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Updated ACIP Recommendations for Use of Smallpox Vaccine

Since smallpox was eradicated in 1980 and no longer occurs naturally, the only potential reemergence of this disease would be as a result of deliberate release in an act of bioterrorism. In June 2002 the Advisory Committee on Immunizations (ACIP) updated their 2001 recommendations for use of smallpox (vaccinia) vaccination in preparation for a possible bioterrorist attack. The following report summarizes the ACIP updated recommendations for smallpox vaccination of the general population and of persons designated to respond to suspected or confirmed cases. In addition, these new guidelines clarify and expand the primary strategy for control and containment of smallpox in the event of an outbreak.

Vaccination protocols remain unchanged for laboratory workers who directly handle recombinant vaccinia viruses derived from vaccinia strains that are not highly attenuated or from other orthopox viruses that infect humans (eg, monkeypox, cowpox, vaccinia, and variola). For aspects still under review (eg, screening for contraindications and care of the vaccination site), the June 2001 recommendations should be used until new ones are published.

ACIP will continue to revise vaccination recommendations as needed to provide new information or developments related to smallpox disease, smallpox (vaccinia) vaccines (including vaccine licensure), risk of smallpox attack, smallpox (vaccinia) vaccine adverse events, and the experience gained in the implementation of the current recommendations.

Smallpox Transmission and Control

Smallpox is transmitted from an infected person once a rash appears. Transmission does not occur during the prodromal period that precedes the rash, but rather by large droplet nuclei; only rarely has airborne transmission been documented. The transmission rate for smallpox is less than that for measles, pertussis, or influenza. The greatest risk of infection occurs among household members and close contacts of persons with smallpox, especially those with prolonged face-to-face exposure.

The primary strategy to control an outbreak of smallpox and interrupt disease transmission is surveillance and containment, which includes ring vaccination and isolation of persons at risk of contracting smallpox. This strategy involves identification of infected persons through intensive surveillance, isolation of infected persons, vaccination of household contacts and other close contacts of infected persons (ie, primary contacts), and vaccination of household contacts of the primary contacts (ie secondary contacts). This strategy was instrumental in the ultimate eradication of smallpox as a naturally occurring disease even in areas that had low vaccination coverage.

Surveillance and containment activities have occasionally been supplemented with voluntary vaccination of other individuals to expand the ring of immune individuals within an outbreak area and to further reduce the chance of secondary transmission from unidentified / unisolated smallpox patients. Such supplemental vaccination activities have been initiated depending upon the size of the smallpox outbreak and the resources that were available for rapid and thorough contact tracing. Regardless of the geographic distribution, number of cases, or

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number of concurrent outbreaks, surveillance and containment activities remain the primary disease control strategy.

Supplemental Vaccine Use: Critical Considerations

Level of disease risk and threat. The risk for smallpox occurring as a result of bioterrorism is considered low, and the at-risk population cannot be determined. Regardless of the mode of release in a bioterrorism event, the epidemiology of subsequent person-to-person transmission would be consistent with prior experience. Additionally, appropriate infection control measures, including use of personal protection equipment (PPE), would provide protection for health care workers.

Expected severe adverse reactions to vaccination. It is assumed that potential vaccinees and their close contacts would be vigorously screened for contraindications to vaccination. Recommended precautions must be taken to minimize the risk of adverse events among vaccinees as well as their close contacts (eg, patients and household members). Additional information on potential adverse reactions is available at www.cdc.gov/mmwr/preview/mmwrhtml/rr5010a1.htm. (See pages 10-11.)

Vaccine and vaccinia immune globulin (VIG) supply. Smallpox (vaccinia) vaccine and VIG are currently available only under investigational new drug (IND) protocols (ie, protocols for products that are not yet licensed). Vaccination would be voluntary and appropriate informed consent, patient follow up, and administrative oversight by federal, state, and local public health officials would be required.

State and local vaccination capacity and capability. Surveillance and containment, including ring vaccination, is the primary strategy for the control and containment of smallpox. In select circumstances, state and local health departments could choose to immunize additional groups, up to and including their entire population.

