PHYSICIAN ALERT

May, 2003

TO: All Clark County Physicians

FROM: Donald S. Kwalick M.D., M.P.H.

RE: SMALLPOX VACCINATION

Clark County has been actively involved in planning for bioterrorism and has a well developed Smallpox Preparedness, Response and Recovery Plan which deals with all aspects of a potential smallpox attack. Although still being developed, there is a muti-phasic approach to providing smallpox vaccinations. Phase I involves vaccinating select public health and hospital-based teams who will be involved in investigation and caring for potential smallpox cases. Phase I is a part of an ongoing preparedness effort and there is no knowledge to suggest any increased threat of smallpox attack other than general concern that nations or groups unfriendly to the United States may possess the smallpox virus.

The purpose of this memorandum is the following: to apprise you of Clark County's plan for Phase I of the National Smallpox Vaccination Program (all physicians should be familiar with this Plan since community physicians may be asked about smallpox vaccination, including general questions, contraindications, and potential adverse reactions among vaccinees or their contacts and since vaccinees with reactions to smallpox vaccine may present to primary care physicians). Mass vaccination is not part of the primary pre-event plan; however vaccinated personnel would become available to respond in an actual smallpox event.

It is important to keep in mind that many of the details of this plan are currently being debated at local. state, and federal levels, and thus there may be changes to the plan. Be assured that Clark County Health District will continue to provide you with as current information as possible. To obtain the full memo, go to the below web site. Listed at the end of this document are websites where you can access the most up-to-date information

Physician's Role

- Be familiar with smallpox vaccination including contraindications and potential adverse reaction in order to counsel patients considering vaccination.
- Serious adverse events that may require treatment with VIG should be reported to the CDC Clinical Consultation Team through the Clinicians Information Hotline at 1-877-554-4625
- Report immediately by telephone to the Clark County Health District any known or suspected adverse reactions to smallpox vaccinations that are serious, life-threatening and/or require hospitalization. 702-383-5160, or 702-385-1291.
- Obtain urgent consultation from the State Adverse Event Coordinator when encountering severe adverse reactions for which Vaccinia Immune Globulin (VIG)/Cidofovir may be required. 775-352-3640.
- To obtain the total 13 page document on smallpox vaccinations go to: http://www.cchd.org/download/fact_sheets/smallpox_vaccination.pdf
- To request a hard copy mailed to you, call Kay Godby RN, Bio-Prep Planner @ 383-5016

Overview of the National Smallpox Vaccination Plan

The National Smallpox Vaccination Plan consists of three phases.

Phase I: The federal government has released approximately 450,000 doses for voluntary vaccination of a limited number of health care workers in public health and hospital settings. These personnel will form public health and hospital-based smallpox response teams. These teams will increase the county's capacity to respond to suspected or actual smallpox cases, should this be necessary. Phase I vaccinations will begin in May 2003. (Phase I is temporarily suspended3/31/03 due to recent cardiac events) In addition, approximately 500,000 military personnel, including reservists, currently are being vaccinated.

Phase II: Expands availability of smallpox vaccination to all healthcare workers and traditional first responders such as pre-hospital emergency medical, law enforcement and fire personnel. The implementation guidelines for Phase II will follow Phase I.

Phase III: Voluntary smallpox vaccination will be available to the general public. Phase III is unlikely to begin before 2004 when the new cell culture is licensed by the Food and Drug Administration (FDA).

Phase I Implementation in Clark County

Each acute care hospital with an Emergency Department in the county was invited to participate in this voluntary program. Participating hospitals are currently screening and recruiting volunteer from a number of disciplines to serve on their Smallpox Health Care Response Teams. We have asked hospitals to develop a team who could potentially provide round the clock care for a case of smallpox for 7-10 days, including physicians, nurses, and other healthcare personnel. For a complete list of the recommended composition of such a team, see http:///www.bt.cdc.gov/agent/smallpox/vaccination/acip-recs-oct2002.asp

About the Vaccine

The smallpox (vaccinia) vaccine is a live virus that multiples in the superficial layers of the skin. The vaccine does not contain variola virus, the virus that causes smallpox, and CANNOT cause smallpox. A successful vaccination in often referred to as a "take". Persons who were vaccinated in the remote past probably no longer have significant immunity. Vaccination after exposure to smallpox is effective in preventing or decreasing the severity of disease, even if given up to 3-4 days after exposure.

