State of Alaska Epidemiology **Bulletin**

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Smallpox Vaccination: Normal and Adverse Reactions to Vaccinia Virus

On February 20, 2003, the Alaska Division of Public Health will hold the first of four smallpox vaccination clinics to vaccinate one health care response and two public health teams. Up to 175 individuals from around the State will be vaccinated as a part of this voluntary program.

Most health care providers have never seen a smallpox vaccination reaction and have no experience with adverse reactions to vaccinia virus, the live virus contained in the smallpox vaccine. **Adverse reactions may occur in vaccinees or in close contacts to vaccinees**. As health care workers and military personnel around the country are vaccinated over the next several weeks to months, providers may be faced with this new clinical challenge.

Normal vaccination progression

Most people who are inoculated with vaccinia will have normal vaccination site progression (Table 1).

Table 1. Normal vaccination reaction timeline

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

Normal vaccination site variants

Approximately 2.4-6.6% of vaccinees will have variants of a normal response, with significant local and systemic signs and symptoms. Findings may include satellite lesions around the vaccination site, lymphangitis from the vaccination site, persistent regional lymphadenopathy, extensive local site edema, and intense erythema (viral cellulitis).

A recent prospective study reported a substantial degree of reactogenicity (Table 2).[1]

Table 2. Systemic symptoms in first time vaccinees

Symptom	% of Vaccinees
Pain at vaccination site	86%
Regional lymphadenopathy	54%
Fatigue	50%
Headache	40%
Missed work, school, sleep or other activities	30%
Muscle aches & chills	20%
Nausea	20%
Fever ≥100F	10%

Robust takes

Large vaccination reactions, defined as >10 cm in diameter, occur in 10% of first-time vaccinees.[1] These unusually large and painful vaccination reactions are called robust takes. Robust takes are a **normal variant** of the typical vaccination reaction, although they may be misdiagnosed as bacterial cellulitis. They improve spontaneously within 3 to 4 days. The key to differentiating robust takes from bacterial cellulitis is the onset interval. Robust takes occur 8-10 days following vaccination while bacterial cellulitis is usually seen within 5 days of vaccination.

Post-vaccination adverse reactions[2]

Adverse reactions to smallpox vaccination are usually mild and self-limited. Mild reactions include most cases of inadvertent inoculation, skin rashes, and generalized vaccinia.

Infrequently, reactions can be life threatening. Some reactions may require vaccinia immune globulin (VIG) for treatment (Table 3). **The Section of Epidemiology is available 24 hours a day to assist in diagnosis, laboratory testing and treatment.**

- ***Eczema vaccinatum***, is seen in persons with a history of atopic dermatitis or eczema. VIG should be initiated immediately.
- ***Progressive vaccinia***, which may be mistaken for a robust take or bacterial super-infection, is seen in persons with humoral or cellular immunodeficiency. It is often fatal even with VIG.
- ***Postvaccinial encephalitis*** (PVE) was historically most common in infants. It had a 25% fatality rate with long-term neurological sequelae in 25% of survivors; VIG is not indicated.
- ***Fetal vaccinia***, a rare event, has been reported among women vaccinated in all three trimesters. VIG may be considered for viable infants with vaccinia lesions.
- One to two ***deaths*** occur for every million primary vaccinations. Of 68 deaths reported during a 9-year period, 52% were due to PVE, 28% to progressive vaccinia, and 18% were contacts with eczema vaccinatum.

Table 3. Adverse reactions, incidence and treatment with VIG

Adverse Reaction	Incidence*	VIG Indicated?
Inadvertent inoculation	25-529	No, for most cases. Yes, for extensive lesions.
Erythema multiforme	164.6	No
Vaccinia keratitis	Unknown	Contraindicated; may cause corneal opacities.
Generalized vaccinia	23-242	No for most cases. Yes, if severe.
Eczema vaccinatum	10-39	Yes
Progressive vaccinia	0.9-1.5	Yes
Post-vaccinial encephalitis	3-12	No
Fetal vaccinia	Unknown	Maybe

* Number of cases per 1 million primary vaccinations

Laboratory diagnosis

When the clinical diagnosis of vaccinia infection is not straight forward (e.g., no known contact to vaccine), laboratory testing for vaccinia may be helpful. DNA amplification (PCR), electron microscopy and viral culture methods have been developed and are awaiting FDA approval. The Alaska State Public Health Laboratories, part of the national Laboratory Response Network, can perform PCR testing and may soon be able to provide electron microscopy. The Section of Epidemiology will facilitate collection of appropriate specimens on a case-by-case basis.

For more information:

- Images of normal and adverse vaccine reactions: www.bt.cdc.gov/agent/smallpox/vaccination/clinicians/asp
- Clinical Management of Adverse Events Following Smallpox Vaccination: A National Training Initiative: www.bt.cdc.gov/agent/smallpox/training/webcast/04feb2003/index.asp
- CDC Clinician Information Line (24/7) – (887) 554-4625

References:

1. Frey et al. Clinical responses to undiluted and diluted smallpox vaccine. NEJM 2002; 346; 17: 1265-74.
2. CDC. Smallpox vaccination and adverse reactions: guidance for clinicians. MMWR Dispatch 2003;52 (January 24, 2003).

Report all suspected adverse smallpox vaccine reactions to the Section of Epidemiology immediately.

Daytime phone number 907-269-8000
After hours number 800-478-0084