

Human Rabies — Missouri, 2014

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On September 18, 2014, the Missouri Department of Health and Senior Services (MDHSS) was notified of a suspected rabies case in a Missouri resident. The patient, a man aged 52 years, lived in a rural, deeply wooded area, and bat sightings in and around his home were anecdotally reported. Exposure to bats poses a risk for rabies. After two emergency department visits for severe neck pain, paresthesia in the left arm, upper body tremors, and anxiety, he was hospitalized on September 13 for encephalitis of unknown etiology. On September 24, he received a diagnosis of rabies and on September 26, he died. Genetic sequencing tests confirmed infection with a rabies virus variant associated with tricolored bats. Health care providers need to maintain a high index of clinical suspicion for rabies in patients who have unexplained, rapidly progressive encephalitis, and adhere to recommended infection control practices when examining and treating patients with suspected infectious diseases.

Case Report

On the morning of September 12, 2014, a Missouri resident, a man aged 52 years, visited hospital A's emergency department for evaluation of acute onset of severe neck pain that radiated down his left arm to his hand. After a cervical spine radiograph, a diagnosis of cervical muscle strain and radiculopathy was made, for which the patient received injections of orphenadrine (a muscle relaxant) and ketolorac (a nonsteroidal anti-inflammatory drug). He was instructed to take ibuprofen and cyclobenzaprine (a muscle relaxant) for pain relief and to return if symptoms worsened. The next day, he awoke with numbness and tingling in his left arm, severe bilateral upper body tremors, and sweating, as well as continued neck pain. He returned to hospital A's emergency department, where he received a diagnosis of a herniated disc and was discharged with instructions to take oral prednisone

and oxycodone HCl/acetaminophen. That same evening, while the patient was at home, his symptoms progressed, and he became anxious and fearful; family members transported him back to the emergency department, during which time he began experiencing visual hallucinations. He was admitted to hospital A with a diagnosis of suspected serotonin syndrome secondary to the cyclobenzaprine.

On September 13, the patient was treated with oral ibuprofen and cyproheptadine and with parenteral lorazepam, diazepam, diphenhydramine, and haloperidol. On September 14, losartan and hydrochlorothiazide were prescribed to be taken orally for hypertension, but the patient was unable to swallow these medications. His condition progressively worsened, with the development of considerable rigidity and action tremors in his upper extremities. That same day, he was transferred to hospital B, a tertiary care referral hospital, for neurologic

INSIDE

- 257 Use of Vaccinia Virus Smallpox Vaccine in Laboratory and Health Care Personnel at Risk for Occupational Exposure to Orthopoxviruses — Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015
- 263 Building and Strengthening Infection Control Strategies to Prevent Tuberculosis — Nigeria, 2015
- 267 Revision to CDC's Zika Travel Notices: Minimal Likelihood for Mosquito-Borne Zika Virus Transmission at Elevations Above 2,000 Meters
- 269 Announcements
- 270 QuickStats

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evaluation. Upon admission, he was febrile (104.9°F [40.5°C]), tachycardic, tachypneic, and hypertensive with bilateral upper extremity tremors and whole body myoclonic jerks. On September 15, he required intubation and mechanical ventilation for airway protection. Before intubation, the patient orally communicated an aversion to water.

During the next 11 days the patient underwent an extensive laboratory evaluation to determine the cause of his encephalopathy, including a urine drug screen, tricyclic antidepressant levels, an arbovirus panel, and testing for antibodies to Rocky Mountain spotted fever, ehrlichiosis, syphilis, and herpes simplex virus; all test results were negative. The peripheral white blood cell count and liver enzymes were both slightly elevated. On September 19, a traumatic lumbar puncture yielded hemorrhagic cerebrospinal fluid (CSF) with elevated glucose, protein, and white blood cells. Electroencephalogram studies indicated generalized slowing of brain activity, minimal reactivity to noxious stimulation, and absent posterior dominant rhythm, consistent with encephalopathy. The patient required dopamine and norepinephrine for cardiovascular support, continuous mechanical ventilation for acute hypoxemic respiratory failure, and hemodialysis for acute kidney injury. Initial treatment included broad-spectrum antibiotics for presumed sepsis and acyclovir for suspected herpes encephalitis.

Family members initially reported that the patient lived in a trailer on 97 densely wooded acres, but his exposure to wildlife was not known at that time. Because of the acute and rapidly progressive clinical course of his illness and the elimination

of the most common etiologies of encephalitis from the differential diagnoses, the possibility of rabies was considered, public health officials notified, and confirmatory laboratory testing initiated on September 18. Serum, CSF, nuchal skin biopsy, and saliva specimens collected on September 19 were submitted to CDC on September 22 for rabies testing.

On September 24, rabies was confirmed by the presence of rabies virus antigen in the skin biopsy, and the detection of rabies virus in saliva and skin by reverse transcription polymerase chain reaction. Genomic sequencing found the variant to be associated with the tricolored bat (*Perimyotis subflavus* [formerly *Pipistrellus subflavus*]). Neither antirabies antibodies (immunoglobulin G or immunoglobulin M) nor rabies virus neutralizing antibodies were detected by indirect fluorescent antibody or rapid fluorescent focus inhibition tests in the serum and CSF specimens collected on September 19. However, both antirabies antibodies and rabies virus neutralizing antibodies were subsequently detected in a serum specimen collected on September 25. Because of the advanced stage of illness and worsening prognosis, the Milwaukee protocol (1) was not initiated. On September 26, the family elected to withdraw life support, and the patient died shortly thereafter.

Public Health Investigation

On September 18, an infectious disease specialist at hospital B notified MDHSS of the suspected human rabies case. After confirmation of the diagnosis, MDHSS, local public

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health agency officials, and infection prevention specialists at hospitals A and B interviewed family members, friends, and hospital personnel in an effort to determine the patient's exposure and travel history and to identify any high-risk exposures that would require rabies postexposure prophylaxis (PEP) (2). Two questionnaires developed by CDC were used to evaluate health care workers and family and community members for possible exposure to the patient.

The variant identified from genetic sequencing of rabies virus from the patient was from *Perimyotis subflavus* (tricolored bat), one of the smallest bats in eastern North America. The rabies variant associated with this bat species occasionally infects other bats (e.g., *Tadarida brasiliensis* [big brown bat]) as well as cats, foxes, and other species. Any of these animal sources could have accounted for the patient's exposure.

Although the exact exposure date is unknown, the patient had reported seeing a bat in his home in late August or early September 2014. He also worked in a warehouse in which coworkers reported that bats are occasionally seen, but no bat sightings in the several weeks before the patient's illness onset were reported. Public health investigators who visited the patient's trailer home noted several places where a small animal, such as a bat, could have entered. A family member reported having observed bats roosting on a utility pole near the trailer in the past. This information, combined with documentation of previous bat-variant rabies cases with undocumented or unidentified exposures (3), makes a bat the most likely source of rabies infection in this patient. Symptom onset was estimated to be September 6, based on a family member's recollection that the patient complained of fatigue and neck pain during that weekend. Rabies infection from a bat exposure during late August or early September would suggest a shorter incubation period than the typical 3–8 weeks (2). Thus an earlier, undetected bat exposure might be more likely.