Vaccination Method

The smallpox vaccine is not given with a hypodermic needle. The vaccine is given using an individually wrapped, sterile, bifurcated (two-pronged) needle that is dipped into the vaccine solution. When removed, the needle retains a droplet of the vaccine. Multiple puncture of the deltoid area of the upper arm with the bifurcated needle is the recommended method of vaccination. The vaccination site will be covered with gauze, which will in turn be covered by a semi permeable dressing for those working in a healthcare setting.

Post-vaccination Site Care

Healthcare workers with direct patient contact who have been vaccinated will be provided with close follow-up and vaccination site care. Trained personnel assess the vaccinee and vaccination site daily. The dressing will be changed as needed, but no less often than every three days. Vaccinees with adverse reactions will be referred to specially trained physicians for further evaluation. Vaccinated healthcare workers may engage in normal patient care activities and do not pose a risk to patients provided that the workers keep their site covered as directed and engage in strict hand washing.

Healthcare workers are to be cautioned to treat contaminated materials as infectious waste (e.g., towels, gauze, instruments, etc.) These materials should be placed in an appropriate biohazard container. In the home environment, contaminated bandages should be placed in a sealed plastic bag. Clothing should be laundered in hot water and detergent (no dry cleaning).

Contraindications to Vaccination against Smallpox

In the event of a bioterrorism attack and exposure to smallpox, there are no contraindications to vaccination. The contraindications detailed in Attachment 1 only apply in the preparedness setting. In addition, there is a continued debate about many details of contraindication, and thus the contraindications listed may change as more information becomes available.

Normal Primary Vaccination, Revaccination and Normal Variants

A normal primary vaccination appears as a papule in 3-4 days, and rapidly progresses to a vesicle with the surrounding erythema by the 5th-6th day. The vesicle center becomes depressed and progresses to a well-formed pustule by the 8th-9th day. By the 12th day, the pustule crusts over forming a brown scab, which progresses from the center of the pustule to the periphery. After 2 ½ to 3 weeks, the scab detaches and a well-formed scar remains. If this reaction, called a "take," does not occur then one should assume that the individual is not immune. Expected systemic symptoms that may occur after vaccination, including pain at the site, fever, malaise, lymphadenopathy and erythema. Please **refer to Attachment 2** for more **information on a normal take, and expected side effects**.

Adverse Reactions

One of the most important roles of the community physician is awareness of potential adverse reactions, and rapid reporting and referral of patients with suspected adverse events. There are several serious or life-threatening adverse reactions described in Attachment 3. These adverse events are rare and most of them are preventable with careful screening, good site care and hygiene.

Severe adverse reactions require immediate telephone notification to the CDC the Clark County Health District and the Adverse Events Coordinator.

Careful screening of potential vaccinees for contraindications will decrease the frequency with which adverse reactions occur. Treatment is available for some of these conditions, and medications can be obtained through the CDC. Vaccinia Immune Globulin (VIG)/ Cidofovir is available for treatment of

certain reactions, consultation is available on a 24-hour basis to assist you in evaluating a potential adverse event

Please refer to Attachment 3.

Additional Information

Extensive resources regarding smallpox and smallpox vaccination are available on the CDC website and satellite broadcasts at www.bt.cdc.gov/agent/smallpox.

For all other questions concerning the county's smallpox vaccination plan, call 383-5016.

For questions regarding the National Smallpox Vaccination Program call the CDC hotline at:

1-888-246-2675 English 1-888-246-2857 Spanish 1-866-874-2646 Hearing Impaired

Contact/Reporting Information

To report known or suspected adverse reactions to smallpox vaccination, call 383-5160 or 383-1291

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Attachment 1

Contraindications to Vaccination Against Smallpox

Eczema or Atopic dermatitis and other acute, chronic, or exfoliative skin conditions

- Persons who have ever been diagnosed with eczema or Atopic dermatitis should not be vaccinated, even if the condition is not currently active. These patients are at high risk of developing eczema vaccinatum, a potentially severe and sometimes fatal complication. Additionally, persons with household contacts that have a history of eczema or Atopic dermatitis, irrespective of disease severity or activity, should not be vaccinated.
- ➤ If the potential vaccinee **or any of their household contacts** have other acute, chronic, or exfoliative skin conditions (e.g., burns, impetigo, chickenpox, contact dermatitis, shingles, herpes, severe acne, or psoriasis), they are at risk for inadvertent autoinoculation of the affected skin with vaccinia virus and should not be vaccinated until the condition(s) resolves.