Smallpox Vaccines and VIG Availability

Prior to the terrorist attacks in the fall of 2001, the Department of Health and Human Services (DHHS) had already begun to increase public health preparedness for potential bioterrorist attacks through expansion of the existing smallpox (vaccinia) vaccine stockpiles. The anthrax attacks in the fall of 2001 resulted in public health activities to further enhance capability to respond to the deliberate release of smallpox. These efforts included accelerated production of additional doses of smallpox (vaccinia) vaccine.

Currently, there are no commercially available (licensed) smallpox vaccines. Smallpox vaccines previously produced by Wyeth (Dryvax) and Aventis-Pasteur are available under CDC's IND protocols. Both vaccines were prepared from calf lymph with a seed virus derived from the New York City Board of Health strain of vaccinia virus. Studies conducted among young adults with no previous smallpox vaccination history showed that a 1:5 dilution of Dryvax (Wyeth Laboratories, Inc) produced take rates among vaccinees equivalent to those among recipients of the undiluted vaccine. (A take rate is a measure of successful vaccination based on reaction at the injection site.)

In October 2001 the federal government contracted with Acambis and Acambis-Baxter Pharmaceuticals for at least 209 million doses of smallpox vaccine produced in cell culture. These vaccines use a clone of the same strain of vaccinia virus (New York City Board of Health), used in the smallpox vaccines produced from calf lymph. These doses are

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expected to be available at the end of 2002 or soon thereafter. Smallpox vaccines are formulated and packaged for administration with a bifurcated needle, which provides a fast, easy, and effective means for adminis-tration. All vaccines are packaged in 100 dose vials, except when Dryvax is diluted 1:5 resulting in vials that contain 500 doses.

The CDC National Pharmaceutical Stockpile (NPS) has developed protocols to allow for the rapid, simultaneous delivery of smallpox vaccine to every state and US territory within 12 to 24 hours. State and local bioterrorism response plans should provide for the rapid distribution of vaccine within their jurisdiction.

Currently, there is enough VIG available under an IND protocol to treat the adverse reactions that would be expected to result from the vaccination of 4 to 6 million people. Contracts for additional supplies of VIG are in progress.

Surveillance

Currently, cases of febrile rash illnesses for which smallpox is considered in the differential diagnosis must be reported immediately to local and/or state health departments. Initial cases of smallpox must be laboratory confirmed. At this time, laboratory confirmation for smallpox is available only at CDC. Clinical consultation and a preliminary laboratory diagnosis can be completed within 8 to 24 hours.

Health professionals in Texas can call 800/252-8239 *to report suspected smallpox and to coordinate testing and control measures.*

Surveillance activities, including notification procedures and laboratory confirmation of cases, would change if smallpox were confirmed. Additional information regarding surveillance activities following laboratory confirmation of a smallpox outbreak can be found in the CDC Interim Smallpox Response Plan and Guidelines, available online at www.bt.cdc.gov/DocumentsApp/Smallpox/RPG/index.asp.

The CDC rash illness assessment algorithm is online at www.cdc.gov/nip/smallpox/Providers.htm#Poster. Since this large poster is difficult to print, a copy can be ordered online at www2.cdc.gov/nchstp_od/PIWeb/niporderform.asp.

Pre-outbreak Smallpox Vaccination Recommendations

For the General Population.

Vaccination of the general population is not recommended when there are no reports of confirmed smallpox and the risk of deliberate release of smallpox is low. In these circumstances the risks of potential complications of vaccination outweigh the potential benefits.

Recommendations regarding pre-outbreak smallpox vaccination are being made on the basis of an assessment that considers the risks of disease and the benefits versus the risks of vaccination. The live smallpox (vaccinia) vaccine virus can be transmitted from person to person. In addition to sometimes causing adverse reactions in vaccinated persons, the vaccine virus can cause adverse reactions in the contacts of vaccinated persons. Currently available vaccines would most likely cause adverse reactions similar to those previously observed, but there could be a greater number people at risk today due to the increased prevalence of altered immune status in the population.

