Vaccinia (Smallpox) Vaccine Related Adverse Reaction

Vaccinia virus is part of the orthopoxvirus genus and has been genetically altered to be used as the agent in the smallpox vaccine[1–3]. The smallpox vaccine is a live-virus vaccine and is generally only recommended for those individuals that are very high risk for infection such as those who handle variola virus[1]. The vaccine is contraindicated for individuals who are immunocompromised, individuals with eczema or other dermatitis, and pregnant women[1–3]. Vaccinia vaccines are very effective at preventing smallpox, but immunity declines 5 to 10 years after first dose[1,2].

A. Agent:
Vaccinia virus (Smallpox Vaccine)[1–3]

B. Clinical Description:
Most individuals will have a normal, typically mild reaction to the smallpox (vaccinia) vaccine. These reactions will include a sore arm, fever, swollen glands, and body aches[2,3]. Other more severe reactions can occur and these need to be reported.

Diffuse dermatologic complications[2,3]:

- Generalized vaccinia is a disseminated vesicular or pustular rash that is often benign and self-limited. Those receiving the vaccine for the first time are at higher risk than those previously vaccinated. Immunocompromised individuals are more at risk for a severe reaction.
- Eczema vaccinatum is a localized or systemic spread of the virus and often occurs in those who have a history of atopic dermatitis. Symptoms include a rash, fever, and lymphadenopathy. Those receiving the vaccine for the first time and children are more at risk for a severe reaction.

Progressive vaccinia is a rare and often fatal complication that occurs when the vaccination site fails to heal and the vaccinia virus continues to replicate. The skin surrounding the vaccination site becomes infected and vaccinia lesions that are necrotic, fungated, or demarcated appear. The reaction is more likely to occur in those who are immunocompromised[2,3].

Rare adverse reactions[2,3]:

- Fetal vaccinia occurs when a pregnant woman receives the vaccine. The transmission of the virus to the fetus can occur at any time during the pregnancy. Symptoms include miscarriage, stillbirth, or a livebirth with a pox-scarred infant.
- Postvaccinial central nervous system disease is common among infants less than one year of age. Symptoms include cerebral or cerebellar dysfunction, headache, vomiting, altered mental status, lethargy, seizures, and coma.

Cardiac adverse events[2,3]:

- Myo/pericarditis results in chest pain, dyspnea, and palpitations.

- Dilated cardiomyopathy and cardiac ischemia are sequelae of viral myocarditis and have been associated with the vaccination; however, there has been no etiologic link.

C. Reservoirs:
Humans – recent recipients of vaccinia vaccine or recent infection with vaccinia virus[1].

D. Mode(s) of Transmission:
Vaccinia can be spread from the vaccination/infection site of one individual to another if they come in close contact with the site before a scab has formed and fallen off or the vaccinated individual can infect another part of their own body[2,3].

E. Incubation Period:
Exposure to a vaccinia vaccine recipient whose vaccine site has not yet fully scabbed can result in secondary spread of vaccinia. Secondary cases have an average incubation period of 11 days with a range of 5–19 days[2].

F. Period of Communicability:
A person who has received vaccinia vaccination or is infected will be able to spread the vaccinia virus until the scab from the vaccination/infection site has fallen off which could take two to three weeks after vaccination/infection[2].

G. Susceptibility and Resistance:
Most individuals will be susceptible to vaccinia virus unless they have previously had the smallpox vaccine. Some individuals are at higher risk of having an adverse reaction to the vaccinia virus including:

- Individuals who have ever had or currently have atopic dermatitis or "eczema"[1–3]
- Individuals have many breaks in their skin such as those caused by chickenpox, shingles, bad burns, severe acne, poison oak, poison ivy, herpes, psoriasis, pityriasis rosea, impetigo, or other rashes[1–3]
- Individuals with Darier disease[3]
- Individuals with a weakened immune system for any reason[1–3]
- Individuals who are pregnant or who might become pregnant within 4 weeks of the close contact's vaccination[1–3].

H. Treatment[4]:
Vaccinia Immune Globulin Intravenous (Human) (VIGIV) can be used to treat eczema vaccinatum, progressive vaccinia, and severe cases of generalized vaccinia. It is not indicated to treat vaccinia keratitis or postvaccinial encephalitis. If treatment alone with VIGIV is insufficient or VIGIV is unavailable, tecovirimat, cidofovir, and brincidofovir can be used.