Nine family members and friends were identified as having potential high-risk exposures to the saliva from the patient through mucous membranes or small, open hand wounds; all received rabies PEP. Among the 73 health care workers who provided care to the patient at hospitals A and B, seven met Advisory Committee on Immunization Practices criteria for rabies PEP (2). Health care-associated exposures primarily occurred through prolonged contact with the patient's face, saliva, or tears with ungloved hands and nonintact skin.

Discussion

This case illustrates the importance of educating the public about potential rabies reservoirs and exposure sources in the United States and of promptly seeking medical attention after any potential rabies exposure. Rabies is preventable after an

Summary

What is already known about this topic?

Human rabies in the United States is rare (one to three cases are reported annually). However, because the virus is endemic in the U.S. wildlife population, susceptible domestic animals and humans exposed to rabid animals are at risk for developing rabies infection.

What is added by this report?

Early diagnosis of human rabies infection might be hampered by delayed recognition, given the rarity of the disease, nonspecific initial symptoms, and difficulty in obtaining animal exposure history once the patient is in the later stages of illness.

What are the implications for public health practice?

To prevent rabies 1) continue to educate the public and health care providers about the risk for exposure to rabies virus from bats and other mammalian species and the importance of prompt medical evaluation and initiation of postexposure prophylaxis and 2) promote consistent adherence to standard precautions among health care providers in the treatment of all potentially infectious patients.

exposure through timely PEP, which includes wound washing and administration of rabies immune globulin and rabies vaccine (2). Bat exposures are high-risk exposures for rabies virus infection, particularly because the wounds inflicted by bats are often minor and easily overlooked. No evidence-based treatment approach for clinical rabies exists. An experimental approach, the Milwaukee protocol, which was first used in 2004 in a Wisconsin patient who survived rabies infection (4), has been implemented with varying outcomes (1).

This case is the second case of human rabies in Missouri in 6 years; during this time, specimens from six humans were referred from the Missouri State Public Health Laboratory to CDC for antemortem rabies testing. In 2008, a male aged 55 years died of rabies in Missouri after being bitten on the ear by a bat (5); before this, the last Missouri rabies case was reported in 1959. During 2008–2011, a total of 11 human rabies cases were reported in the United States and Puerto Rico, including five cases with infections acquired overseas (6). Among the six domestically acquired cases, five were associated with bat variant rabies viruses; in three cases, a confirmed bat bite was reported. In Missouri, bats and skunks are principal reservoirs of rabies (7). Given that wild animals might not display obvious signs of rabies illness, it is important that, whenever possible, all bats and wild terrestrial carnivores implicated in a potential rabies exposure be euthanized and tested for rabies. This testing can ensure that PEP is appropriately administered to prevent rabies in persons with exposures to confirmed rabid animals, and might avoid misadministration of PEP to nonexposed persons.

A review of human rabies cases in the United States during 1960–2010 found that a median of 39 contacts per case (range = 1–180) received PEP (8). Sixteen persons with possible exposure to the 2014 Missouri patient were identified (seven health care workers and nine community members). According to the indications for rabies PEP (2), human-to-human transmission of rabies virus can occur through exposure to virus in saliva through mucous membranes or fresh, open cuts in the skin. Consistent adherence to standard precautions should minimize the need for rabies PEP in health care settings (9).

Public education campaigns aimed at raising rabies awareness should address misconceptions about risk associated with bat encounters (e.g., lack of knowledge that bats can transmit rabies through small, undetected bites) that can lead to a delay in the timely response to potential rabies virus exposures. These campaigns should also emphasize the importance of completing the full rabies PEP series once initiated, unless the exposure source is determined not to be rabid through laboratory testing or successful (i.e., remains healthy) completion of a 10-day observation period for a dog, cat, or ferret (2). In addition to the importance of public education, health care workers should consider rabies in the differential diagnosis of any patient with acute, unexplained encephalitis, and use appropriate infection control practices when examining and treating patients with a suspected infectious disease.

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Use of Vaccinia Virus Smallpox Vaccine in Laboratory and Health Care Personnel at Risk for Occupational Exposure to Orthopoxviruses — Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015

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On June 25, 2015, the Advisory Committee on Immunization Practices (ACIP) recommended routine vaccination with live smallpox (vaccinia) vaccine (ACAM2000) for laboratory personnel who directly handle 1) cultures or 2) animals contaminated or infected with replication-competent vaccinia virus, recombinant vaccinia viruses derived from replication-competent vaccinia strains (i.e., those that are capable of causing clinical infection and producing infectious virus in humans), or other orthopoxviruses that infect humans (e.g., monkeypox, cowpox, and variola) (recommendation category: A, evidence type 2 [Box]). Health care personnel (e.g., physicians and nurses) who currently treat or anticipate treating patients with vaccinia virus infections and whose contact with replication-competent vaccinia viruses is limited to contaminated materials (e.g., dressings) and persons administering ACAM2000 smallpox vaccine who adhere to appropriate infection prevention measures can be offered vaccination with ACAM2000 (recommendation category: B, evidence type 2 [Box]). These revised recommendations update the previous ACIP recommendations for nonemergency use of vaccinia virus

smallpox vaccine for laboratory and health care personnel at risk for occupational exposure to orthopoxviruses (1). Since 2001, when the previous ACIP recommendations were developed, ACAM2000 has replaced Dryvax as the only smallpox vaccine licensed by the U.S. Food and Drug Administration (FDA) and available for use in the United States (2). These recommendations contain information on ACAM2000 and its use in laboratory and health care personnel at risk for occupational exposure to orthopoxviruses.

Background

Smallpox vaccines containing vaccinia virus were used to successfully eradicate smallpox as a disease of humans (3). Eradication was made possible by the ability of vaccinia virus to induce cross-protective immunity against other viruses within the orthopoxvirus genus capable of producing human infection (e.g., variola, monkeypox, and cowpox) (3). ACAM2000 (Smallpox [Vaccinia] Vaccine, Live) is currently the only smallpox vaccine licensed by FDA and available for use in the United States. The license for Dryvax vaccine, the smallpox vaccine previously recommended by ACIP, was withdrawn in

Recommendations for routine use of vaccines in children, adolescents, and adults are developed by the Advisory Committee on Immunization Practices (ACIP). ACIP is chartered as a federal advisory committee to provide expert external advice and guidance to the Director of the Centers for Disease Control and Prevention (CDC) on use of vaccines and related agents for the control of vaccine-preventable diseases in the civilian population of the United States. Recommendations for routine use of vaccines in children and adolescents are harmonized to the greatest extent possible with recommendations made by the American Academy of Pediatrics (AAP), the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG). Recommendations for routine use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, the American College of Physicians (ACP), and the American College of Nurse-Midwives (ACNM). ACIP recommendations adopted by the CDC Director become agency guidelines on the date published in the Morbidity and Mortality Weekly Report (MMWR). Additional information regarding ACIP is available at <http://www.cdc.gov/vaccines/acip>.

BOX. The U.S. Advisory Committee on Immunization Practices system for grading evidence and recommendations*

Recommendation categories

Category A: Recommendation that applies to all persons in an age- or risk-based group.

Category B: Recommendation for individual clinical decision-making.