For Smallpox Response Teams.

To enhance public health preparedness and response for smallpox control, specific teams at the federal, state, and local level should be established to investigate and facilitate the diagnostic work-up of the initial suspect case/s of smallpox and initiate control measures.

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These smallpox response teams might include persons designated as medical team leaders, public health advisors, medical epidemiologists, disease investigators, diagnostic laboratory scientists, nurses, personnel who would administer smallpox vaccines, and security/law enforcement personnel. Such teams may also include medical personnel who would assist in the evaluation of suspected smallpox cases.

Each state and territory should establish and maintain at least one smallpox response team. Members of these response teams should receive smallpox vaccination.

Considerations for additional teams should take into account population and geographic considerations and should be developed in accordance with federal, state, and local bioterrorism plans.

Designated Smallpox Healthcare Personnel at Designated Hospitals. Smallpox vaccination is recommended for selected personnel in facilities designated to serve as referral centers to provide care for the initial cases of smallpox. These facilities would be chosen by the appropriate bioterrorism and public health authorities, and personnel within these facilities would be designated by the hospital.

As outlined in the CDC Interim Smallpox Response Plan and Guidelines, state bioterrorism response plans should designate initial smallpox isolation and care facilities. In turn, these facilities should choose individuals who would care for the initial smallpox cases. To staff augmented medical response capabilities, additional personnel should be identified and trained to care for smallpox patients.

Implementation of Recommendations

Implementing the ACIP recommendations requires attention to a number of issues, which include the following: health care provider and public education, provider training, availability of vaccine and VIG, appropriate IND protocols, screening, strategies to minimize vaccine wastage, vaccine adverse event surveillance, and other logistical and administrative issues.

The latest draft of the current ACIP recommendations, Use of Smallpox (Vaccinia) Vaccine, June 2002, was approved by ACIP on June 20. It is now under consideration by CDC and the Department of Health and Human Services. This document is available online at www.cdc.gov/nip/smallpox/supp_recs.htm.

F*or further information regarding Texas Department of health readiness for potential bioterroristic release of smallpox, contact the Office of the State Epidemiologist at* 512/458-7219 *and visit the TDH Immunization Division website:* www.immunizetexas.com

First US Case of VRSA Identified

In June 2002 vancomycin resistant *S. aureus* (VRSA) was identified at a hospital laboratory in Michigan. The first clinical isolate of *S. aureus* with reduced susceptibility to vancomycin was reported from Japan in 1996.[1] As of June 2002, 8 cases of clinical infection caused by vancomycin-intermediate resistant *S. aureus* (VISA) had been confirmed in US patients.[2,3]

This DPN report is adapted from the July 5, 2002, MMWR report on the first clinical isolate in the US of *S. aureus* found to be fully resistant to vancomycin. Testing was done using interpretive criteria defined by the National Committee for Clinical Laboratory Standards.[4]

Background

Staphylococcus aureus causes a wide range of human infections and is an important cause of health-care associated infections.[5,6] The introduction of new classes of antimicrobials usually has been followed by emergence of resistance in *S. aureus*.

The resistance level of an antibiotic is expressed in terms of minimum inhibitory concentration (MIC). The MIC breakpoints for vancomycin are as follows: sensitive, MIC $\leq$ 4 µg/mL; intermediate, MIC=8 µg/mL; and resistant, $\geq$32 µg/mL. The result reported for the 1996 isolate identified in Japan was identified as having intermediate resistance. The result for the first VRSA isolate to be identified in the US was MIC $\geq$ 128 µg/mL.