Diseases or conditions which cause immunodeficiency or immunosuppression

- ➤ If a potential vaccinee **or any of their household contacts** have conditions such as HIV/AIDS, solid organ or stem cell transplant, generalized malignancy, leukemia, lymphoma, agammaglobulinemia, or autoimmune disease, they should not be vaccinated.
- ➤ HIV testing is recommended for persons who have any history of a risk factor for HIV infection and who are not sure if their HIV infection status. Anyone who is concerned that they could have HIV infection also should be tested.
- > Patients with autoimmune disease such as lupus or any of their household contacts should not be vaccinated.

Treatments which cause immunodeficiency of immunosuppression

➤ If a potential vaccinee **or any of their household contacts** are undergoing treatment with radiation, antimetabolites, alkaylating agents, systemic corticosteroids, (i.e. doses of prednisone higher than 2mg.kg/day or 20 mg/day for more than 14 days in the last 3 months) chemotherapy agents, or organ transplant medications, they should not be vaccinated. People who are receiving these therapies are at greater risk of serious adverse reactions to the smallpox vaccine.

Pregnancy

- ➤ Before vaccination, potential vaccinees should be asked if they **or any of their household contacts** are pregnant or intent to become pregnant in the next 4 weeks; those who respond positively should not be vaccinated.
- ➤ In addition, women who are vaccinated should be counseled not to become pregnant during the 4 weeks after vaccination.
- Routine pregnancy testing of women of childbearing age is not recommended.

Breastfeeding mothers

➤ Breastfeeding mothers should not receive the vaccine due to unknown risk of possible virus transmission in breast milk and due to the close contact with young infants which could increase the risk of inadvertent inoculation of their infants.

Previous allergic reaction to smallpox vaccine or any of the vaccine's components

- ➤ Vaccina vaccine (Dryvax) contains small amounts of polymixin B sulfate, streptomycin sulfate, chlortetracycline hydrochloride, neomycin sulfate, phenol and latex. Anyone who has experienced an anaphylactic reaction to these components should not be vaccinated.
- ➤ In addition, anyone who has experienced a previous allergic reaction to the smallpox vaccine should not be vaccinated.

Moderate or severe acute illness

- Moderate or severe acute illness is generally considered a contraindication to vaccination.
- > Vaccination should be deferred until the acute illness has resolved.

Children

- The advisory committee on Immunization Practice (ACIP) advises against non-emergency use of smallpox vaccine in persons younger than 18 years of age.
- > Child less than 12 months of age, in the household. The caregiver should not be vaccinated.

Ophthalmic disease

➤ Patients with inflammatory eye disease on ocular steroids, or post-surgical treatment on ophthalmologic steroids should not be vaccinated.

Cardiac History

- Have been diagnosed by a doctor as having a heart condition with or without symptoms, including conditions such as previous myocardial infarction (heart attack), angina (chest pain caused by lack of blood flow to the heart), congestive heart failure, cardiomyopathy (heart muscle becomes inflamed and doesn't work as well as it should), stroke or transient ischemic attack (a "mini-stroke" that produces stroke-like symptoms but not lasting damage), chest pain or shortness of breath with activity (such as walking up stairs), or other heart conditions being treated by a doctor. (While this may be a temporary exclusion, these people should not get the vaccine at this time.)
- Have 3 or more of the following risk factors: high blood pressure diagnosed by a doctor; high blood cholesterol diagnosed by a doctor; diabetes or high blood sugar diagnosed by a doctor; a first degree relative (for example, mother, father, brother, sister) who had a heart condition before the age of 50; and, you smoke cigarettes now. (While this may be a temporary exclusion, these people should not get the vaccine at this time.)

