

Varicella Death of an Unvaccinated, Previously Healthy Adolescent — Ohio, 2009

Varicella usually is a self-limited disease but sometimes can result in severe complications and death. Although infants, adults, and immunocompromised persons are at increased risk for severe disease, before varicella vaccine was introduced in 1995, the majority of hospitalizations and deaths from varicella occurred among healthy persons aged <20 years (1). Introduction of varicella vaccine has substantially decreased varicella incidence, hospitalizations, and deaths in the United States (2). This report describes a varicella death in an unvaccinated, previously healthy adolescent aged 15 years. In April 2012, as part of the routine review of vital statistics records, the Ohio Department of Health identified a 2009 death with the International Classification of Diseases, 10th Revision code for varicella as the underlying cause. Because varicella deaths are nationally reportable, the Ohio Department of Health conducted an investigation to validate that the coding was accurate. Investigators learned that, on March 12, 2009, the adolescent girl was admitted to a hospital with a 3-day history of a rash consistent with varicella and a 1-day history of fever and shortness of breath. The patient was started on intravenous acyclovir (on day 4 of illness) and broad-spectrum antibiotics and antifungals, but she died 3 weeks later. The case underscores the importance of varicella vaccination, including catch-up vaccination of older children and adolescents, to prevent varicella and its serious complications.

On admission, the patient had a fever of 101.1°F (38.4°C), dyspnea, facial edema, generalized petechial rash, and hypotension; she received a diagnosis of septic shock. She was awake and alert, and noninvasive mechanical ventilation was implemented during the first 6 hours of admission. However, her respiratory function continued to deteriorate with increasingly labored breathing, requiring invasive mechanical ventilation.

The patient's laboratory results at admission indicated thrombocytopenia (platelet count: $30,000/\mu$ L; normal: 140,000–400,000/ μ L) and leukopenia (white blood cell count: 1,400/ μ L; normal: 3,800–10,600/ μ L); blood cultures

were negative. Vesicular fluid from a skin specimen collected on March 14 was positive for varicella-zoster virus (VZV) by direct fluorescent antibody test. Over the course of hospitalization, the patient developed pneumonia complicated by acute respiratory distress syndrome, pancytopenia, multiorgan dysfunction, health-care–acquired bacterial colonization and infection (including respiratory tract colonization with *Enterobacter cloacae* and urinary tract infection with *Pseudomonas aeruginosa*), and sepsis (blood cultures on hospital days 19 and 20 were positive for *Stenotrophomonas maltophilia*). Other blood cultures were negative, but they had been collected while she was on antibiotics.

Multiple chest radiographs showed diffuse, tiny nodules in the lung parenchyma consistent with alveolar consolidation. A computed tomography scan did not find any intracranial lesions, and electroencephalography ruled out any subclinical seizures. In addition to initial treatment with intravenous acyclovir, the patient's treatment included ciprofloxacin, meropenem, trimethoprim-sulfamethoxazole, ticarcillin-clavulanate, and tigecycline. During her last week in the hospital, her respiratory function deteriorated progressively, requiring high levels of pressure and oxygen. On hospital day 21, she died.

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U.S. Department of Health and Human Services Centers for Disease Control and Prevention The source of the patient's VZV exposure remains unknown. She had previously received 4 doses of diphtheria-tetanuspertussis vaccine; 1 dose of *Haemophilus influenzae* type b vaccine; and 2 doses of measles-mumps-rubella vaccine, but lived in a community with low rates of varicella vaccination. She did not have any known underlying medical conditions. An aspirate of bone marrow obtained during her hospitalization showed no evidence of leukemia.

Reported by

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Editorial Note

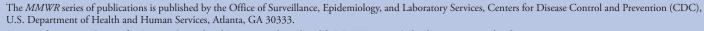
Varicella vaccine is highly effective (>95%) in preventing severe varicella and deaths (2). VZV infection has the potential, even among healthy persons, to cause severe complications, including secondary bacterial infection and sepsis, pneumonia, encephalitis, cerebellar ataxia, and thrombocytopenia; these complications can occur within a few days of rash onset (1,3).

The Advisory Committee on Immunization Practices recommends routine administration of the first dose of varicella vaccine at age 12–15 months and the second dose at age 4–6 years. Catch-up vaccination also is recommended. Unvaccinated persons who do not have evidence of immunity to varicella* should receive 2 doses of varicella vaccine at appropriate intervals, and those who have received 1 dose previously should receive a second dose (*2*).

Before varicella vaccination was included in routine childhood immunization, approximately 11,000 varicella-related hospitalizations and 100–150 deaths were reported annually in the United States (2). Implementation of the varicella vaccination program in the United States has led to declines of >95% in varicella-related illnesses, hospitalizations, and deaths in populations that received routine vaccination. However, of 24,488 varicella-related hospitalizations during 2000–2006, a total of 17,142 (70%) were among healthy persons with no contraindications for vaccination (4). Among 112 varicellarelated deaths during 2002–2007, a total of 100 (89%) were among persons with no high-risk preexisting conditions, such as cancer, immunodeficiency, or pregnancy (5).

The case described in this report can serve as a reminder of the importance of catch-up vaccination of older children and adolescents (2) to prevent varicella and its serious complications later in life when disease can be more severe. Approaches that are used to implement catch-up vaccination include

^{*} Evidence of immunity to varicella includes any of the following: 1) documentation of age-appropriate vaccination with varicella vaccine, 2) laboratory evidence of immunity or laboratory confirmation of disease, 3) birth in the United States before 1980, or 4) diagnosis or verification by a health-care provider of a history of varicella or herpes zoster disease.



