

## **Important Information About Vaccinia (Smallpox) Vaccine**

*Please Read This Carefully*

### **Introduction**

Vaccinia vaccine, previously known as smallpox vaccine, is highly effective in producing immunity to smallpox (variola), and other closely related viruses of the *Orthopox* genus, such as monkeypox and cowpox. The use of vaccinia vaccine led to the global eradication of smallpox in 1977. Because of the low risk of smallpox, the routine use of vaccinia vaccine in the United States was discontinued in 1971. In 1976, the recommendation for routine vaccination of health-care workers was also discontinued. In 1983, the only active producer of vaccinia vaccine in the United States discontinued distribution of vaccinia vaccine for civilians.

In the US, only the WHO Collaborating Center for Smallpox and Other Poxvirus Infections at the Centers for Disease Control in Atlanta is authorized to work with smallpox virus; the CDC and a few laboratories may be working with other human orthopoxviruses, including vaccinia virus and recombinant vaccinia viruses, for which vaccination is recommended. The recombinant vaccinia viruses are genetically modified to express foreign proteins, and are known as recombinants. Much of the work with recombinant vaccinia viruses is part of an effort to produce new vaccines, or to promote the production of other proteins in cell culture. A recombinant vaccinia virus which expresses portions of human immunodeficiency virus (HIV) is now being used in trials in humans at several research centers.

The risk of a laboratory-acquired infection with vaccinia virus is not known with certainty. However, several laboratory-acquired infections have been reported, including infections with recombinant vaccinia viruses. Because human trials are being conducted with experimental vaccinia-HIV recombinant vaccines, it is also possible that other health care workers, such as nurses and physicians, could be exposed to both vaccinia and recombinant vaccinia viruses.

Since 1980, the United States Public Health Service has recommended the use of vaccinia vaccine to protect laboratory workers from infection with orthopoxviruses, including persons working with animals infected with orthopoxviruses.

### **Vaccinia (smallpox) vaccine**

The vaccinia vaccine licensed in the United States contains live vaccinia virus, derived from the New York City Board of Health strain of vaccinia. Vaccine is administered using the multiple puncture technique with a bifurcated needle. Use of vaccinia vaccine to treat herpes simplex 1 and 2 constitutes misuse of the vaccine.

More than 95% of primary vaccinees (i.e., persons receiving their first dose of vaccine) will develop neutralizing and/or hemagglutination inhibition antibody at a titer of  $>1:10$ . Neutralizing antibody appears to persist for many years, with antibody titers of  $\geq 1:10$  found in 75% of persons 10 years following a second dose, and up to 30 years following three doses of vaccine. The level of antibody required for protection against vaccinia infection is not known. However, fewer than 10% of persons with neutralizing titers of  $\geq 1:10$  will have a primary-type response to revaccination, suggesting that these persons are protected from viral replication, and presumably infection.

### **Who should receive vaccinia vaccine?**

The United States Public Health Service recommends vaccinia vaccine for the following persons:

1. Laboratory workers who directly handle cultures contaminated or infected with vaccinia, recombinant vaccinia, or other orthopoxviruses (such as monkeypox, cowpox, and others);
2. Laboratory workers who directly handle animals contaminated or infected with vaccinia, recombinant vaccinia, or other orthopoxviruses.

Other health-care workers (such as physicians and nurses) whose contact with these viruses is limited to contaminated materials (for example, dressings), but who adhere to appropriate infection control measures, are probably at lower risk for inadvertent infection than laboratory workers. However, because a theoretical risk of infection exists, vaccination may be considered for this group.



**Because of the low risk of infection, vaccination is not recommended for persons who do not directly handle virus cultures, or who do not work with materials or animals contaminated or infected with these viruses (for example, security guards, janitorial and engineering personnel).**

**How often should I be revaccinated?**

Antibody to vaccinia following vaccination appears to persist for many years. The Public Health Service recommends that persons working with vaccinia, recombinant vaccinia viruses or other non-variola orthopoxviruses be revaccinated every 10 years.

**What are the benefits of vaccinia vaccination?**

The immunity to vaccinia should help protect recipients against infection resulting from uncontrolled, inadvertent exposure to vaccinia, recombinant vaccinia, or other orthopoxviruses. These unintentional exposures could occur by unusual routes (for example, splashes into the eye or inhalation of an aerosol). These exposures could also involve a large dose of virus which is more likely to cause illness. In addition, persons with preexisting immunity to vaccinia may be protected against seroconversion to the foreign antigen expressed by a recombinant virus.