Case Report

VRSA was isolated in June 2002 from a swab obtained from the catheter exit site of a Michigan resident aged 40 years. This patient had diabetes, peripheral vascular disease, and chronic renal failure. The patient received dialysis at an outpatient facility (dialysis center A). Since April 2001 the patient had been treated for chronic foot ulcerations with multiple courses of antimicrobial therapy, some of which included vancomycin. In April 2002 the patient underwent amputation of a gangrenous toe and subsequently developed methicillin-resistant *S. aureus* bacteremia caused by an infected arteriovenous hemodialysis graft. The infection was treated with vancomycin, rifampin, and removal of the infected graft.

In June the patient developed a suspected catheter exit-site infection, and the temporary dialysis catheter was removed. Cultures of the exit site and catheter tip subsequently grew *S. aureus* resistant to oxacillin (MIC >16 µg/mL) and vancomycin (MIC >128 µg/mL). A week after catheter removal, the exit site appeared healed; however, the patient's chronic foot ulcer appeared infected. VRSA, vancomycin-resistant *Enterococcus faecalis* (VRE), and *Klebsiella oxytoca* also were recovered from a culture of the ulcer. Swab cultures of the patient's healed catheter exit site and anterior nares did not grow VRSA. To date, the patient is clinically stable, and the infection is responding to outpatient treatment consisting of aggressive wound care and systemic antimicrobial therapy with trimethroprim/sulfamethoxazole.

The VRSA isolate recovered from the catheter exit site was identified initially at a local hospital laboratory using commercial MIC testing and was confirmed by the Michigan Department of Community Health and CDC. Identification methods used at CDC included traditional biochemical tests and DNA sequence analysis of gyrA and the gene encoding 16S ribosomal RNA. Molecular tests for genes unique to enterococci were negative. The MIC results for vancomycin, teicoplaninin, and oxacillin were >128 µg/mL, 32 µg/mL, and >16 µg/mL, respectively, by the broth microdilution method. The isolate

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contained the vanA vancomycin resistance gene from enterococci, which is consistent with the glycopeptide MIC profiles. It also contained the oxacillin-resistance gene mecA. The isolate was susceptible to chloramphenicol, linezolid, minocycline, quinupristin/dalfopristin, tetracycline, and trimethoprim/sulfamethoxazole.

Epidemiologic and laboratory investigations are under way to assess the risk for transmission of VRSA to other patients, health care workers, close family, and other contacts. To date, no VRSA transmission has been identified.

Infection control practices in dialysis center A were assessed; all health care workers followed standard precautions consistent with CDC guidelines.[7] After the identification of VRSA, dialysis center A initiated special precautions on the basis of CDC recommendations,[8] including using gloves, gowns, and masks for all contacts with the patient; performing dialysis with a dedicated dialysis machine during the last shift of the day in an area separate from other patients; having a dialysis technician dedicated to providing care for the patient; using dedicated, noncritical patient-care items; and enhancing education of staff members about appropriate infection control practices. Assessment of infection control practices in other health care settings in which the patient was treated is ongoing.

MMWR Editorial Note

The introduction of new classes of antimicrobials usually has been followed by emergence of resistance in *S. aureus*. After the initial success of penicillin in treating *S. aureus* infection, penicillin-resistant *S. aureus* became a major threat in hospitals and nurseries in the 1950s, requiring the use of methicillin and related drugs for treatment of *S. aureus* infections. In the 1980s, methicillin-resistant *S. aureus* emerged and became endemic in many hospitals, leading to increasing use of vancomycin. In the late 1990s, cases of VISA were reported.

Although the acquired vancomycin-resistance determinants vanA, vanB, vanD, vanE, vanF, and vanG have been reported from VRE, these resistance determinants have not previously been identified in clinical isolates of *S. aureus*.[9] Conjugative transfer of the vanA gene from enterococci to S. aureus has been demonstrated in vitro.[10] The presence of vanA in this VRSA suggests that the resistance determinant might have been acquired through exchange of genetic material from the vancomycin-resistant enterococcus also isolated from the swab culture. This VRSA isolate is susceptible in vitro to several antimicrobial agents, including antimicrobials recently approved by the Food and Drug Administration (ie, linezolid and quinupristin/dalfopristin) with activity against glycopeptide-resistant Gram-positive microorganisms.