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Exposure to VZV can occur when persons are exposed to patients with varicella (chickenpox) or herpes zoster (shingles). Unvaccinated children, adolescents, and adults are at risk for acquiring varicella; severe varicella can develop among healthy persons, and which patients might develop an especially severe course often is unpredictable at disease onset. Health-care providers should remind parents about vaccination during routine visits for children and adolescents, and parents should be informed of the risks, including potentially severe complications, from vaccine-preventable diseases. Resources for discussions with parents regarding vaccination are available.[†] Adult patients who have no evidence of varicella immunity should be offered varicella vaccine. For otherwise healthy persons aged >12 years who develop varicella, oral acyclovir is recommended. Treatment should be initiated as soon as possible, ideally within the first 24 hours (7). Intravenous acyclovir therapy is recommended for immunocompromised patients, and also in cases with serious, viral-mediated complications (7).

What is already known on this topic?

Although varicella usually is a self-limited disease, it can lead to severe complications and death, even among persons without underlying conditions that put them at increased risk for severe disease. The varicella vaccine is highly effective in preventing severe varicella and death.

What is added by this report?

This report describes a varicella-related death that occurred in an unvaccinated, previously healthy adolescent aged 15 years. The case described in this report can serve as a reminder of the importance of catch-up vaccination of older children and adolescents to prevent varicella and its serious complications later in life when disease can be more severe. The case underscores the fact that severe complications of varicella and death can occur among persons without high-risk conditions for severe varicella.

What are the implications for public health practice?

Severe varicella can develop among unvaccinated healthy persons, and which patients might develop an especially severe course often is unpredictable. Persons without evidence of immunity to varicella should receive 2 doses of varicella vaccine, or a second dose if they have received only 1 dose, to prevent varicella and its severe complications.

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[†]Available at http://www.cdc.gov/vaccines/hcp/patient-ed/conversations/ index.html.

Transmission of *Strongyloides stercoralis* Through Transplantation of Solid Organs — Pennsylvania, 2012

Strongyloides stercoralis is an intestinal nematode endemic in the tropics and subtropics. Immunocompetent hosts typically are asymptomatic, despite chronic Strongyloides infection. In contrast, immunocompromised patients are at risk for hyperinfection syndrome and disseminated disease, with a fatality rate >50% (1–3). The infection source for immunocompromised patients, such as solid organ transplant recipients, is not always apparent and might result from reactivation of chronic infection after initiation of immunosuppressive therapy or transmission from the donor. In October 2012, the United Network for Organ Sharing (UNOS) notified CDC of a left kidney and pancreas recipient in Pennsylvania diagnosed with strongyloidiasis. This report summarizes the results of the investigation of the source of Strongyloides infection in three of four organ recipients. Testing of pretransplant donor and recipient sera confirmed that infection in the recipients was donor derived. This investigation underscores the importance of prompt communication between organ procurement organizations, transplant centers, and public health authorities to prevent adverse events in recipients when transmission is suspected. Additionally, it emphasizes the utility of stored pretransplant samples for investigation of suspected transplant-transmitted infections and the need to consider the risk for Strongyloides infection in organ donors.

Case Investigation

On October 4, 2012, UNOS notified CDC of a left kidney and pancreas transplant recipient diagnosed with strongyloidiasis. UNOS also identified three additional organ recipients: the right kidney recipient, who received his transplant at the same institution as the index case; the liver recipient, who died within a few days after the transplantation; and the heart recipient, who was diagnosed with suspected reactivation of chronic strongyloidiasis 2 weeks earlier. CDC requested stored pretransplant serum from all organ recipients, along with stored donor serum for testing, to determine if infection with *Strongyloides* in the recipients was donor derived or reactivation of chronic infection. Evaluation of these specimens revealed that no recipient had detectable *Strongyloides* antibody before transplantation, but the donor had evidence of chronic infection based on positive serologic results.

Organ donor. In July 2012, a Puerto Rico-born Hispanic man, aged 24 years, was admitted to a local emergency department with multiple gunshot wounds. After a 9-day hospitalization, he died, and his heart, kidneys, pancreas, and liver were transplanted into four recipients the next day. History obtained from his mother indicated that the donor was a healthy young male who often visited Puerto Rico. *Strongyloides* infection risk was not considered; therefore, testing was not performed before organ recovery.

Kidney and pancreas recipient. This recipient is a U.S.born white man, aged 64 years, with end-stage renal disease secondary to long-standing diabetes mellitus who had never traveled outside the United States. Nine weeks posttransplant, he developed severe nausea, anorexia, and abdominal distention and was admitted to the hospital. Stool studies and biopsies performed during an esophagogastroduodenoscopy revealed *S. stercoralis* adult worms; larvae were found in urine studies. The patient was treated with ivermectin and albendazole, and after a hospitalization complicated by *Enterobacter cloacae* bacteremia, periduodenal abscess, and loss of pancreatic transplant function, he was discharged in stable condition on ivermectin. Repeat stool analyses were negative 3 days after starting therapy.

Kidney recipient. This recipient is a U.S.-born adolescent, aged 14 years, with end-stage renal disease as a result of a single dysplastic kidney; he had never traveled outside the United States. He was contacted for evaluation 10 weeks posttransplant, after the left kidney and pancreas recipient received a diagnosis of strongyloidiasis. He was discovered to be ill with fever, rash, malaise, anorexia, nausea, vomiting, and diarrhea. He was diagnosed with strongyloidiasis via esophagogastroduodenoscopy-obtained biopsy and stool testing. He was treated with ivermectin for 4 weeks and albendazole for 2 weeks. Repeat stool specimens were negative 3 days after starting therapy and remained negative as of November 2012.