Type or quality of evidence

1. Randomized controlled trials (RCTs), or overwhelming evidence from observational studies.
2. RCTs with important limitations, or exceptionally strong evidence from observational studies.
3. RCTs with notable limitations, or observational studies.
4. RCTs with several major limitations, observational studies with important limitations, or clinical experience and observations.

* Adopted from the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system.

2008, and all remaining supplies of this vaccine were subsequently destroyed (2).

ACAM2000 is a vaccinia virus vaccine derived from a plaque-purified clone of the same New York City Board of Health strain that was used to manufacture Dryvax vaccine. ACAM2000 is grown in African green monkey kidney (Vero) cells and tested to be free of known adventitious agents (4). Safety data from ACAM2000 clinical trials indicate a similar safety profile to Dryvax, including a risk for serious adverse events (e.g., progressive vaccinia, postvaccinial encephalitis, and eczema vaccinatum) (5,6). Myopericarditis has also been associated with ACAM2000 and is estimated to occur at a rate of 5.7 per 1,000 primary vaccinees based on clinical trial data (6).

ACAM2000 is provided as a lyophilized preparation of purified live virus containing the following nonactive excipients: 6 mM–8 mM HEPES (pH 6.5–7.5), 2% human serum albumin United States Pharmacopeia (USP), 0.5%–0.7% sodium chloride USP, 5% mannitol USP, and trace amounts of neomycin and polymyxin B (6). Diluent for ACAM2000 contains 50% (v/v) glycerin USP and 0.25% (v/v) phenol USP in water for injection USP. Diluent is supplied as 0.6 mL of liquid in 3 mL clear glass vials (6).

ACAM2000 is administered in a single dose by the percutaneous route (scarification) using 15 jabs of a stainless steel bifurcated needle that has been dipped into the reconstituted vaccine (6). Following successful administration of vaccine, ACAM2000 produces vaccination site lesions containing infectious vaccinia virus capable of transmission through autoinoculation and inadvertent inoculation of close contacts of vaccinees. The development of vaccination site lesions may be modified or greatly reduced in revaccinees (3,6).

Poxviruses are increasingly being used in biomedical research for a wide range of purposes. Vaccinia virus is the most frequently studied poxvirus and serves as the prototype of the orthopoxvirus genus. It has not only been used in the area of basic virology but also as both an immunology tool and potential vaccine vector because of its ability to serve as a vector for the expression of foreign genes (antigens) (7,8). Many strains of vaccinia virus exist with different levels of virulence in humans and animals. Distinguishing between replication-competent and replication-deficient poxvirus strains is useful in establishing the risk they pose to persons who might be occupationally exposed to such viruses. Replication-deficient poxvirus strains can be defined as those that do not produce infectious virus in humans (and therefore do not cause clinical infection), and as such, pose a substantially lower risk compared with replication-competent poxvirus strains, which are capable of causing clinical infection in humans as well as producing infectious virus that can be transmitted to others. Modified vaccinia Ankara (MVA), NYVAC, TROVAC, and

ALVAC are examples of replication-deficient poxvirus strains (9,10). The categories replication-competent and replication-deficient replace the previous poxvirus strain categories of highly attenuated and nonhighly attenuated to add clarity and specificity to the vaccination recommendations (1). Persons at risk for occupational exposure to orthopoxviruses might include laboratory personnel who have contact or work with live orthopoxviruses or clinical samples from suspected cases of orthopoxvirus infection, animal care personnel who have direct contact with orthopoxvirus-inoculated or -infected animals or their secretions, and health care personnel (e.g., physicians and nurses) involved in caring for orthopoxvirus-infected persons or administering biological agents containing orthopoxviruses.

Methods

These recommendations were developed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (Box) (11–13). GRADE steps include defining specific questions, identifying important health outcomes, summarizing evidence for important outcomes, assessing quality of evidence, and formulating recommendations. Principal considerations for formulating recommendations include balance of benefits and harms; quality of evidence; values and preferences; and health economic analyses. The central policy question for this policy note was whether routine vaccination with ACAM2000 should be recommended for laboratory and health care personnel at risk for occupational exposure to orthopoxviruses (13).

Rationale and Evidence

ACIP considered the risk for infection, the risk for an adverse event following vaccination, and the benefit from vaccination in developing these recommendations. Vaccinia virus smallpox vaccine has been recommended by ACIP for the protection of laboratory personnel against orthopoxviruses since 1980. However, 14 orthopoxvirus infections were reported in laboratory personnel in the United States during 2004–2014; 13 of these infections occurred in laboratory personnel who were not vaccinated according to ACIP recommendations (8) (CDC unpublished data 1/1/2015). Although these data indicate the presence of risk, it is difficult to quantify the absolute number of persons at risk for occupational exposure to orthopoxviruses because the size of the population at risk is not known and vaccinia virus and cowpox virus exposures and infections among this population are not notifiable events. During the same 2004–2014 period, no reports of preventable vaccine-associated serious adverse events (e.g., eczema vaccinatum, progressive vaccinia, or contact transmission) were documented among laboratory and health care personnel at risk for occupational exposure who had been vaccinated with

smallpox vaccine. Furthermore, data from U.S. military personnel and civilian first responders vaccinated during smallpox vaccination campaigns that were initiated in 2002 indicate that the incidence of serious adverse events overall was lower than previously reported in 1968 (14–16). Although serious adverse events have occurred, this decrease in incidence is likely attributable to more stringent prevaccination screening procedures to identify persons who should not receive the vaccine, to increased use of protective bandages to cover the vaccination site, and to enhanced education of vaccinees compared with the routine vaccination practices in place in the 1960s. Vaccination with ACAM2000 is expected to provide benefit to persons at risk for occupational exposure to orthopoxviruses, given the ability of vaccinia virus smallpox vaccines to induce cross-protective immunity against other viruses within the orthopoxvirus genus.

Recommendations

Laboratory and health care personnel at risk for occupational exposure to orthopoxviruses should follow recommended biosafety guidelines and adhere to published infection prevention and control procedures (17–19). Laboratories using both replication-competent and replication-deficient vaccinia virus strains where working areas for these viruses cannot be clearly segregated should follow increased biosafety precautions because laboratory infections caused by contamination have been previously documented (8,17). Persons with immunocompromising conditions or other contraindications to vaccination are at increased risk for severe disease if an occupational exposure occurs.

Routine vaccination with ACAM2000 is recommended for laboratory personnel who directly handle 1) cultures or 2) animals contaminated or infected with replication-competent vaccinia virus, recombinant vaccinia viruses derived from replication-competent vaccinia strains (i.e., those that are capable of causing clinical infection and producing infectious virus in humans), or other orthopoxviruses that infect humans (e.g., monkeypox, cowpox, and variola) (recommendation category: A, evidence type 2 [Box]). However, vaccination with ACAM2000 is not recommended for persons who work only with replication-deficient poxvirus strains (e.g., MVA,

NYVAC, TROVAC, and ALVAC) (recommendation category: A, evidence type 2 [Box]).

