



ACR HOTLINE

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Smallpox: Relevance to Rheumatology

Introduction

On December 13, 2002, in response to growing concern regarding potential bioterrorism threats, President Bush announced a plan for a program of smallpox vaccinations for persons in the United States. The first groups to be vaccinated will be those in the military, along with certain medical personnel. The initial group of medical personnel to receive smallpox vaccination will include those 'first responders' (e.g. emergency room and ICU staff). This is in keeping with federal and state strategies for controlling smallpox outbreaks, which call for: 1) pre-event vaccination of public health and health care workers who would investigate a smallpox case or provide care to patients and 2) post-event response to an outbreak of smallpox. Smallpox vaccination of these 'first responder' teams will likely begin in mid-January 2003. Vaccinations would next be offered to the general public, probably in 2004.

Why do rheumatologists need to know about this?

As healthcare providers, our patients depend on us to explain and interpret medical information disseminated by the lay press. Perhaps most importantly, immune responsiveness is central to vaccination strategies. Impaired immunity, that may be induced by anti-rheumatic therapies or that may be associated with rheumatic diseases themselves may impact the potential risks and benefits of vaccination. Potential concerns related to vaccination of patients with abnormal immunity include:

- a failure to respond adequately to vaccination, with resultant lack of protection from the target disease, or a requirement for more frequent vaccination
- more severe or more frequent adverse effects related to the vaccination; particularly with live virus or bacterial vaccines (e.g. smallpox, oral polio virus, measles-mumps-rubella, BCG, oral typhoid, varicella, yellow fever)

What should we know about smallpox and smallpox vaccination?

Smallpox is a disease caused by the *Variola* virus. The disease is highly infectious, typically manifests with nonspecific symptoms including fever and rash, and may be fatal in 1 out of 3 unvaccinated patients. Smallpox vaccine is live vaccinia virus. Ironically, smallpox was the target for the initial validation of vaccination as a medical therapy, dating to Edward Jenner's use of cowpox inoculation in 1798. Smallpox vaccination was so successful that natural disease was eradicated worldwide by 1977; the specter of its use as an agent of bioterrorism has reawakened interest in smallpox vaccination. Smallpox vaccination can be associated with a number of adverse effects, some of which can be severe or even fatal. These include eczema vaccinatum, generalized vaccinia, inadvertent inoculation, progressive vaccinia, vaccinia encephalopathy, and fetal vaccinia.

Contraindications to receiving the vaccine include eczema, atopic dermatitis and other significant skin conditions (these patients are at higher risk of developing eczema vaccinatum). Other contraindications include severe immunodeficiency or immunosuppression, pregnancy, breastfeeding, age <1 year, allergy to the vaccine's components (polymyxin B, streptomycin, chlortetracycline, neomycin, phenol) and moderate or severe acute illness at the time of vaccination. Because the vaccinia virus used in smallpox vaccines can be spread to others from the vaccine site of immunized persons, these contraindications apply not only to vaccine recipients, but also to their household and other close contacts. The vaccination site should be considered infectious until complete healing occurs.

What should we tell our patients?

Various experts uniformly recommend that immunosuppressed patients NOT receive smallpox vaccination. However, there are still a number of key questions that remain unanswered regarding patients with rheumatic diseases. For example, apart from the effects of treatment, it is not clear to what extent patients with various autoimmune diseases might be immunosuppressed such that they would not respond to vaccination or would suffer more severe adverse effects. Since disease effects on the immune system often vary with disease severity, the effects of immunomodulatory anti-rheumatic therapies probably outweigh those of the condition itself, and untreated patients with mild disease could be considered similar to normal persons.

More important to patients with rheumatic disease are questions related to immunomodulatory therapies? Guidelines specifically recommend that patients receiving radiation, antimetabolites, alkylating agents, high-dose corticosteroids, and chemotherapeutic agents NOT receive smallpox vaccine due to concern about severe side effects. There are no specific recommendations regarding low dose prednisone or DMARDs (including antimetabolites at lower doses). It would certainly seem prudent that patients receiving anticytokine therapies (e.g. inhibitors of TNF or IL-1) or other biologic agents avoid smallpox vaccination as well as other live vaccines. However, the question of how to best counsel an RA patient on methotrexate alone, or on another DMARD and low dose prednisone, for example, remains unanswered. It may be prudent to withhold vaccination from such patients until further information becomes available.

Where can we go for further information?

The Centers for Disease Control (CDC) and state departments of health are developing standardized forms for screening potential vaccine recipients, which should be generally available soon. State health departments will be among agencies that will monitor for adverse events and intervention, including obtaining vaccinia immune globulin and/or cidofivir through an investigational new drug protocol from CDC. Vaccine recipients will be counseled in appropriate care of the vaccination site (gauze and semi permeable dressing) and meticulous hand washing. Vaccine recipients will be monitored for “take” (indicating immunity) and adverse reactions.

Rheumatologists should become familiar with smallpox vaccine, including contraindications and adverse effects. Further, we should all keep abreast of the emerging information in this area, some of which will be forthcoming from various state and federal agencies. The CDC has a good deal of information on the CDC Web site at <http://www.bt.cdc.gov/agent/smallpox/vaccination/index.asp>.

Information includes the smallpox vaccination and adverse events training module, smallpox vaccine contraindications, adverse reactions following smallpox vaccination, management of adverse reactions, Advisory Committee on Immunization Practices (ACIP) recommendations (most recent October 2002), and visual aids helping to distinguish illnesses associated with rashes.

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