Liver recipient. This recipient was a Hispanic man, aged 66 years, with a history of hepatic failure secondary to chronic hepatitis C infection. He tolerated surgery and was clinically stable until postoperative day 4, when his heart stopped and he was unresponsive to attempts at resuscitation. At autopsy, no evidence of *Strongyloides* infection was found; cause of death was undetermined.

Heart recipient. This recipient was a U.S.-born Hispanic man, aged 59 years, with ischemic cardiomyopathy; he lived in Puerto Rico for 6 months as a teenager. He remained clinically stable posttransplant and was discharged 11 days after surgery. He experienced multiple episodes of organ rejection and was treated with high doses of steroids. Seven weeks posttransplant, he was readmitted to the hospital with fever and a respiratory illness and required intubation in response to rapid decompensation. He was diagnosed with a viral respiratory illness and given oseltamivir and antibiotic and antifungal medications. A bronchoscopy performed on hospital day 3 showed *S. stercoralis* larvae. He was started on ivermectin and albendazole for treatment of suspected reactivated chronic strongyloidiasis. He developed gram-negative and enterococcal bacteremia and vancomycin-resistant enterococcal meningitis and became neurologically compromised. Life support was withdrawn, and he died 11 weeks posttransplant.

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Editorial Note

Most *Strongyloides* infections in organ transplant recipients are thought to be caused by reactivation of chronic infection after initiation of immunosuppressive therapy. Donor-derived infection has been reported, but the incidence of transmission is unknown (4,5). During 2009–2012, CDC assisted in seven investigations of organ donors and associated recipients with strongyloidiasis determined to be donor derived. Donorderived infection is difficult to prove, especially if the infected recipient is from a region in which *Strongyloides* is endemic. Archived pretransplant serum samples were available for recipient testing in this investigation. Results of that testing contributed to the determination that infection was donor derived and not reactivated chronic infection in the recipients.

This investigation revealed several gaps in current understanding and assessment of the risk for transplant-transmitted strongyloidiasis. Specific recommendations are lacking for *Strongyloides* testing of organ donors from areas in which it is endemic. The parasitic infections sections of the American Society for Transplantation's guidelines for screening prior to solid organ transplantation recommend testing donors and recipients for *Toxoplasma* and *Trypanosoma cruzi* (the cause of Chagas disease), but only recommend screening for *Strongyloides* in recipients from areas in which the nematodes are endemic, with no mention of donor screening (6,7). These guidelines are not policy, thus screening of donors and recipients for parasitic infections is voluntary, resulting in varied practices among organ procurement organizations and

What is already known on this topic?

Strongyloides infections in organ transplant recipients are thought to be caused mainly by reactivation of chronic infection after initiation of immunosuppressive therapy, which can lead to hyperinfection or disseminated disease. The American Society for Transplantation's guidelines are in place to screen solid organ transplant recipients, but not donors, to assess the risk for reactivation of chronic infection in those from areas in which Strongyloides is endemic.

What is added by this report?

Donor-derived *Strongyloides* infection might be more common than previously believed. In these investigations, a single donor was the source of infection for three of four organ recipients. Testing of pretransplant serum contributed to the determination that infection was donor derived.

What are the implications for public health practice?

Screening of donors from *Strongyloides*-endemic areas might help to protect organ recipients. Rapid communication among transplant centers and organ procurement organizations is vital to protect the health of organ recipients when potential transmission of disease or medical conditions from the donor is a concern.

transplant centers based on the perceived risk in their respective patient populations. The growing evidence of transplant transmission of *Strongyloides*, reported here and in the recent literature, might support development of recommendations for specific testing of donors and recipients from endemic regions to prevent severe strongyloidiasis in recipients (1,4,5). A minimum of three serial stool examinations for larvae, using specialized concentration techniques, is the gold standard for diagnosis of *Strongyloides* infection, but this might not be feasible in patients who have poor gastrointestinal function or are brain dead. Tests to detect parasite-specific antibody, such as an enzyme-linked immunoassay, also are available and are valuable in identifying *Strongyloides* infection (8). If infection is confirmed in the donor, prophylaxis could be given to recipients to avert adverse outcomes.

Rapid communication among transplant centers with patients who received organs from a single donor also is essential. The Organ Procurement and Transplant Network encourages organ procurement organizations and transplant programs to communicate promptly through its Patient Safety System, especially when there is concern for potential transmission of disease or medical conditions to the organ recipient from the donor. Such communication ideally should occur within 24 hours after knowledge of or concern for transmission, because multiple recipients might be adversely affected (9).

This investigation illuminates two gaps that need to be filled to improve transplant safety in solid organ recipients at risk for *Strongyloides* infection: 1) developing recommendations for screening of donors from *Strongyloides*-endemic areas, and 2) improving communication among transplant centers and organ procurement organizations. Advances in these areas might be life-saving for immunocompromised hosts.

