SMALLPOX FACT SHEET – *Information for Clinicians*

Adverse Reactions Following Smallpox Vaccination

Smallpox vaccination (vaccinia) is generally a safe and effective means of preventing smallpox. However, in a number of individuals, smallpox vaccination can result in untoward effects and adverse reactions. Most are totally benign, but may be alarming in appearance. Some are serious, but treatable. A few, which rarely occur, are serious, life threatening and can be fatal. Severe adverse reactions are more common in persons receiving primary vaccination compared to those being revaccinated.

Local Reactions

- Primary vaccination can produce swelling and tenderness of regional lymph nodes beginning 3 to 10 days after vaccination and in some cases persisting up to 2 to 4 weeks after the skin lesion has healed.
- Other normal local reactions can include
    - local satellite lesions (which appear similar to the primary lesion),
    - considerable local edema,
    - what may be confused with bacterial cellulitis, but is simply intense inflammation accompanying the vaccination (viral cellulitis).
- In a recent study of adult primary vaccinees, 36% were sufficiently ill to miss work, school, or recreational activities or to have trouble sleeping.

Systemic Reactions

- In a recent study, 17% of adult primary vaccinees experienced fever of at least 100°F within two weeks of vaccination; 7% had a fever of 101°F or more, and 1.4% experienced a fever of 102°F or more. Beyond two weeks, fever was recorded in 0.3% of vaccinees.
- Other expected systemic reactions include malaise, soreness at the vaccination site, myalgia, local lymphadenopathy, and intense erythema ringing the vaccination site.
- A variety of erythematous or urticarial rashes occur approximately 10 days after primary vaccination in one person per 3700 vaccinated.
    - Vaccinees who develop these rashes are usually afebrile and the rash resolves spontaneously within 2 to 4 days.
    - Rarely, a more serious rash, called bullous erythema multiforme (or Stevens-Johnson syndrome) occurs.
- In a recent study of adult primary vaccinees, 36% were sufficiently ill to miss work, school, or recreational activities or had trouble sleeping.

Inadvertent Inoculation

Successful vaccination produces a lesion at the vaccination site. Beginning about four days after vaccination, the florid site contains high titers of vaccinia virus. This surface is easily transferred to the hands and to fomites, especially since itching is a common part of the local reaction.

- Accidental implantation occurs due to transfer of vaccinia virus from the primary site to other parts of the body, or to other individuals.
- This is the most frequent complication of smallpox vaccination (529 per million primary vaccinees), accounting for approximately half of all complications of primary vaccination and revaccination.*
- Lesions of inadvertent inoculation can occur anywhere on the body, but the most common sites are the face, eyelid, nose, mouth, genitalia, and rectum. Lesions in eczematous skin, in disrupted skin

and in the eye pose special hazards, as the infection can be extensive in skin lesions and a threat to eyesight in the eye.
- Most lesions heal without specific treatment.

Generalized Vaccinia

- Generalized vaccinia consists of vesicles or pustules appearing on normal skin distant from the vaccination site.
- In the past, it was estimated to occur in 242 per million primary vaccinees.*
- It is believed to result from a vaccinia viremia with skin manifestations.
- Most rashes labeled as generalized vaccinia produce only minor illness with little residual damage.
- The rash is generally self-limited and usually requires only supportive therapy. However, patients with underlying immunosuppressed illnesses may have a toxic course and require Vaccinia Immune Globulin (VIG).

Eczema Vaccinatum

- Eczema vaccinatum is a localized or systemic spread of vaccinia virus.
- In the past, it was estimated to occur in 10-39 per million primary vaccinees.*
- Transfer of vaccinia virus can occur from autoinoculation or from contact with a vaccinee whose lesion is in the florid stages.
- Individuals with eczema or atopic dermatitis are at increased risk. Eczema vaccinatum can occur regardless of whether the eczema/atopic dermatitis is active at the time of vaccination.
- Virus implanted in disrupted skin (may be at multiple sites) spreads from cell to cell producing extensive lesions dependent on extent of abnormal skin.
- Treatment should include hospitalization and urgent treatment with VIG. Mortality has been prevented in patients treated promptly and adequately.
- Severe cases and fatalities have been observed after contact of recently vaccinated persons with persons who have active eczema/atopic dermatitis or a history of eczema/atopic dermatitis.