I. Clinical Case Definition[5]:

Adverse events may include one or more of the following:

- Common adverse reactions
  - Local skin reaction
  - Nonspecific rashes, e.g., reticular maculopapular, generalized urticarial rash
  - Erythema migrans
- Vaccinia-specific reactions
  - Inadvertent inoculation
  - Ocular vaccinia infection (keratitis)
  - Generalized vaccinia: disseminated, non-centrifugal maculopapular or vesicular rash
  - Progressive vaccinia/vaccinia necrosum: an initial lesion which continues to progress without healing for more than 15 days after the vaccination; painless progressive necrosis at the site with or without metastases to other distant sites
  - Eczema vaccinia: localized or generalized popular, vesicular or pustular rash anywhere on the body, especially at sites of previous atopic dermatitis lesions
  - Encephalopathy or encephalomyelitis: most common in infants; symptoms include fever, headache, change in mental status, lethargy, seizures, coma, and is diagnosed by exclusion of other causes
- Other adverse effects
  - Cardiac, e.g., myocarditis, pericarditis
  - Osteomyelitis
  - Transverse myelitis, seizures, paralysis and neuritis
  - Fetal vaccinia: transmission from mother to fetus resulting in skin diseases and other organ involvement leading to fetal or neonatal death
  - Wound complications

Exposure Criteria

- Vaccination with smallpox vaccine within the three months preceding symptom onset; OR
- Contact exposure to someone vaccinated with smallpox vaccine within the three months preceding symptom onset.

J. Laboratory Criteria for Diagnosis:

None

Case Classification[5]	
Confirmed	A person who has at least one of the clinical features and meets at least one of the exposure criteria

K. Classification of Import Status:

N/A

L. Laboratory Testing:
PCR testing can be done but will be considered on a case by case basis[3].

M. Assessing Laboratory Results:
N/A

N. Outbreak Definition:
An outbreak is defined as ≥2 cases (epi-link outside household or common exposure source/ setting), occurring within a 19-day period.

Investigation Guidelines

O. Time frame[6]:
Providers must submit a report to the Local Health Department within 1 working day after a case or suspect case is diagnosed, treated, or detected.

Local health agencies must notify ADHS within 1 working day after receiving a report.

Local health agencies must submit an epidemiologic investigation report to ADHS within 30 calendar days after receiving a report.

P. Forms:
- Vaccine Adverse Event Reporting System (VAERS) Form

Q. Steps
For a local health agency[6]:

A.A.C. .R9-6-3100. . Vaccinia-related Adverse Event
Case control measures: A local health agency shall:
1. Upon receiving a report under R9-6-202 of a case or suspect case of a vaccinia-related adverse event, notify the Department within one working day after receiving the report and provide to the Department the information contained in the report;
2. Conduct an epidemiologic investigation of each reported case or suspect case of a vaccinia-related adverse event; and
3. For each case of a vaccinia-related adverse event, submit to the Department, as specified in Table 2.4, the information required under R9-6-206(D).

1. **Confirm diagnosis**
   - Before contacting the patient or family, determine what information is available from medical records, physicians, etc.
   - For hospitalization, obtain medical records, including admission notes, progress notes, lab report(s), and discharge summary.
   - Obtain information that supports clinical findings in the case definition including:
     - Adverse reaction or clinical presentation

- Possible exposure to smallpox vaccination
- Smallpox vaccination history

2. **Conduct case investigation**
   - Interview case to determine source, risk factors and transmission settings
   - Collect the following information:
     - Demographic information (birth date, county, sex, race/ethnicity)
     - Vaccination information (date of vaccination, exposure to individual with recent vaccination)
     - Risk factors
     - Type of symptoms
     - Date of onset of symptoms
     - Name, date of birth, and contact information of possible exposures

3. **Conduct contact investigation**
   - Consider individuals who have been in contact with those individuals who were vaccinated within 3 months of illness onset.
   - Determine if the contact is a high risk individual:
     - History of eczema
     - Individuals who are currently pregnant
     - Individuals who are immunocompromised for any reason

4. **Initiate control and prevention measures**
   - Advise the individual who was vaccinated/infected to keep the vaccination/infection site covered with a loose bandage until the site has scabbed and the scab has fallen off[2,3]
   - Vaccinated persons should wash their hands with warm, soapy water or a hand-rub solution containing ≥60% alcohol immediately after they touch their vaccination site or change their vaccination-site bandages[3].
   - Take special care not to touch the vaccination/infection site and the eye area[2,3]
   - Contact precautions for anyone in the household or close contacts[2,3]
   - Take special care when washing linens or clothing of the vaccinated/infected individual. Use hot water and bleach[3]
   - The vaccinated/infected individual as well as household or close contacts should use good hand hygiene practice[2,3]

5. **Isolation, Work and Child Care Restrictions**

- Vaccinia vaccine recipients/infected individuals who will have close contact at work with individuals at high-risk for complications from vaccinia (e.g., pregnant women, children ≤ 12 months old, immune compromised individuals, or individuals with a chronic skin condition such as eczema) should have their work assignment assessed on a case-by-case basis with input from health care personnel or public health workers who are knowledgeable in vaccinia infection control issues[3].

6. **Case Management**
   - Cases should be followed to determine compliance of control measures.
   - Provider should complete Vaccine Adverse Event Reporting System (VAERS) Form.

7. **Contact Management, Including Susceptible Contacts**
   - Monitor an individual that is considered to be exposed for 19 days to ensure there was no spread[3]

8. **Notifications**
   - As appropriate, use the notification letter(s) and the disease fact sheet to notify the case, contacts and other individuals or groups.
   - ADHS is responsible for notifying CDC upon identification of a confirmed case.

R. Outbreak Guidelines:
Refer to the general outbreak guidelines section for general information on conducting an outbreak investigation.

Additional Information & Resources

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