In 1997 the Healthcare Infection Control Practices Advisory Committee published guidelines for the prevention and control of staphylococcal infection associated with reduced susceptibility to vancomycin;[8] plans to contain VISA/VRSA on the basis of CDC recommendations have been established in some state health departments. In the health care setting, a patient with VISA/VRSA should be placed in a private room and have dedicated patient-care items. Health care workers providing care to such patients should follow contact precautions (ie, wearing gowns, masks, and gloves and using antibacterial soap for hand washing). These control measures were adopted by dialysis center A immediately following confirmation of the VRSA isolate. To date, there has been no documented spread of this microorganism to other patients or health care workers.

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The emergence of VRSA underscores the need for programs to prevent the spread of antimicrobial-resistant microorganisms and to control the use of antimicrobial drugs in health care settings. Strategies to improve adherence to current guidelines to prevent transmission of antimicrobial resistant microorganisms in health-care settings should be a priority for all health-care facilities in the United States. *S. aureus* should be tested for resistance to vancomycin using a MIC method. The isolation of *S. aureus* with confirmed or presumptive vancomycin resistance should be reported immediately to the Texas Department of Health Infectious Disease Epidemiology and Surveillance Division by calling 800/252-8239 or 512/458-7676.

Adapted from CDC. *Staphylococcus aureus* Resistant to Vancomycin—United States, 2002. MMWR 2002;51(26).

This issue is available online at this CDC website: www.cdc.gov/mmwr/preview/mmwrhtml/mm5125a1.htm.

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Texas Department of Health
1100 West 49th Street
Austin, TX 78756-3199
Phone: (512) 458-7677
Fax: (512) 458-7340
Email: dpn@tdh.state.tx.us

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Central Texas Floods: Summer 2002

Worldwide, floods account for an estimated 40% of all natural disasters. Flash flooding, the leading cause of weather related mortality in the United States, causes approximately 200 deaths per year. By July 10, 2002, flooding in Central Texas left 9 people dead and 24 counties declared as disaster areas eligiblefor state and/or federal emergency relief. In October 1998, 60 (24%) Texas counties reported flooding as a result of an unusual storm system that also spawned several tornados; 36 counties became eligible for federal and/or state assistance. Estimated damages from the 1998 floods were reported at just over $900 million; public property, almost 12,000 homes, and 700 businesses were affected. A total of 31 flood related deaths were reported from 9 Texas counties. (Go to www.tdh.state.tx.us/injury/reports/storms/st_disc.htm for complete TDH reports on the Texas floods of 1998.)

Although the physical devastation and drowning risk associated with flooding is of foremost concern, other public health concerns that arise during and after a flood are also important. The recent flooding in Central Texas resulted in a July 3 alert from the San Antonio Metropolitan Health District (SAMHD) that residents of several northern areas of the metropolitan area should boil all water for consumption. It was also advised that private well water in the entire SA metropolitan area should not be consumed until it is tested and disinfected after flood waters recede. Free bottled water has been provided to residents in targeted areas. Residents in all flooded areas should be alerted to listen for public announcements regarding the safety of their local water supplies.

Food safety is also of concern: electrical problems can result in refrigeration lapses, and even containers for nonrefrigerated food can be damaged and the contents potentially contaminated. Downed power lines can create significant health risks, and clean-up efforts following flooding necessitate precautions to prevent disease and injury. Often overlooked in the wake of a flood are the personal physical and emotional stresses such as sleeplessness, anxiety, anger, depression, lethargy, and fatigue that can progress to more serious ill health.

Updates on the current flooding situation in Texas are availabe online at www.txdps.state.tx.us/dem. A list of TDH recommendations on life-saving precautions during floods is available at www.tdh.state.tx.us/injury/reports/storms/st_disc.htm. The CDC brochure, "Flood: A Prevention Guide to Promote Your Personal Health and Safety," is available online at www.cdc.gov/nceh/emergency/flood/default.htm.