Careful screening is essential to minimize complications from the smallpox vaccine. Further information regarding vaccine contraindications can be found on the CDC website at www.cdc.gov/smallpox

Remember, people who have been directly exposed to the smallpox virus should get the vaccine, regardless of their health status.

Attachment 2

Normal Primary Vaccination, Revaccination, and Normal Variants

Normal Reaction Timeline

A normal primary vaccination appears as a papule in 3-4 days, and rapidly progresses to a vesicle with surrounding erythema by the 5^{th} - 6^{th} day. The vesicle center becomes depressed and progresses to a well-formed pustule by the 8^{th} - 9^{th} day. By the 12^{th} day, the pustule crusts over forming a brown scab, which progresses form the center of the pustule to the periphery. After $2\frac{1}{2}$ to 3 weeks, the scab detaches and a well-formed scar remains.

For more information with detailed photographs of normal reactions as well as adverse reactions, see http://www.bt.cdc.gov/training/smallpoxvaccine/reactions/
http://www.labt.org/pdfs/SmallpoxVaccinationGuide.pdf

No Reaction

Rarely, appropriate vaccination techniques may result in no reaction. The individual is not immune and vaccination must be repeated.

Systemic Symptoms

Systemic symptoms are expected and occur about a week after vaccination. These symptoms are more common after primary vaccination. These may include:

Fever, malaise, myalgia, headache, chills, nausea, fatigue, soreness at the vaccination site, lymphadenopathy (local), Intense erythema ringing he vaccination site

The occurrence of these normal reactions varies considerably form study to study. The prevalence is as follows:

Lymphadenopathy 25.0-50.0% Myalgia, headache, chills, nausea, fatigue 0.3-37% Fever > 37.7 C 2.0-16.0%

Normal Variants

Normal variants (rate:2.4%-6.6%) of vaccination are **NOT** adverse events and require no specific treatment. They include:

- ➤ Local satellite lesions (that are normal in appearance)
- > Lymphangitis form the site to regional nodes
- > Regional lymphadenopathy
- > Considerable local edema at the site
- > Viral cellulites (intense inflammation surrounding the papule and often confused with bacterial cellulitis)

Revaccination

The nature of the response to revaccination depends on the degree of residual immunity following previous vaccination. Revaccinees may either exhibit the typical primary reaction described above, which may progress through the stages more rapidly, or an equivocal reaction. Revaccination is indicated for an equivocal reaction.

If a patient has never had a successful take, the patient should not be informed that he/she is most likely NOT immune.

Attachment 3

Adverse Reactions

While most patients may have side effects such as pain, puritis, malaise and fever as described above, there are several serious of life-threatening adverse reactions described below. These events are rare and most of them are preventable with careful screening, good site care and hygiene. Careful screening of potential vaccinees for contraindications will decrease the frequency with which adverse reactions occur. Treatment available for some of these conditions can be obtained through the Clark County Health District by calling the following numbers. Hospitalization of patients with adverse events should be based on the degree of severity and infectivity. If patients are hospitalized, they should be under contact isolation.

Serious adverse events that may require treatment with VIG should be reported to the CDC Clinical Consultation Team through the Clinicians Information Hotline at 1-877-554-4625. Severe adverse reactions also require telephone notification to CCHD 383-5160 or 385-1291 and the State Adverse Event Coordinator 775-352-3640.

Rashes following smallpox vaccination:

Rarely, toxic and or/ hypersensitivity rashes may occur 1-2 weeks after vaccination (1/30,000 primary vaccinations). The rash varies form erythematous macular lesions to vesicles, urticaria, pustules, and typical bulls-eye lesions, all under the rubric "erythema multiforme." These are benign lesions that do not progress. Itching may accompany the rash. The most serious hypersensitivity reaction, Stevens Johnson Syndrome (SJS), is rare.

The diagnosis is made when the typical rash is seen in temporal association with primary vaccination. In the vesicular and pustular forms, it is necessary to distinguish these from generalized vaccinia or inoculation vaccinia. Treatment is symptomatic, usually employing an antihistamine and other measures to counteract itching. Mucosal involvement and evolution to SJS requires hospitalization and supportive care.

Severity: benign (except SJS-severe)

Frequency 1/30,000 primary vaccinations, SJS-rare)

VIG: not recommended

Reporting: report to CCHD and the State Adverse Event Coordinator.