**What are the risks of vaccination?**

Successful vaccination, particularly in persons receiving their first dose of vaccine, is associated with tenderness, redness, swelling, and a lesion at the vaccination site, and may cause fever for a few days. The lymph nodes in the axilla of the vaccinated arm may become enlarged and tender. These symptoms are more common in persons receiving their first dose of vaccine (15%-20%) than in persons being revaccinated (5%-10%).

The overall risks of serious complications of vaccinia vaccination are low, and occur more frequently in persons receiving their first dose of vaccine, and among young children. The most frequent serious complications of vaccination are encephalitis (brain inflammation), vaccinia necrosum (progressive destruction of skin and other tissues at the vaccination site), and eczema vaccinatum (severe and destructive infection of skin affected by eczema or other chronic skin disorder caused by spread of vaccinia virus).

Among adults receiving their first dose of vaccine, the following serious complications have been observed:

- Encephalitis - about one in 300,000 doses.
- Vaccinia Necrosum - this complication has been limited to recipients who have abnormalities of their immune system, for whom the vaccine is contraindicated.
- Eczema Vaccinatum - this complication has been limited to recipients who have eczema or other chronic skin conditions, for whom the vaccine is contraindicated.

Among adults being revaccinated, the following serious complications have been observed:

- Encephalitis - about one in 200,000 doses.
- Vaccinia Necrosum - this complication has been limited to recipients who have abnormalities of their immune system, for whom the vaccine is contraindicated.
- Eczema Vaccinatum - this complication has been limited to recipients who have eczema or other chronic skin conditions, for whom the vaccine is contraindicated.

Other less serious complications include generalized vaccinia (vaccination lesions developing away from the vaccination site), and inadvertent transfer of vaccinia from the vaccination site to other parts of the body. These complications occur in adults approximately one in 5,000 and one in 1,700 primary vaccinations, respectively, and one in 110,000 and 40,000 revaccinations, respectively. Generalized vaccinia in persons without underlying illness (such as immune deficiency) is generally self limited and requires little or no therapy. Inadvertent transfer of vaccinia from the vaccination site to other parts of the body can be prevented by handwashing after touching the vaccination site.

Since the majority of persons receiving vaccinia vaccination are likely to have been born prior to 1970, most will have been vaccinated as children. Therefore, most doses of vaccinia vaccine given to laboratory workers will be revaccinations, and generally lower rates of complications are expected.



On rare occasions, almost always after primary vaccination, vaccinia virus has been reported to cause fetal infection after vaccination of a pregnant woman. Fewer than 50 instances of fetal vaccinia are known, but cases have been observed as recently as 1978. Fetal vaccinia usually results in stillbirth or death of the infant shortly after delivery. Vaccinia vaccine is not known to cause congenital malformations.

Because the vaccinia virus is present at the vaccination site, other persons can become infected if they come in direct contact with the vaccinee's lesions. Vaccinees can also transfer virus from the vaccination site to another person by touching the lesion and then touching the other person. The exact risk of infection by such routes of transmission is unknown; however, virus can be cultured from the vaccination site until the skin heals. Most instances of contact transmission of vaccinia do not lead to serious illness in the contact. However, about 30% of contact transmission results in eczema vaccinatum.

### **Treatment of complications of vaccinia vaccine**

The only product currently available for the treatment of complications of vaccinia vaccination is vaccinia immune globulin (VIG). VIG is an isotonic sterile solution of the immunoglobulin fraction of plasma from persons vaccinated with vaccinia vaccine. In 1998 a slight discoloration was noted in this product and the FDA placed a hold on its release. Consequently, VIG can no longer be entered into interstate commerce under terms of the approved license and must therefore revert to IND (investigational new drug) status.

VIG is effective in the treatment of eczema vaccinatum and some cases of progressive vaccinia, and may be useful in the treatment of ocular vaccinia resulting from accidental implantation. It is also recommended for severe generalized vaccinia if the patient has a toxic condition or has a serious underlying disease. VIG is of no benefit in the treatment of postvaccinal encephalitis.