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Human Contacts with Oral Rabies Vaccine Baits Distributed for Wildlife Rabies Management — Ohio, 2012

Baits laden with oral rabies vaccines are important for the management of wildlife rabies in the United States (1). In August 2012, the Wildlife Services program of the U.S. Department of Agriculture's Animal and Plant Health Inspection Service began a field trial involving limited distribution of a new oral rabies vaccine bait in five states, including Ohio. The vaccine consisted of live recombinant human adenovirus type 5 vector, expressing rabies virus glycoprotein (AdRG1.3) (Onrab). A previously used oral rabies vaccine consisting of a live recombinant vaccinia vector, expressing rabies virus glycoprotein (V-RG) (Raboral V-RG) (2,3), was distributed in other areas of Ohio. To monitor human contacts and potential vaccine virus exposure, surveillance was conducted by the Ohio Department of Health, local Ohio health agencies, and CDC. During August 23-September 7, 2012, a total of 776,921 baits were distributed in Ohio over 4,379 square miles (11,341 square kilometers). During August 24-September 12, a total of 89 baits were reported found by the general public, with 55 human contacts with baits identified (some contacts involved more than one bait). In 27 of the 55 human contacts, the bait was not intact, and a barrier (e.g., gloves) had not been used to handle the bait, leaving persons at risk for vaccine exposure and vaccine virus infection. However, no adverse events were reported. Continued surveillance of human contacts with oral rabies vaccine baits and public warnings to avoid contact with baits are needed because of the potential for vaccine virus infection.

Wildlife accounts for more than 90% of the rabid animals reported in the United States, and raccoons are the species most frequently reported (4). Oral rabies vaccination is an effective strategy to prevent the spread of rabies in reservoirs such as raccoons, coyotes, and foxes. Baits laden with oral rabies vaccine are distributed in strategic areas where target species can find and consume the baits, thereby releasing vaccine into their oral cavity. Oral rabies vaccination has contributed to the elimination of the red fox rabies virus variant and the canine rabies virus variant from several European countries and the United States, respectively, and has helped to prevent any appreciable spread of the raccoon rabies virus variant in the eastern United States (1). V-RG has been used in the United States since 1990, with approximately 138 million doses released to date. Baiting strategies have attempted to minimize human contact with V-RG baits because of the risk for infection with the V-RG vaccine virus; only two human vaccinia infections have been reported from V-RG exposure (3,5,6). AdRG1.3 is an alternative to V-RG that might have a different human safety profile given the high prevalence of antibodies in humans to human adenovirus type 5 and the mild illness that typically results from infection with this virus (7). AdRG1.3 has been integrated successfully into raccoon rabies management programs in Canada and has shown promise when used at higher bait densities for eliminating residual rabies foci in skunks (8,9).

Before and during the 2012 distribution of baits, the Ohio Department of Health, Wildlife Services, and Ohio local health jurisdictions used print media, television, radio, and the Internet to raise awareness and provide guidance to the public regarding what to do if a bait was found by a person or domestic animal. Despite these efforts, 75% of persons who came in contact with a bait were unaware of the baiting operation. A human contact was recorded when a person reported either seeing or coming into physical contact with a single bait or multiple baits with or without a barrier such as gloves. Contacts were reported by calling the toll-free telephone numbers printed on all baits or by contacting local health departments directly.

Persons who came into physical contact with an intact bait (i.e., a bait that was neither punctured nor leaking) did not require further follow-up, even if they did not use a barrier such as gloves, because vaccine exposure was not likely to have occurred. However, persons who came into physical contact with a bait that was not intact and who did not use a barrier such as gloves were considered to be potentially exposed to vaccine and at risk for vaccine virus infection. Attempts were made to contact all persons potentially exposed to vaccine 21 days after the event to ensure that their symptoms, if any, were reported. Persons who were immunocompromised, pregnant, aged <12 years, or cognitively impaired and persons with dermatologic conditions or a history of vaccine exposure to a mucosal membrane were contacted sooner than 21 days after the potential exposure.

During August 23–September 7, 2012, a total of 776,921 baits (272,034 AdRG1.3 and 504,887 V-RG baits) (Figure) were distributed by automobile in urban areas and by aircraft in rural areas of Ohio over an area of 4,379 square miles (11,341 square kilometers). A total of 89 baits were reported found by the general population during August 24–September 12 (11.5 baits found per 100,000 baits distributed). Fifteen of the baits found were AdRG1.3 (5.5 per 100,000 AdRG1.3 baits distributed), and 74 were V-RG (14.7 per 100,000 V-RG baits distributed) (p<0.001).

FIGURE. Types of oral rabies vaccine baits* distributed by Wildlife Services of the U.S. Department of Agriculture's Animal and Plant Health Inspection Service — Ohio, 2012



Photo/U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Wildlife Services

* Two types of oral rabies vaccines were distributed in different areas of Ohio: a new oral rabies vaccine (AdRG1.3) and one that has been in use since 1990 (V-RG). Clockwise from upper left: two V-RG coated sachets, two V-RG fishmeal polymer blocks, two AdRG1.3 polyvinyl chloride blister packs. A U.S. quarter is shown to illustrate the size of the baits.

Among the 89 baits found, 55 human contacts occurred (some human contacts involved more than one bait). Fourteen of the human contacts were with AdRG1.3 baits, and 41 were with V-RG baits. Among the 55 human contacts, 27 involved potential vaccine exposures. Among the AdRG1.3 bait contacts, 79% resulted in potential vaccine exposure, compared with 39% of V-RG bait contacts (odds ratio: 5.7; 95% confidence interval: 1.4–23.8) (Table 1). Only 5.8% of persons physically contacting a bait used a barrier such as gloves.