Laboratory personnel working with replication-competent vaccinia viruses and recombinant viruses developed from replication-competent vaccinia viruses should be revaccinated with ACAM2000 at least every 10 years (recommendation category: A, evidence type 2 [Box]). To ensure an increased level of protection against more virulent orthopoxviruses (e.g., variola, monkeypox), revaccination with ACAM2000 every 3 years is recommended for personnel handling these viruses (recommendation category: A, evidence type 2 [Box]) (Table 1). Public health and health care volunteers who were vaccinated as responders in the U.S. Civilian Smallpox Preparedness and Response Program should refer to the October 2008 *CDC Interim Guidance for Revaccination of Eligible Persons who Participated in the US Civilian Smallpox Preparedness and Response Program* (<http://emergency.cdc.gov/agent/smallpox/revaxmemo.asp>).

Health care personnel (e.g., physicians and nurses) or animal care personnel whose contact with replication-competent vaccinia viruses is limited to contaminated materials (e.g., dressings or cages), but who adhere to appropriate infection prevention measures, are at lower risk for inadvertent infection than laboratory personnel. Similarly, persons administering ACAM2000 smallpox vaccine to laboratory and health care personnel at risk for occupational exposure to orthopoxviruses can decrease the risk for inadvertent infection through recommended infection prevention measures. However, because of a theoretical risk for infection, vaccination with ACAM2000 can be offered to health care or animal care personnel, provided individual persons have no specified contraindications to vaccination (recommendation category: B, evidence type 2 [Box]). Persons with an orthopoxvirus exposure should be evaluated by a health care provider and clinical management decisions, including postexposure smallpox vaccination should be made on a case-by-case basis in consultation with public health authorities.

Precautions and Contraindications

Nonemergency use of ACAM2000 should be avoided in persons with increased risk for adverse events following

TABLE 1. Recommendations for revaccination of laboratory and health care personnel at risk for occupational exposure to orthopoxviruses

| Orthopoxvirus | Revaccination schedule |
|---|-------------------------|
| Replication-competent vaccinia viruses and recombinant viruses developed from replication-competent vaccinia viruses | At least every 10 years |
| More virulent orthopoxviruses (e.g., variola, monkeypox) | Every 3 years |
| Replication-deficient vaccinia viruses and recombinant viruses developed from replication-deficient vaccinia viruses* | Not recommended |

* Laboratories that use both replication-competent and replication-deficient vaccinia virus strains but where working areas for these viruses cannot be clearly segregated should follow increased biosafety precautions because laboratory infections due to contamination have previously been documented. Sources: MacNeil A, Reynolds MG, Damon IK. Risks associated with vaccinia virus in the laboratory. *Virology* 2009;385:1–4; Chosewood LC, Wilson DE. *CDC National Institutes of Health. Biosafety in microbiological and biomedical laboratories*. 5th ed. Washington, DC: US Department of Health and Human Services, Public Health Service, CDC, National Institutes of Health; 2009.

administration of smallpox vaccine. Contraindications for nonemergency use of ACAM2000 include persons with a history or presence of atopic dermatitis, persons with other active exfoliative skin conditions (e.g., eczema, burns, impetigo, varicella zoster virus infection, herpes simplex virus infection, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease [keratosis follicularis]); persons with conditions associated with immunosuppression (e.g., human immunodeficiency virus [HIV] infection or acquired immune deficiency syndrome [AIDS], leukemia, lymphoma, generalized malignancy, solid organ transplantation, or therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor [TNF] inhibitors, or high-dose corticosteroids [≥ 2 mg/kg body weight or ≥ 20 mg/day of prednisone or its equivalent for ≥ 2 weeks], hematopoietic stem cell transplant recipients < 24 months post-transplant or ≥ 24 months, but who have graft-versus-host disease or disease relapse, or autoimmune disease [e.g. systemic lupus erythematosus] with immunodeficiency as a clinical component); persons aged < 1 year; women who are pregnant or breastfeeding; persons with a serious allergy to any component of ACAM2000; persons with known underlying heart disease with or without symptoms (e.g., coronary artery disease or cardiomyopathy); and primary vaccinees with three or more known major cardiac risk factors (i.e., hypertension, diabetes, hypercholesterolemia, heart disease at age 50 years in a first-degree relative, and smoking) (recommendation category: A, evidence type 2). Data from clinical trials and epidemiologic studies suggest that primary vaccinees might be at increased risk for myopericarditis (20,21). Although the specific risk factors for myopericarditis following smallpox vaccination have

not been identified, the consequences of myopericarditis are more likely to be severe in persons with known heart disease or cardiac risk factors than in persons without these conditions.

Given the risk for vaccinia virus transmission from recently vaccinated persons through inadvertent inoculation, non-emergency use of ACAM2000 is also contraindicated in persons with household contacts with a history or presence of atopic dermatitis, other active exfoliative skin conditions (e.g., eczema, burns, impetigo, varicella zoster, herpes, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease [keratosis follicularis]); conditions associated with immunosuppression (e.g., HIV/AIDS, leukemia, lymphoma, generalized malignancy, solid organ transplantation, or therapy with alkylating agents, antimetabolites, radiation, TNF inhibitors, or high-dose corticosteroids [i.e., ≥ 2 mg/kg body weight or 20 mg/day of prednisone or its equivalent for ≥ 2 weeks], hematopoietic stem cell transplant recipients < 24 months post-transplant or ≥ 24 months, but who have graft-versus-host disease or disease relapse, or autoimmune disease [e.g. systemic lupus erythematosus] with immunodeficiency as a clinical component); household contacts aged < 1 year; and household contacts who are pregnant (recommendation category: A, evidence type 2 [Box]). Household contacts include persons with prolonged intimate contact with the potential vaccinee (e.g. sexual contacts) and others who might have direct contact with the vaccination site or with potentially contaminated materials (e.g., dressings or clothing) (Table 2). ACIP also does not recommend nonemergency vaccination with ACAM2000 for children and adolescents aged < 18 years.

TABLE 2. Contraindications to using ACAM2000 smallpox vaccine in laboratory and health care personnel at risk for occupational exposure to orthopoxviruses

| Contraindication | Primary vaccinees | Revaccinees | Household contacts* |
|--|-------------------|-------------|---------------------|
| History or presence of atopic dermatitis | √ | √ | √ |
| Other active exfoliative skin conditions [†] | √ | √ | √ |
| Conditions associated with immunosuppression [‡] | √ | √ | √ |
| Pregnancy | √ | √ | √ |
| Aged < 1 yr [¶] | √ | √ | √ |
| Breastfeeding | √ | √ | √ |
| Serious vaccine component allergy | √ | √ | √ |
| Known underlying heart disease (e.g., coronary artery disease or cardiomyopathy) | √ | √ | √ |
| Three or more known major cardiac risk factors** | √ | √ | √ |

* Household contacts include persons with prolonged intimate contact with the potential vaccinee (e.g., sexual contacts) and others who might have direct contact with the vaccination site or with potentially contaminated materials (e.g., dressings or clothing).

[†] Conditions include eczema, burns, impetigo, varicella zoster, herpes, severe acne, severe diaper dermatitis with extensive areas of denuded skin, psoriasis, or Darier disease (keratosis follicularis).

[‡] Conditions include human immunodeficiency virus/acquired immune deficiency syndrome infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, high-dose corticosteroids, being a recipient with hematopoietic stem cell transplant < 24 months post-transplant or ≥ 24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component.