Inadvertent Inoculation

The vaccination site contains high titers of vaccinia virus. Transfer of this virus from the primary site to other parts of the body, or to other individuals can occur if care is not taken. Autoinoculation historically occurred mainly in children, in 1/1800 primary vaccinations, and most frequently occurs on the face, eyelid, nose, mouth, rectum and genitalia. Lesions typically follow the same course as the primary vaccination. If there are only a few lesions, no specific treatment is required. Multiple lesions, especially if they are confluent and cover large portions of the body, warrant treatment with VIG. For lesions in or near the eye, refer immediately to an ophthalmologist to rule out vaccinia keratitis.

Severity: mild to severe hospitalize severe Frequency: 1/1800 primary vaccinations

VIG: indicated for extensive lesions, or ocular lesions without keratitis, not recommended for mild instances

Reporting: report to CCHD and the State Adverse Event Coordinator.

Vaccinia Keratitis

Although a rare occurrence, vaccinia virus can be implanted into diseased or injured conjunctivae and cornea resulting initially in viral replication with ulceration and ultimately in an antigen-antibody interaction leading to corneal cloudiness. Ten days after transfer the clinical signs of infection (a central, grayish, disciform corneal lesion) can be seen. **VIG is contraindicated for use in vaccinia keratitis.**Topical antiviral agents are the treatment of choice in consultation with an experienced ophthalmologist.

Severity: severe-if untreated

Frequency: rare VIG: contraindicated

Reporting: report immediately to CCHD and the State Adverse Event Coordinator

Bacterial Infection

Staphylococci and streptococci would be the most likely organisms encountered. Enteric or anaerobic organisms are the cause of bacterial superinfections of vaccinations. Infection should be preventable with good hygiene. The use of non-permeable dressings may result in increased maceration of the skin. Bacterial cultures should be obtained from the site by swabbing or aspiration.

Treatment is with antibiotics specific to the agent.

Severity: mild

Frequency: **uncommon** VIG: **not recommended**

Reporting: report to CCHD and the State Adverse Event Coordinator.

Eczema Vaccinatum

Individuals with eczema or Atopic dermatitis are at special risk for implantation of vaccinia virus into the diseased skin, sometimes with a fatal outcome. Atopic dermatitis implies both a skin abnormality and an immunologic difference, ill-defined, in individuals subject to this disease. Transfer of Vaccina virus can occur by autoinoculation or from contact with a vaccinee whose lesion is in the florid stages. Because most individuals have large contiguous patches of skin in the affected area, confluent lesions are the rule (on the face and limbs primarily). Scarring may be extensive.

With early recognition and prompt treatment with VIG, mortality can be reduced to zero, and morbidity alleviated.

Severity: **severe**, **especially if untreated** Frequency: **1/25,000 primary vaccinations**

VIG: indicated

Reporting: report immediately to CCHD and the State Adverse Event Coordinator

Generalized Vaccinia

Generalized vaccinia is rare, usually benign, and the result of a viremia. With in a week, lesions appear on any part of the body (most often on the trunk and abdomen, less commonly on the face, limbs, palms and soles). Lesions undergo rapid evolution to scarring. Subtle minor immunologic abnormalities, particularly of the immunoglobulin B-cell stem, are suspected to be present.

The illness should be differentiated from erythema multiforme, eczema vaccinatum, progressive vaccinia, severe chickenpox, and smallpox.

Consultation with and immunologist/allergist is strongly recommended.

Most instances of generalized vaccinia, particularly if the lesions are few, require no specific therapy. In some cases, with extensive lesions, or in recurrent disease, VIG should be administered.

Severity: benign, no hospitalization (exception: recurrent generalized vaccinia-hospitalize)

Frequency: 1/4000 primary vaccination

VIG: Indicated if severe or recurrent; not recommended if mild or limited – most instances

Reporting: report immediately to CCHD and the State Adverse Event Coordinator

Progressive Vaccinia

Progressive Vaccinia (also known as vaccinia necrosum) is a rare complication occurring primarily in T-cell deficient persons. Patients with T-cell deficiencies (cancer, HIV/AIDS, or those receiving immunosuppressive drugs) are at risk. The primary vaccination fails to heal and spreads both locally and through the blood stream to other parts of the body. Each lesion spreads without an inflammatory response. Untreated patients may succumb to viral infection or to a secondary fungal, bacterial, or parasitic infections. Complications include septic shock, disseminated intravascular coagulation, and superimposed microbial infections.