Fifty-four of the human contacts were reported through 47 telephone calls on the toll-free numbers (more than one human contact was reported on some calls). An additional human contact was reported directly to a local health department. The total report rate was 6.2 reports per 100,000 baits distributed, with 4.4 reports per 100,000 AdRG1.3 baits distributed and 7.1 reports per 100,000 V-RG baits distributed (Table 2).

Five of the persons who had potential vaccine exposures also had one of the conditions that required closer follow-up. Three of these incidents occurred with AdRG1.3 and involved a boy aged 11 years, a pregnant woman, and a woman with eczema. The other two incidents occurred with V-RG in women who had autoimmune conditions and were on immunosuppressive medications. No adverse events were reported among these five persons or among the other persons who contacted baits.

A total of 38 (79%) of the 48 reports of human contact involved domestic animals, and all of the animals were dogs. One animal adverse event resulted from an AdRG1.3 bait TABLE 1. Reported number of human contacts with oral rabies vaccine baits and number and percentage of contacts with potential vaccine exposure, by year and bait type — Ohio, 2010–2012

Year/Bait type	No. of human contacts	No. of contacts with potential vaccine exposure	(%)
2010*	83	37	(45)
2011*	83	29	(35)
2012 (total)	55	27	(49)
AdRG1.3	14	11	(79)
V-RG	41	16	(39)

Abbreviations: AdRG1.3 = human adenovirus type 5-rabies glycoprotein recombinant vaccine; V-RG = vaccinia-rabies glycoprotein recombinant vaccine. * During 2010 and 2011, only V-RG was distributed.

TABLE 2. Reported number of oral rabies vaccine baits distributed and later found and numbers of human contacts and reports received, by bait type — Ohio, 2012

Bait type	No. of baits distributed	No. of baits found	No. of human contacts reported	No. of reports received	Reports received per 100,000 baits		
AdRG1.3	272,034	15	14	12	4.4		
V-RG	504,887	74	41	36	7.1		

Abbreviations: AdRG1.3 = human adenovirus type 5-rabies glycoprotein recombinant vaccine; V-RG = vaccinia-rabies glycoprotein recombinant vaccine.

temporarily obstructing a dog's airway, but the dog survived. Two other adverse events were reported for V-RG baits in which the dogs regurgitated the baits.

Reported by

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Editorial Note

Surveillance during rabies vaccine baiting operations in Ohio suggests that human and domestic animal contacts with baits are rare. In 2010 and 2011, totals of 774,714 and 863,215 baits were distributed in Ohio, respectively, compared with 776,921 in 2012 (*10*). Overall, fewer human contacts with baits were reported in 2012 than in the preceding 2 years: 55 in 2012, compared with 83 in both 2010 and 2011 (Ohio Department of Health, unpublished data, 2012).

Multistate surveillance of contacts with V-RG baits during 2001–2009 revealed 6.9 V-RG baits found per 100,000 V-RG baits distributed for the study period, compared with 14.7 V-RG baits found per 100,000 V-RG baits distributed in Ohio in 2012. This same multistate surveillance system found 3.5 reports of V-RG bait contacts per 100,000 V-RG baits distributed during 2001–2009 (*3*), compared with 7.1 reports per 100,000 V-RG baits distributed in Ohio in 2012. Similar report rates have been observed previously in other states (*3*).

In 2012, AdRG1.3 was distributed for the first time in Ohio. The rate of 4.4 reports of AdRG1.3 bait contacts per 100,000 baits distributed was higher than rates observed in Canada (8,9) and in the first AdRG1.3 field trial in the United States in rural West Virginia in 2011 (Wildlife Services, U.S. Department of Agriculture, unpublished data, 2012). However, no adverse events were reported as a result of human contacts with baits in Ohio, Canada, or West Virginia (Wildlife Services, U.S. Department of Agriculture, unpublished data, 2013) (8,9). Because the risk for infection arises from exposure to vaccine virus rather than from contact with an intact bait, the higher proportion of human contacts that resulted in potential vaccine exposure with AdRG1.3 baits compared with V-RG baits deserves further evaluation.

The low percentage of persons who were aware of the baiting operation at the time of bait contact suggests that public outreach strategies should be evaluated and modified to enhance public awareness. Similar low rates of awareness about baiting operations have been reported in the past (*3*). In addition, only 5.8% of persons physically contacting a bait reported using a barrier such as gloves to handle baits, underscoring the need to raise awareness about the potential risk of handling baits without protection.

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Jay Becker, Geauga County Health Dept; Sandy Swann, Trumbull County Health Dept; Kelly Lewis, Ohio State Univ. Dennis Slate, Timothy Algeo, Wildlife Svcs, US Dept of Agriculture. Ermias Belay, Inger Damon, Robert Holman, Andrea McCollum, Lynda Osadebe, Brett Petersen, Mary Reynolds, Div of High-Consequence Pathogens and Pathology; Celia Quinn, EIS Officer, CDC.

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What is already known on this topic?

Baits laden with oral rabies vaccine play an important role in the management of rabies in wildlife. An oral rabies vaccine consisting of a recombinant vaccinia vector (V-RG) has been used in the United States for over 20 years; during this time only two cases of human vaccinia infection from human contact with vaccine in the baits have been reported. An oral rabies vaccine consisting of a recombinant human adenovirus type 5 vector (AdRG1.3) is now being field tested in the United States to assess its safety and immunogenicity.

What is added by this report?

This is the first published report of human contacts with AdRG1.3 baits in the United States. In 2012, a total 272,034 AdRG1.3 and 504,887 V-RG baits were distributed in Ohio. A total of 55 human contacts with the baits were reported, with potential vaccine exposure in 27 of the human contacts (11 with AdRG1.3 and 16 with V-RG). No adverse events were reported.