[¶] Vaccination of infants aged < 1 year is contraindicated. Additionally, the Advisory Committee on Immunization Practices does not recommend vaccinating children and adolescents aged < 18 years.

** Major cardiac risk factors include hypertension, diabetes, hypercholesterolemia, heart disease at age 50 years in a first-degree relative, and smoking.

Summary**What is currently recommended?**

In 2001, the Advisory Committee on Immunization Practices approved revised recommendations that laboratory and health care personnel occupationally exposed to vaccinia virus, recombinant vaccinia viruses, and other orthopoxviruses that can infect humans be vaccinated with Dryvax smallpox vaccine.

Why are the recommendations being modified now?

In 2007, ACAM2000 was licensed by the U.S. Food and Drug Administration and replaced Dryvax as the only smallpox vaccine available for use in the United States. The evidence supporting routine vaccination with ACAM2000 for laboratory personnel at risk for occupational exposure to orthopoxviruses was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation framework and determined to be type 2 (moderate level of evidence); the recommendation was designated as a Category A recommendation.

What are the new recommendations?

Routine vaccination with ACAM2000 is recommended for laboratory personnel who directly handle 1) cultures or 2) animals contaminated or infected with replication-competent vaccinia virus, recombinant vaccinia viruses derived from replication-competent vaccinia strains (i.e., those that are capable of causing clinical infection and producing infectious virus in humans), or other orthopoxviruses that infect humans (e.g., monkeypox, cowpox, and variola) (recommendation category: A, evidence type 2). Health care personnel (e.g., physicians and nurses) who currently treat or anticipate treating patients with vaccinia virus infections and whose contact with replication-competent vaccinia viruses is limited to contaminated materials (e.g., dressings) and persons administering ACAM2000 smallpox vaccine who adhere to appropriate infection prevention measures can be offered vaccination with ACAM2000 (recommendation category: B, evidence type 2).

Persons with inflammatory eye disease might be at increased risk for inadvertent inoculation as a result of touching or rubbing the eye. Therefore, deferring vaccination is prudent for persons with inflammatory eye diseases requiring steroid treatment until the condition resolves and the course of therapy is complete (recommendation category: B, evidence type 4 [Box]).

Adverse events occurring after administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reports can be submitted to VAERS online, by fax, or by mail. Additional information about VAERS is available by telephone (1-800-822-7967) or online (<https://vaers.hhs.gov>).

ACAM2000 Availability

CDC is the only source of ACAM2000 for civilians. CDC will provide ACAM2000 to protect laboratory and other health care and animal care personnel whose occupations place them at risk for exposure to vaccinia and other orthopoxviruses, including recombinant vaccinia viruses. Vaccine should be administered under the supervision of a physician selected by the requesting institution. Vaccine will be shipped to the responsible physician. Requests for vaccine, including the reason for the request, should be referred to the following: CDC Drug Service, Division of Scientific Resources, National Center for Emerging and Zoonotic Infectious Diseases, Office of Infectious Diseases, Mailstop D-09, Atlanta, GA 30329; telephone: 404-639-3670; fax: 404-639-3717; e-mail: drug-service@cdc.gov.

Future Directions

ACIP will review these recommendations as new information or developments related to orthopoxvirus disease, smallpox vaccines (including licensure of additional smallpox vaccines), smallpox vaccine adverse events, and the experience gained in the implementation of these recommendations becomes available. Revised recommendations will be developed as needed.

Acknowledgments

Members of the Advisory Committee on Immunization Practices (ACIP); members of the ACIP Smallpox Vaccine Workgroup (ACIP member roster for July 2014–June 2015 is available online [<http://www.cdc.gov/vaccines/acip/committee/members.html>]); Faruque Ahmed, Nancy M. Bennett, Maria Cano, Mark D. Challberg, Paul Chaplin, Emily A. Cloessner, Limone C. Collins, Inger K. Damon, Michael D. Decker, Renata J. Engler, Doran L. Fink, Jesse R. Geibe, Richard L. Gorman, Richard N. Greenberg, Laura Hughes-Baker, Stuart N. Isaacs, M. Shannon Keckler, Grace Kubin, Alison C. Mawle, Michael M. McNeil, Sharon Medcalf, Michael Merchlinsky, Howard L. Minkoff, Jay R. Montgomery, Richard W. Moyer, Lynda Osadebe, Larry K. Pickering, Greg A. Poland, James M. Schmitt, Eric M. Sergienko, Jean C. Smith, Neil M. Vora, Sixun Yang.

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Building and Strengthening Infection Control Strategies to Prevent Tuberculosis — Nigeria, 2015

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Tuberculosis (TB) is the leading cause of infectious disease mortality worldwide, accounting for more than 1.5 million deaths in 2014, and is the leading cause of death among persons living with human immunodeficiency virus (HIV) infection (1). Nigeria has the fourth highest annual number of TB cases among countries, with an estimated incidence of 322 per 100,000 population (1), and the second highest prevalence of HIV infection, with 3.4 million infected persons (2). In 2014, 100,000 incident TB cases and 78,000 TB deaths occurred among persons living with HIV infection in Nigeria (1). Nosocomial transmission is a significant source of TB infection in resource-limited settings (3), and persons with HIV infection and health care workers are at increased risk for TB infection because of their routine exposure to patients with TB in health care facilities (3–5). A lack of TB infection control in health care settings has resulted in outbreaks of TB and drug-resistant TB among patients and health care workers, leading to excess morbidity and mortality. In March 2015, in collaboration with the Nigeria Ministry of Health (MoH), CDC implemented a pilot initiative, aimed at increasing health care worker knowledge about TB infection control, assessing infection control measures in health facilities, and developing plans to address identified gaps. The approach resulted in substantial improvements in TB infection control practices at seven selected facilities, and scale-up of these measures across other facilities might lead to a reduction in TB transmission in Nigeria and globally.

To address the risk for TB transmission to uninfected persons, the World Health Organization (WHO) recommends implementation and scale-up of TB infection control measures, including managerial (leadership and commitment for establishing and implementing infection control policies at the health facility), administrative (prompt identification and separation of persons with presumptive TB, with timely diagnosis and treatment of TB patients), and environmental (optimization of building design and patient flow to reduce the concentration of TB droplet nuclei in the air and control directional flow of potentially infectious aerosols) measures and personal protective equipment (PPE) use, implemented in conjunction with other infection control measures, to reduce the risk for TB transmission in health care facilities

(6). Preventing nosocomial TB transmission, aimed at reducing the impact of TB on persons living with HIV, is also a priority for the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) (7). However, infection control measures to prevent TB transmission in health care facilities have not been adequately implemented, especially in settings with high incidence of TB and limited resources (8,9).

A four-phase TB infection control initiative, *Building and Strengthening Infection Control Strategies* (TB BASICS), was developed by CDC to assess and improve health care facility infection control practices in countries with high numbers of TB cases, using a continuous quality improvement approach. The initiative includes 1) TB infection control training of health care workers, 2) baseline health facility assessments and development of intervention plans, 3) implementation, and 4) monitoring and evaluation through engagement of local health officials and health care workers to encourage commitment to the initiative. The pilot project was conducted in seven health care facilities in Ebonyi, Enugu, and Imo states that are supported by a PEPFAR implementing partner in southeastern Nigeria. These facilities provide services to 1.48 million persons and, during the past year, treated 1,600 TB patients.

