctivitis
- Weigh risks and benefits if keratitis present
- Use VIG for other severe vaccinia disease, even if keratitis present
- Consider prophylaxis against bacterial infection
- Enroll in studies