Vaccinia Keratitis

- Vaccinia keratitis results in lesions of the cornea due to accidental implantation of vaccinia virus, and is potentially threatening to eyesight.
- Symptoms appear ten days after transfer of vaccinia virus.
- Left untreated, considerable corneal scarring may result as lesion heals resulting in significant impairment of vision.
- Topical antiviral agents are the treatment of choice; therapy should be determined in immediate consultation with an experienced ophthalmologist.

Progressive Vaccinia

- Progressive vaccinia, also known as vaccinia necrosum, is a severe, potentially fatal illness characterized by progressive necrosis in the area of vaccination, often with metastatic lesions (e.g., lesions at places other than the vaccination site).
- In the past, it was estimated that progressive vaccinia occurred in approximately 1 to 2 per million primary vaccinations, and was almost always fatal before the introduction of VIG and antiviral agents.*
- Rare in the past, it may be a greater threat today, given the larger proportion of susceptible persons in the population and the greater number with immunocompromise. Nearly all instances have been in people with defined cell-mediated immune defect (T-cell deficiency).
- Prompt hospitalization and aggressive use of VIG are required.
- Massive doses of VIG are necessary to control viremia. Up to 10 ml per kg of intramuscular VIG has been used.
- There is no proven antiviral therapy. Preliminary studies with cidofovir show some antiviral effect in vitro; studies in animals are pending.

- Immediate consultation with the CDC is recommended to determine if any experimental antiviral drugs are available.

Post-Vaccinial Encephalitis

- Encephalitis or meningoencephalitis following vaccination has been reported in about 3 to 12 per million primary vaccinees; how many such cases are coincidental in time and how many are related to the vaccination itself is impossible to know.*
- Because many different infectious agents and non-infectious processes can be responsible, it is often impossible to establish the etiology. Most cases are believed to result from autoimmune or allergic reactions rather than direct viral invasion of the nervous system.
- In general, this is a severe disease with high mortality and morbidity. Approximately 15-25% percent of affected vaccinees with this complication die, and 25% develop permanent neurological sequelae.
- There is no specific therapy. Supportive care, anticonvulsants and hospitalization in intensive care may be required in individual cases.
- VIG is **not** effective and is **not** recommended.

Fetal Vaccinia

- Fetal vaccinia is a rare complication of smallpox vaccination.
- Fewer than 50 cases of fetal vaccinia infection have been reported, usually after primary vaccination of the mother in early pregnancy.
- Fetal vaccinia usually results in stillbirth or death of the infant soon after delivery. Smallpox vaccine is not known to cause congenital malformations.

Death

- Death resulting from smallpox vaccination is rare, in the past approximately 1 to 2 primary vaccinees died per million vaccinated.*
- Death is most often the result of postvaccinial encephalitis or progressive vaccinia.

Possible Causal Association Between Smallpox Vaccination and Myopericarditis

- Data from recent smallpox vaccinations have been found to be consistent with a causal association between vaccination and myopericarditis, although this is not proven. Persons receiving smallpox vaccine should be informed that myopericarditis is a potential complication of smallpox vaccination and that they should seek medical attention if they develop chest pain, shortness of breath, or other symptoms of cardiac disease after vaccination.

** Adverse event rates presented here are primarily from data collected in the 1960s. Rates in the United States today may be higher because there may be more persons at risk from 1) immune suppression from cancer, cancer therapy, organ transplantation, and other illnesses, such as HIV/AIDS, and 2) eczema or atopic dermatitis. Rates may be lower for persons previously vaccinated.*

This fact sheet is a brief overview of reactions following smallpox vaccination. Additional details for clinicians regarding diagnosis and management of patients with adverse reactions are available at the CDC smallpox website. Visual images of expected and adverse reactions can be viewed at www.bt.cdc.gov/training/smallpoxvaccine/reactions.

For more information, visit www.cdc.gov/smallpox, or call the CDC public response hotline at (888) 246-2675 (English), (888) 246-2857 (Español), or (866) 874-2646 (TTY)
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