A 3-day training workshop based on the WHO policy on TB infection control in health care facilities, congregate settings, and households (6) and delivered by MoH and CDC was conducted for 50 health care workers, including physicians, nurses, residents from the Nigeria Field Epidemiology and Laboratory Training Program (NFELTP), TB and HIV program coordinators, and TB/HIV program officers from the MoH. A precourse assessment identified environmental and administrative measures for infection control as the main gaps in participant knowledge. Training materials, videos, and job aids* were provided to all participants to facilitate their training of other staff members in their respective health facilities.

Teams[†] conducted baseline assessments of TB infection control practices at each of the seven facilities using a standardized facility assessment tool that included staff interviews, observation of

* <http://www.cdc.gov/globalaids/Resources/pmtct-care/tuberculosis-infection-control.html>.

[†] The seven teams included state, regional, and federal MoH officials, NFELTP residents, PEPFAR implementing partners, WHO staff members, and CDC staff members and were led by health care providers from the pilot health facilities.

routine practices, and review of available policies and procedures on infection control. After completion of the baseline assessments and identification of programmatic areas for strengthening, each team developed a facility-specific intervention plan with a timeline for implementation. Implementation of TB infection control measures at each facility was reassessed at 2, 4, and 6 months after the baseline assessment. Monitoring of 14 managerial measures, 13 administrative measures, seven environmental measures, and three PPE measures was conducted by NFELTP residents, and the final evaluations were performed by the teams that conducted the baseline assessments. Data were displayed in a color-coded dashboard (<http://stacks.cdc.gov/view/cdc/38109>) that indicated elements that were not implemented (and for which there was no implementation plan) in red, elements that were planned but not yet implemented in yellow, elements that were not applicable or assessed in blue, and elements that were fully implemented in green. Site-specific feedback and a copy of the dashboard were provided to the facilities immediately after the baseline assessment was completed and at each of the bimonthly evaluations so that staff members could visually track their own progress.

Baseline Assessment of TB Infection Control Measures

At baseline, managerial measures were lacking in almost all facilities. Only one site had national infection control policy and guidelines or facility-specific plans available. There were no infection control committees or designated practitioners, no routine risk assessments or daily monitoring of infection control activities, no ongoing or planned operational research to improve infection control practices, and no occupational health programs. All facilities had systems in place for reporting all new TB diagnoses, and all patients with diagnosed TB disease were referred for treatment. In accordance with the national TB treatment policy, directly observed therapy was provided for TB patients; however, staff members did not know how to properly educate patients and their visitors or provide them with information on infection prevention. Administrative measures also were generally not in place. Only three facilities had posters describing proper cough etiquette, and most did not have tissue or hygiene supplies for coughing patients, staff members designated to identify coughing patients and separate them from other patients to reduce possible exposure to TB, or systems in place for patients with presumptive TB to be prioritized for clinical evaluation. None of the facilities provided routine TB evaluation, HIV testing or secure documentation of health information for their staffs, and most did not have WHO-recommended isoniazid preventive therapy available for staff members with HIV infection.[§]

[§]http://www.who.int/hiv/strategy2016-2021/Draft_global_health_sector_strategy_hiv_01Dec2015.pdf?ua=1&ua=1.

Collection of sputum in a designated location away from other patients and timely processing of sputum samples were in place in five of the seven facilities. Although all of the facilities had outdoor patient waiting areas with good ventilation, other environmental measures were poorly implemented. None of the facilities routinely checked airflow in examination rooms and waiting areas to ensure adequate air exchange; signage reinforcing the opening of doors and windows for cross-ventilation was not displayed, and the facilities did not have extractor fans to facilitate removal of infectious aerosols or use ultraviolet germicidal irradiation of TB droplet nuclei. PPE was not consistently used in any of the facilities. Coughing patients were not provided masks to cover the nose and mouth. Staff members had not undergone respirator fit testing and did not routinely wear respirators when interacting with patients with presumptive or diagnosed TB disease.

Implementation of TB Infection Control Improvements

Interventions to improve infection control practices were carried out at each site to promote and enable facility-driven program changes. No-cost interventions were immediately put in place, and providers who had attended the training used workshop materials to train other staff members at their facilities. Posters and pamphlets with information on cough etiquette, hygiene, and handwashing were provided to each facility for display in patient waiting areas. Purchase of supplies and minor renovations, including the construction of designated sputum collection booths in remote areas of the facilities, were undertaken. Facilities developed plans to monitor average patient wait times and ensure that presumptive TB patients received expedited care to reduce the amount of time they spent around other patients and health care workers. Occupational health programs were established at each facility, including routine TB evaluations for health care workers, which led to the diagnosis of TB in three staff members at two of the pilot facilities.

As measured by the dashboard, progress from predominantly red indicators at baseline (indicating nonimplementation of recommended measures), to almost all green indicators (indicating full implementation) at the 6-month evaluation reflected improvements made by the seven pilot facilities. At baseline, only two of the 14 managerial measures were implemented at all seven facilities. At the 6-month evaluation, 13 of the 14 managerial indicators had been implemented at all of the facilities. Of the 13 administrative measures, the number implemented increased from zero at baseline to 10 at the 6-month evaluation. Of the seven environmental measures, the number implemented increased from one to four, and of the three PPE measures, the number implemented increased from zero to three. As of February 2016, NFELTP residents, health care providers, and health officials from the initial training

Summary**What is already known about this topic?**

Tuberculosis (TB) is the leading cause of infectious disease mortality globally. Nosocomial transmission is a significant source of TB infection and of particular risk for health care workers and persons living with human immunodeficiency virus infection. TB infection control measures to reduce the transmission of TB in health care facilities have not been well implemented in settings with high numbers of cases and limited resources.

What is added by this report?

An intervention in Nigeria that focused on training health care workers, identifying TB infection control gaps, and using continuous quality improvement measures to monitor strategies in health care facilities was effective in improving TB infection control.

What are the implications for public health practice?

Increasing health care worker knowledge and implementation of TB infection control measures in health facilities are key to preventing the nosocomial spread of TB and reducing the incidence of TB globally. Ongoing support will be required to ensure that gains are maintained and that the infection control program is sustainable.

workshop had trained approximately 200 health care workers, using materials and videos developed by CDC. The experiences of participants in the project helped to inform revisions being made to the TB infection control section of the Nigeria MoH guidelines for TB/HIV collaborative activities.

Discussion

TB prevention is a key element in the strategy to end the global TB epidemic (10) and an important component of prevention is TB infection control. In Nigeria, as in many countries with high numbers of cases and limited resources, implementation of TB infection control measures has been inadequate (8). An initiative aimed at increasing health care worker knowledge about TB infection control and implementing measures to reduce nosocomial transmission in Nigeria resulted in substantial improvement in managerial, administrative, environmental, and personal protective measures and in demonstrable country and facility commitment to the initiative during a 6-month implementation period. Managerial and administrative measures mainly involved implementation of existing policies and change in practices and were rapidly put into place. Environmental improvements and PPE use were instituted at minimal cost.