What are the implications for public health practice?

Ongoing surveillance is needed of human contacts with AdRG1.3 and V-RG baits. The low level of awareness about baiting operations among those who came into contact with baits suggests a need for improved public outreach before distributing baits.

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Evaluating Surveillance Indicators Supporting the Global Polio Eradication Initiative, 2011–2012

The Global Polio Eradication Initiative (GPEI) was established in 1988 by the World Health Assembly to interrupt transmission of wild poliovirus (WPV); completion of this initiative was declared a programmatic emergency of public health in January 2012 (1,2). Polio cases are detected through surveillance for acute flaccid paralysis (AFP) with linked stool specimens tested for polioviruses (PVs) at accredited laboratories within the Global Polio Laboratory Network (GPLN). AFP surveillance findings are supplemented by testing sewage samples (environmental surveillance) collected at selected sites. Virologic data guide where targeted immunization activities should be conducted or improved. Key performance indicators are used to 1) monitor AFP surveillance quality at national and subnational levels to identify gaps where PV transmission could occur undetected; 2) provide evidence of where PV circulation has been interrupted; and 3) allow timely detection of an outbreak. Standardized surveillance indicators allow progress to be monitored over time and compared among countries (3). This report presents AFP surveillance performance indicators at national and subnational levels for countries affected by polio during 2011-2012, and trends in environmental surveillance, updating previous reports (4,5). In the 19 countries with transmission of PV (WPV and/ or circulating vaccine-derived poliovirus [cVDPV]) during 2011–2012, national performance indicator targets were met in 12 (63%) countries in 2011 and 13 (68%) countries in 2012. Seven countries (37%) in 2011 had ≥80% of the population living in areas meeting performance indicators, increasing to nine countries (47%) in 2012. Performance indicators for timely reporting of PV isolation and characterization were met in four of six World Health Organization (WHO) regions in 2011 and five regions in 2012. To achieve global polio eradication, efforts are needed to improve and maintain AFP surveillance and laboratory performance.

AFP Surveillance

AFP surveillance detects recent paralytic illness of any cause, including poliomyelitis caused by WPV or VDPV. The indicator used to determine if surveillance is sufficiently sensitive to detect PV circulation is the annual proportion of AFP cases that are negative for WPV and VDPV (nonpolio AFP [NPAFP]) among children aged <15 years. Countries in WHO regions certified as polio-free* should achieve an annual NPAFP rate of ≥1 case per 100,000 population aged <15 years; all other countries[†] should achieve annual rates of ≥ 2 . To ensure sufficiently complete and reliable laboratory analysis, $\geq 80\%$ of AFP cases should have two stool specimens collected ≥ 24 hours apart, within 14 days of paralysis onset, arriving in good condition at an accredited GPLN laboratory (adequate specimen). Because national data can mask heterogeneous subnational performance, the AFP surveillance indicators described in this report can be applied to subnational areas and assessed both individually and in combination. To assess population coverage in surveillance, the proportion of the national population residing in the subnational areas where both indicator targets are met is considered. Both national and subnational surveillance performance indicators are used to track GPEI progress.

In 2011, AFP surveillance detected WPV transmission in 16 countries: four countries with uninterrupted endemic transmission (Afghanistan, India, Nigeria, and Pakistan), three previously polio-free countries with reestablished transmission (Angola, Chad, and Democratic Republic of the Congo [DRC]), and nine countries with outbreaks following importation (Central African Republic [CAR], China, Côte d'Ivoire, Gabon, Guinea, Kenya, Mali, Niger, and Republic of the Congo) (Table 1) (6). In 2012, WPV transmission was detected in five countries (Afghanistan, Chad, Niger, Nigeria, and Pakistan); because the most recent confirmed WPV case in India had onset in January 2011, WHO removed India from the list of polio-endemic countries in February 2012.

In 2011, cVDPV cases were detected in seven countries (Afghanistan, DRC, Mozambique, Niger, Nigeria, Somalia, and Yemen) and in eight countries in 2012 (Afghanistan, Chad, DRC, Kenya, Nigeria, Pakistan, Somalia, and Yemen) (Table 1). All cVDPV outbreaks during 2011 and 2012 were type 2 except in Mozambique (type 1) and Yemen (type 3). cVDPV isolates detected in Kenya were genetically similar to cVDPV isolates detected in Somalia (*7*).

All 19 countries reporting PV transmission during 2011– 2012 met the national target of an annual rate of \geq 2 NPAFP cases per 100,000 population aged <15 years for both years (Table 1); the national target of \geq 80% of AFP cases with adequate specimens was met by 12 (63%) countries in 2011 and 13 (68%) countries in 2012. The geographic distribution of subnational AFP surveillance quality indicators varied among countries with PV circulation (Table 1, Figure). In the African Region, \geq 80% of the population lived in areas meeting both AFP surveillance quality indicators only in Nigeria in 2011, and in Angola, CAR, Kenya, and Nigeria in 2012. In addition, DRC, Mali, and Mozambique had substantial

^{*}American, European, and Western Pacific regions.

[†]Countries in the African, Eastern Mediterranean, and South-East Asian regions.