Viral and immunologic laboratory investigation is necessary.

Therapy consists of intensive administration of antibody, usually in the form of VIG, in addition to supportive care.

Severity: severe-hospitalize

Frequency: 1/600,000 primary vaccinees

VIG; INDICATED

Reporting: report immediately to CCHD and the State Adverse Event Coordinator

Post-Vaccinia Encephalitis

Post-vaccinial encephalitis is a rare complication of primary vaccination (15 per million primary vaccinations). Encephalitis occurs 10-14 days after vaccination with headache, vomiting, drowsiness and fever as the first symptoms. In severe cases, life-threatening complications can develop.

Severity: severe-hospitalize

Frequency: 1/80,000 primary vaccinees

VIG: not indicated

Reporting: report immediately to CCHD and the State Adverse Event Coordinator

Fetal Vaccina

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

Severity: severe hospitalize

Frequency: rare VIG: unknown

• Reporting: report immediately to CCHD and the State Adverse Event Coordinator

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 post-vaccinia encephalitis or progressive vaccinia.

• Reporting: report immediately to CCHD and the State Adverse Event Coordinator

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Smallpox	Vaccine	Adverse	Reactions	Rates	- (ner millini	ı nrımar	v vaccinations)
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Adverse Reaction	Rate per Primary Vaccination			
Inadvertent inoculation	25-529			
Generalized vaccinia	23-242			
Eczema vaccinatum	10-39			
Progressive vaccinia	0.9-1.5			
Post-vaccinia encephalitis	3-12			
Death	1			

Vaccinia Immune Globulin (VIG)

Vaccinia Immune Globulin (VIG) was produced in the 1960's from plasma obtained from recently vaccinated donors and was administered intramuscularly.

Vials of intramuscular VIG (IM-VIG) are stored at the CDC and are available only under investigational New Drug (IND) protocols. An effort is underway to produce new lots that will meet the standards for intravenous VIG (IV-VIG).

- Serious adverse events that may require treatment with VIG should be reported to the CDC Clinical Consultation Team through the Clinicians Information Hotline at 1-877-554-4625
- Report immediately by telephone to the Clark County Health District any known or suspected adverse reactions to smallpox vaccinations that are serious, life-threatening and/or require hospitalization. During work hours: 702-383-5160, after hours 702-385-1291.
- Obtain urgent consultation from the State Adverse Event Coordinator when encountering severe adverse reactions for which Vaccinia Immune Globulin (VIG)/Cidofovir may be required. 775-352-3640.

VIG Administration

	Autoinoculation (extensive lesions)
Indicated	Eczema vaccinatum
	Generalized vaccinia (if severe or recurrent)
	Progressive vaccinia (also known as vaccinia necrosum)
	Autoinoculation (mild instances)
Not-Recommended	Generalized vaccinia (mild or limited – most instances)
	Erythema multiforme
	Post-vaccinia encephalitis
Contraindicated	Vaccinia keratitis (may produce severe corneal opacities)

Dosage

The usual dose of IM-VIG is 0.6 ml/kg-body weight. As much as 1-10 ml/kg body weight has been used in serious, life threatening complications.

The exact dose of IV-VIG has not been determined but most likely will be administered at lower dose that the intramuscular preparation.

Adopted from the CDC and the County of Los Angeles Department of Health Services

Web sites

http://www.bt.cdc.gov/index.asp

http://www.bt.cdc.gov/agent/smallpox/reference/resource-kit.asp

http://www.bt.cdc.gov/agent/smallpox/response-plan/files/annex-2.pdf

http://www.cidrap.umn.edu/cidrap/

http://www.who.int/emc/diseases/smallpox/factsheet.html

http://www.nlm.nih.gov/medlineplus/smallpox.html

http://jama.ama-assn.org/cgi/content/short/281/22/2127

http://www.os.dhhs.gov/

http://www.cdc.gov/nip/ed/smallpox-trg/clinician-should-know/default.htm