The investigational VIG product was made before the FDA required specific viral safety tests on certain licensed products, but a review of past analyses of the product supports the conclusion that the product is safe. However, the following medical screening will be required before administration of VIG and at 3 and 6 months following administration of the VIG:

- Routine physicals
- Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV) testing (pre and post HIV test counseling will be provided by attending physician as required)
- Liver function tests to include serum alanine aminotransferase (ALT), serum creatinine, and complete blood count (About four tubes of blood will be drawn for the laboratory tests)
- Daily doctor visit for first 5 days following administration of the VIG in order to monitor the status of possible lesions.

The recommended dosage for treatment of complications is 0.6 milliliter per kilogram of body weight. VIG must be given intramuscularly, and should be given as early as possible after the onset of symptoms. Because therapeutic doses of VIG may be large (e.g., 42 milliliters for a person weighing 70 kg), the product should be given in divided doses over a 24- to 36-hour period. Doses may be repeated, usually at intervals of 2-3 days, until recovery begins (e.g., no new lesions appear).

The only source of VIG for civilians is the CDC.

### **Who should not be vaccinated?**

As described above, persons with certain conditions are more likely to develop severe complications of vaccinia vaccine and should not be vaccinated. These include:

- Persons who have ever been diagnosed as having eczema, even if the condition is mild or is not presently active.
- Persons whose household contacts have eczema, or a history of eczema.
- Persons with other acute or chronic skin conditions, such as atopic dermatitis, burns, impetigo, or varicella zoster (shingles) should not be vaccinated until the condition resolves.
- Persons whose household contacts have an immunodeficiency disease or therapy listed above.



- Persons with diseases or conditions which cause immunodeficiency, such as leukemia, lymphoma, generalized malignancy, agammaglobulinemia, or therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids.
- Women who are pregnant, or who are planning to become pregnant within a month following vaccination.
- Persons with serious, life-threatening allergies to the antibiotics polymyxin B, streptomycin, tetracycline, or neomycin.

The risk of severe complications after vaccinia vaccination for persons infected with human immunodeficiency virus (HIV) is not known. At present, there is no evidence that vaccinia vaccination accelerates the progression of HIV-related disease. Nevertheless, until additional information becomes available, it is prudent that persons who have HIV infection not be vaccinated.

### What to look for and do after the vaccination

Three to five days following primary vaccination, a small bump develops at the site of vaccination. The bump becomes a blister, which then becomes pus-filled, and reaches its maximum size by 8-10 days. The pus-filled blister dries and forms a scab, which separates by 14-21 days after vaccination, leaving a typical scar. Vaccinia virus is shed from the site from 4 days following vaccination until the scab separates from the skin. Persons being revaccinated may not develop a blister, and the progression of the lesion at the site of vaccination may be shorter.

The main objectives in caring for a smallpox vaccination are to avoid spread of virus from the vaccination site to another area of the body such as the eye, to avoid spread to another person, and to keep the area clean and dry.

- (1) Keep the site covered with a bandage, such as a Band-Aid<sup>1</sup>, at all times until the scab has fallen off and the underlying skin is healed. An occlusive (air-tight) cover should not be used.
- (2) Keep the site dry. When showering, cover the site with plastic and rubber bands or tape the plastic down with adhesive tape to prevent wetting. Do not direct shower water to the vaccinated area. After drying off, replace the occlusive plastic cover with a simple bandage.
- (3) After changing the bandage, or any time the vaccination site is touched, wash your hands thoroughly with soap and water. **This is the most important measure to prevent transmission of vaccinia to another person, or another part of the body.**
- (4) Avoid contact with anyone at risk of complications of smallpox vaccination listed above until the scab has fallen off.

### Where can I get more information about vaccinia vaccine?

If you have questions about vaccinia vaccination, you should ask your doctor, or the person responsible for vaccination in your facility. In December 1991, the United States Public Health Service published its recommendations for the use of vaccinia vaccine in the *Recommendations and Reports* series of *Morbidity and Mortality Weekly Report*. A copy of these recommendations may be obtained by writing the CDC Drug Service, National Center for Infectious Diseases, Mailstop D-09, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, or going to CDC Website at <http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/00042032.htm>, or by calling (404) 639-3670.

<sup>1</sup> Use of trade names is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