		2011								2012						
WHO region [†] / Country	No. of AFP cases	National NPAFP rate [§]	% subna- tional areas with NPAFP rate ≥2 [¶]		% subna- tional areas with ≥80% adequate specimens	% population in areas meeting both indica- tors ^{††}	No. of confirmed WPV cases (No. of cVDPV cases) ^{§§}	No. of AFP cases	National NPAFP rate [§]	% subna- tional areas with NPAFP rate ≥2 [¶]		tional areas with ≥80% adequate	% population in areas meeting both indicators	No. of confirmed WPV cases (No. of cVDPV cases) ^{§§}		
African	16,636	4.4	_	88	_	_	350 (48)	18,032	4.8	_	90	_	_	127 (40)		
Angola ^{†††}	256	2.3	56	91	89	43	5	319	3.1	94	90	94	95	_		
CAR***	142	6.0	100	80	71	68	4	124	6.3	100	85	86	88	_		
Chad ^{†††}	465	5.7	100	75	39	33	132	418	6.7	100	71	22	20	5 (12)		
Côte d'Ivoire***	511	5.1	95	64	0	0	36	331	3.5	74	77	29	25	_		
DRC ⁺⁺⁺	2,222	4.9	100	79	27	33	93 (11)	1,858	4.4	100	83	64	70	(17)		
Gabon***	30	2.9	0	60	33	10	1	25	2.4	0	12	0	0			
Guinea***	205	3.8	100	68	0	0	3	187	3.3	100	62	0	0	_		
Kenya***	559	3.0	88	84	75	49	1	715	4.2	100	91	100	100	(3)		
Mali***	210	2.7	100	84	67	64	7	266	3.4	75	91	75	77	_		
Mozambique	314	2.7	80	87	80	59	(2)	337	3.1	100	88	70	77	_		
Niger***	319	4.0	88	73	25	20	5 (1)	365	4.5	100	68	0	0	1		
Nigeria ⁺⁺⁺	6,099	7.9	100	93	100	100	62 (34)	7,223	8.7	100	94	97	96	122 (8)		
Republic of the Congo***	93	3.1	60	75	55	20	1	62	2.9	50	76	55	16	—		
Eastern Mediterranean	11,742	5.7	_	90	—	—	278 (19)	10,956	5.2	—	91	—	—	95 (27)		
Afghanistan ^{†††}	1,831	10.0	100	92	91	91	80 (1)	1,829	10.2	100	92	94	91	37 (8)		
Pakistan ^{†††}	5,767	7.1	100	88	88	95	198	4,878	6.3	100	89	88	98	58 (16)		
Somalia	172	3.2	94	98	95	81	(9)	148	2.8	75	98	100	56	(1)		
Yemen	386	3.4	100	91	95	93	(9)	477	4.0	100	93	95	98	(2)		
South-East Asia	65,331	12.1	_	85	_	_	1	66,067	12.2	_	87	_	_	0		
India ⁺⁺⁺	60,540	13.5	91	84	82	89	1	60,994	14.0	100	87	86	97	_		
Western Pacific	7,303	2.1	_	90	_	_	21	7,569	2.2	_	91	_	_	0		
China***	6,182	2.8	81	94	97	91	21	6,181	2.8	77	94	97	87	_		
Total	101,012	5.6		88	_	_	650 (67)	102,624			90			223 (67)		

TABLE 1. National and subnational acute flaccid paralysis (AFP) surveillance indicators and number of confirmed wild poliovirus (WPV) and circulating vaccine-derived poliovirus (cVDPV) cases, by World Health Organization (WHO) region and polio-affected country, 2011 and 2012*

Abbreviations: NPAFP = nonpolio AFP; CAR = Central African Republic; DRC = Democratic Republic of Congo.

* Data as of February 5, 2013.

⁺ Regional NPAFP rates use United Nations Development Program population estimates as denominators; these tend to be higher than country rates, which use their summed subnational population estimates as denominators. Regional data available at http://apps.who.int/immunization_monitoring/en/diseases/poliomyelitis/case_count.cfm.

[§] Per 100,000 persons aged <15 years.

[¶] For subnational areas (states and provinces) with populations >100,000.

** Standard WHO target is adequate stool specimen collection from ≥80% of AFP cases, in which two specimens are collected ≥24 hours apart, and within 14 days of paralysis onset, and arriving in good condition (received by reverse cold chain and without leakage or desiccation) in a WHO-accredited laboratory. Stool adequacy proportions from the WHO regions and China do not include criteria of good stool specimen condition.

⁺⁺ For all subnational areas regardless of population size.

^{§§} cVDPV is associated with two or more cases of AFP. Kenya cVDPVs in 2012 are linked to the Somalia outbreak. VDPV type 2 cases with greater than or equal to six nucleotide differences from AFP sources. Nigeria data include one case in 2011 with WPV1/cVDPV mixture.

11 Countries with reestablished WPV transmission.

*** Countries with WPV outbreaks.

⁺⁺⁺ Countries with endemic WPV transmission.

improvements in the proportion of the population living in areas meeting both AFP surveillance quality indicators from 2011 to 2012 (Table 1).

Six countries with PV circulation during 2011–2012 in the African Region had low proportions of subnational areas meeting the indicator for adequate specimen collection and low proportions of the population living in areas meeting subnational indicators in both years without substantial improvement (Chad, Republic of the Congo, Côte d'Ivoire, Gabon, Guinea, and Niger) (Table 1). Among neighboring countries with surveillance data available and without reported PV circulation during 2011–2012, quality gaps occurred in subnational AFP surveillance performance in 2012 (Figure).