Commitment from MoH and the conscientiousness of participating health care workers were critical to the success of this project. The limited knowledge of health care providers and minimal implementation of infection control measures at baseline was challenging. However, country capacity was built by engaging local stakeholders in all aspects of the project,

including training, facility assessment, intervention planning and implementation, monitoring, and evaluation. In addition, many of the implemented practices required minimal intervention. Continuing education and training of health care workers, as well as monitoring of infection control practices, will help to ensure that the progress attained is sustained.

The findings in this report are subject to at least two limitations. First, the pilot project was conducted in PEPFAR-supported facilities in southeastern Nigeria and might not be representative of other facilities or sites in other parts of the country. Second, although the initial achievements have been encouraging, the long-term impact and sustainability of the TB infection control practices implemented have not yet been assessed.

The incidental diagnoses of TB among health care workers as a result of this project highlight the value of routine health care worker screening and underscore the importance of TB infection control in health care settings. The outcome of the pilot project and recommendations have been shared with the government of Nigeria and in-country TB stakeholders, and will guide ongoing capacity-building efforts, scale-up of infection control practices in other health facilities in Nigeria, and long-term monitoring plans.

Preventing TB infection is key to reducing the number of TB cases worldwide, but there are still critical infection control gaps in health facilities, posing a continued risk to persons living with HIV infection, health care workers, and uninfected persons. Widespread implementation of infection control measures, especially in settings with high numbers of cases, should help prevent further TB transmission and ultimately bring the global TB epidemic to an end.

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Revision to CDC's Zika Travel Notices: Minimal Likelihood for Mosquito-Borne Zika Virus Transmission at Elevations Above 2,000 Meters

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Since May 2015, when Zika virus, a flavivirus transmitted primarily by *Aedes aegypti* mosquitoes, was reported in Brazil, the virus has rapidly spread across the Region of the Americas and the Caribbean. The association between maternal Zika virus infection and adverse fetal and reproductive outcomes, including microcephaly, prompted CDC to issue a Level 2 alert travel notice* for the 37 countries and U.S. territories (at the national and territorial level) that have reported recent Zika virus transmission as of March 11, 2016. In addition to mosquito bite precautions for all travelers, CDC advises that pregnant women postpone travel to affected countries and U.S. territories. Within a nation's borders, ecologic characteristics, which determine the distribution of mosquito vectors, can vary considerably. CDC conducted a spatial analysis, focusing on the probability of occurrence of *Ae. aegypti*, to support the demarcation for subnational travel alerts. Based on results of this analysis, travel that is limited to elevations higher than 2,000 m (6,562 ft) above sea level is considered to have minimal (approximately 1%) likelihood for mosquito-borne Zika virus transmission, even within countries reporting active transmission. Women who are pregnant should avoid travel to elevations <2,000 m in countries with active Zika virus transmission.

Zika virus is a flavivirus primarily transmitted by *Aedes* species mosquitoes (1). In May 2015, the Pan American Health Organization (PAHO) issued an alert regarding the first confirmed Zika virus infections in Brazil (2). Currently, outbreaks of Zika virus disease are occurring in many countries and U.S. territories, and as of March 11, 2016, CDC had issued 37 Level 2 travel notices for areas with ongoing Zika virus transmission.† Currently, when laboratory-confirmed local Zika virus transmission is first reported, travel notices are issued for the entire country or U.S. territory. Establishing more precisely defined areas of Zika virus risk in a country or U.S. territory

is complicated by incomplete surveillance data on the disease and the presence of the mosquito vector.

In an effort to develop more precise guidance for travelers, CDC evaluated whether subnational travel notices could be based on an ecologic indicator of the probable absence of the predominant Zika virus mosquito vector, *Ae. aegypti*. Within a nation's borders, ecologic factors, such as temperature, precipitation, vegetation, and human population density, that define suitable habitats for *Aedes* species vary. Where habitat is unsuitable, the mosquito vector is likely to be absent, and risk for mosquito-borne Zika virus transmission is likely to be negligible.

The first step in developing subnational travel notices required identification of a single, easily quantifiable ecologic variable that could be used as a substitute for the likely absence of *Ae. aegypti*. Of the many ecologic factors affecting habitat suitability and *Ae. aegypti* survival as a vector for Zika virus, temperature has been the most frequently investigated and rigorously quantified (3); however, temperature varies widely and is difficult to predict locally and over the long term. Historically, elevation has served as a reasonable proxy for temperature. Because it is static and relatively easy to measure (4), elevation was selected for further investigation. Previous reports from various global regions suggest that *Ae. aegypti* is present, but rare, between elevations of 1,700–2,100 m (5,6). Therefore, this analysis was restricted to countries and U.S. territories that have 1) ongoing Zika virus transmission and 2) areas with high elevations (starting at >1,500 m). Sixteen countries, including Bolivia, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, and Venezuela have areas which fit these criteria.§ No U.S. territories had elevations at that level.

Spatial analyses were conducted using multiple data sets: global data on predicted probabilities of the presence of *Ae. aegypti* based on 20,000 observed occurrences during 1960–2014 (7); remotely sensed data on human population density (8); global geographic data on human dengue cases

*CDC provides updated travel information on areas with ongoing Zika virus transmission. <http://wwwnc.cdc.gov/travel/notices>.

†American Samoa, Aruba, Barbados, Bolivia, Bonaire, Brazil, Cape Verde, Colombia, Costa Rica, Curacao, Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Marshall Islands, Martinique, Mexico, New Caledonia, Nicaragua, Panama, Paraguay, Puerto Rico, Saint Martin, Saint Vincent and Grenadines, Samoa, Sint Maarten, Suriname, Tonga, Trinidad and Tobago, U.S. Virgin Islands, and Venezuela.

§CDC provides updated travel notice maps for areas with ongoing Zika virus transmission, including Bolivia, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, and Venezuela. <http://wwwnc.cdc.gov/travel/page/zika-travel-information>.

during 1960–2012 (9); and a digital elevation model (10); zonal statistics were used to relate the data sets. Within each of the 16 countries, the area of land suitable for *Ae. aegypti*, and the human population counts within each area were quantified. The quantification was done in 100-m elevation segments for elevations between 0 m and 2,500 m. Across all 16 countries, at elevations >2,000 m, *Ae. aegypti* was predicted to be largely absent. Because of sparse current geographic data on Zika virus cases, cases of dengue, another vector-borne viral disease spread primarily by *Ae. aegypti*, were examined as a proxy for Zika cases. Only 1.1% (28/2,682) of dengue cases in the global data set (9) were reported to have occurred at elevations >2,000 m in the 16 countries.

A CDC Zika virus travel notice is currently applied to an entire country or U.S. territory when transmission is confirmed by a local public health authority. However, *Ae. aegypti* might not be uniformly present because of differences in ecologic suitability. Recent advances in scientific modeling have allowed for more precision in geospatial analyses. CDC applied these approaches to previously published and rigorously evaluated data to determine if more precise guidance to travelers and persons living in affected regions could be established. The results from the spatial analyses of 16 countries with ongoing Zika virus transmission and elevation points >1,500 m indicate that *Ae. aegypti* is unlikely to be found at elevations >2,000 m because of unsuitable ecologic factors, including but not limited to, low temperatures. Consequently, at elevations above 2,000 m, the risk for mosquito-borne exposure to Zika virus is considered to be minimal. These findings support revising the Zika travel notice to reflect enhanced geographic precision regarding the likelihood of Zika virus presence at certain elevations.

With this revision, CDC recommends that women who are pregnant should postpone travel to areas that are at elevations <2,000 m above sea level in countries and U.S. territories with ongoing Zika virus transmission. Because Zika virus is primarily spread by mosquitoes, CDC recommends that travelers protect themselves from mosquito bites.[‡] Travel that is entirely limited to elevations >2,000 m is considered to pose minimal likelihood for mosquito-borne Zika virus transmission.** As additional geographic data specific to Zika virus cases in relation to elevation become available, these recommendations will be reviewed and revised as needed.

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[‡] <http://wwwnc.cdc.gov/travel/page/avoid-bug-bites>.

** The low oxygen levels found at high elevations can cause problems for travelers who are going to elevations above 2,400 m (8,000 ft). The best way to prevent altitude illness is to ascend slowly and take time to get used to the lower oxygen levels. Pregnant women should avoid strenuous activities at high elevations, and some doctors recommend that pregnant women not spend the night at altitudes above 3,650 m (12,000 ft). Pregnant women should also consider whether they will have access to medical care at a high-elevation destination.

Announcements

Diabetes Alert Day — March 22, 2016

March 22 is Diabetes Alert Day, dedicated to raising awareness about type 2 diabetes, its risk factors, and its prevention. Type 2 diabetes, which accounts for 90%–95% of all cases of diagnosed diabetes in U.S. adults, might be prevented through lifestyle changes, such as losing weight and increasing physical activity (1,2). In the United States, 86 million adults have prediabetes, putting them at increased risk for developing type 2 diabetes, heart disease, and stroke. Only 10% of adults with prediabetes know they have it (1,3).

In partnership with the Ad Council, the American Diabetes Association, and the American Medical Association, CDC's Division of Diabetes Translation developed and launched the first national prediabetes awareness campaign to encourage people to take steps to prevent type 2 diabetes. The website DoIHavePrediabetes.org (<https://doihaveprediabetes.org>) features a short test for people to find out their prediabetes risk and includes lifestyle tips and links to CDC-recognized prevention programs across the country that are part of the National Diabetes Prevention Program (<http://www.cdc.gov/diabetes/prevention/index.html>). The U.S. Diabetes Surveillance System includes an updated Diabetes State Atlas (<http://www.cdc.gov/diabetes/data>) that allows users to view data and trends on any mobile device. In addition to containing the latest state-level data, the atlas now presents estimates of the percentage of adults without diagnosed diabetes who report having had a test for diabetes or high blood glucose in the past 3 years. Additional information about diabetes prevention and control is available from CDC (<http://www.cdc.gov/diabetes>).

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World Water Day — March 22, 2016

World Water Day 2016, sponsored by the United Nations, is focused on water and jobs. Approximately half of workers around the world (1.5 billion persons) have jobs in water-related industries (1). Many industries rely on water to perform jobs, such as fishing, agriculture, manufacturing, and food service. Societies and economies depend on the men and women who work to keep the world's drinking water safe.

Climate change affects the economies and infrastructure that provide access to safe drinking water around the world. The World Health Organization estimates that during 2030–2050, an additional 250,000 persons will die each year as a result of climate change (2). Diarrheal diseases from contaminated water and lack of adequate sanitation and hygiene will be a major cause of these additional deaths (3). Now is the time to address these challenges and commit to the responsible management of water resources to ensure sustainable development in the present and for generations to come.

Information is available about World Water Day, including ideas on how to get involved (<http://www.unwater.org/worldwaterday>). Information on CDC's efforts to ensure global access to improved water, sanitation, and hygiene is also available (<http://www.cdc.gov/healthywater/global>).

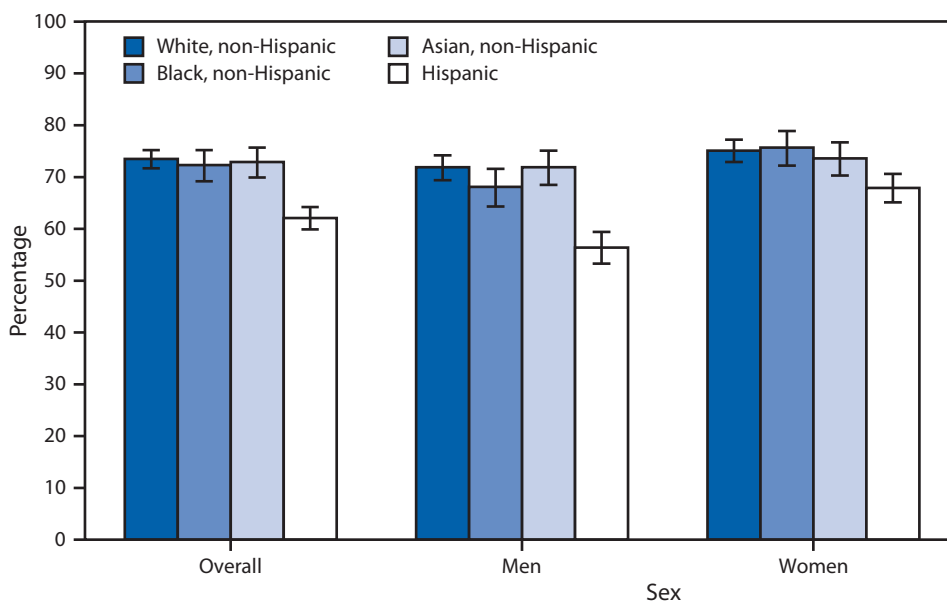
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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Percentage^{*,†} of Adults Aged ≥20 Years Who Had Their Cholesterol Checked in the Past 5 Years,[§] by Sex and Race/Ethnicity — National Health and Nutrition Examination Survey, United States, 2011–2014



* With 95% confidence intervals indicated with error bars.

† Age-adjusted using the direct method to the year 2000 projected Census population using three age groups: 20–39 years, 40–59 years, and ≥60 years.

§ Defined by an affirmative response to the question, “Have you ever had your blood cholesterol checked?” and a response indicating <5 years ago to the question, “About how long has it been since you last had your blood cholesterol level checked?”

During 2011–2014, 71.2% of adults aged ≥20 years had their blood cholesterol checked in the past 5 years. A smaller percentage of Hispanic adults (62.1%) had their cholesterol checked in the past 5 years compared with non-Hispanic white (73.5%), non-Hispanic black (72.3%), and non-Hispanic Asian (72.9%) adults. This pattern was observed for both men and women. A larger percentage of non-Hispanic white, non-Hispanic black, and Hispanic women had their cholesterol checked compared with their male counterparts, but there was no difference between non-Hispanic Asian men and women.

Source: Carroll MD, Kit BK, Lacher DA, Yoon SS. Total and high-density lipoprotein cholesterol in adults: National Health and Nutrition Examination Survey, 2011–2012. NCHS Data Brief no. 132; 2013. <http://www.cdc.gov/nchs/data/databriefs/db132.htm>.

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