Environmental Surveillance

The sampling and testing of sewage can identify PV circulation in populations serviced by the sewage system and is used to complement AFP surveillance (8). Environmental surveillance has been established in two currently polio-endemic countries: Nigeria since 2011 (currently 11 sites in three states) and Pakistan since 2009 (currently 23 sites in four states), and in 22 countries without active WPV transmission: India (currently 15 sites in four states), Egypt (currently 34 sites in 11 cities), and multiple sites in 20 countries of the WHO European Region.

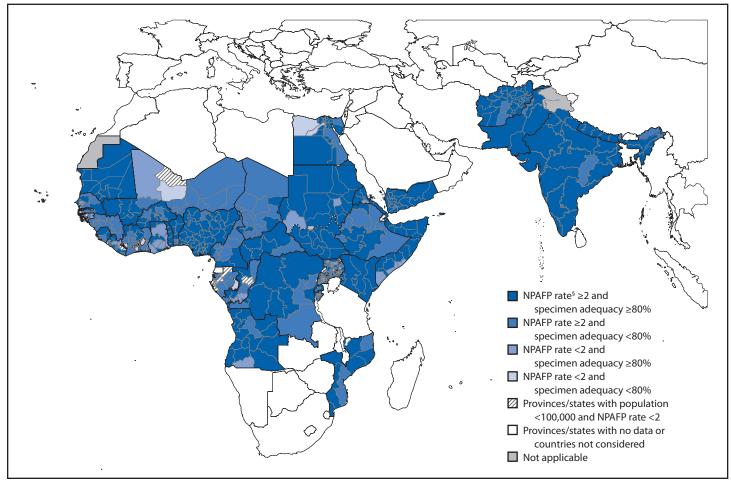


FIGURE. Combined performance indicators for the quality of acute flaccid paralysis (AFP) surveillance* in subnational areas (states and provinces) of 16 polio-affected countries and neighboring countries, 2012[†]

Abbreviation: NPAFP = nonpolio AFP.

* The Global Polio Eradication Initiative 2010–2012 strategic plan sets the following targets for countries with current or recent wild poliovirus transmission and their states/provinces: 1) NPAFP detection rate of two or more cases per 100,000 persons aged <15 years, and 2) adequate stool specimen collection from ≥80% of AFP cases, with specimen adequacy defined as two specimens collected ≥24 hours apart, both within 14 days of paralysis onset, shipped on ice or frozen packs, and arriving in good condition (without leakage or desiccation) at a World Health Organization–accredited laboratory.

⁺ Data are for AFP cases with onset during 2012, reported as of February 13, 2012.

§ Per 100,000 persons aged >15 years.

In Nigeria, WPV type 1 (WPV1) and VDPV type 2 (VDPV2) were isolated from sewage samples taken from four sites in Sokoto during March–December 2012, including periods when no PV was isolated from persons with AFP. In Kano, sewage sampling began in 2011 at three sites; VDPV2, WPV1, and WPV type 3 isolates were detected during January–September 2012.

In Pakistan, the number of environmental surveillance sampling sites increased from 17 in 2011 to 23 in 2012. WPVs have been isolated from sewage samples since testing began in 2009 from all major cities, even in the absence of confirmed WPV cases detected through AFP surveillance. Samples from Sindh consistently have yielded WPV isolates in the absence of associated WPV-positive AFP cases in the vicinity. In contrast, WPV cases were not detected in Quetta during the second half of 2012; environmental samples from the two Quetta sites also were negative during that period.

In Egypt, WPV1 was isolated from two samples collected in Cairo in December 2012; WPV1 was not detected from samples collected subsequently. The WPV1 sequences from these isolates were similar to WPV1 circulating in northern Sindh, Pakistan. WPV has not been detected in persons with AFP in Egypt since 2004.

Global Polio Laboratory Network

GPLN consists of 146 WHO-accredited PV laboratories in all six WHO regions (5). GPLN member laboratories follow standardized protocols to 1) identify and isolate PV to confirm WPV cases; 2) differentiate the three PV serotypes (1-3), and WPV, Sabin-like PV,§ and VDPV (intratypic differentiation [ITD]); and 3) conduct genomic sequencing to monitor pathways of PV transmission by comparing the nucleotide sequence of the VP1 region of the genome from PV isolates (9,10). The two standard laboratory timeliness indicators for stool specimen processing are to report \geq 80% ITD results within 7 days of receipt of specimen and $\geq 80\%$ of sequencing results within 7 days of receipt of specimen. The independent programmatic indicator standard is to report ITD results for ≥80% of isolates within 60 days of paralysis onset of persons with AFP cases; this indicator takes into account the entire interval from onset of paralysis through case notification, investigation, and specimen collection, transport, and testing (the WHO Eastern Mediterranean Region uses a 45-day timeframe). In addition to timeliness, the accuracy and quality of laboratory testing are monitored through an annual accreditation program of onsite reviews and proficiency testing (9). During 2011–2012, GPLN laboratories in five WHO regions met timeliness indicators for PV isolation. Reporting indicators for onset to ITD results were met in four WHO regions in 2011 and in all WHO regions in 2012 (Table 2). GPLN tested 215,629 stool specimens in 2012, compared with 206,981 specimens in 2011 (4% increase). In 2012, a total of 395 WPV isolates were detected from all sources (AFP and environmental sample specimens), compared with 1,570 WPV isolates in 2011 (a 75% decrease). In addition, 7,349 Sabin-related PV and 125 VDPV isolates were detected in 2012, compared with 8,569 Sabin-related PV and 93 VDPV isolates detected in 2011.

During 2012, genomic sequencing identified two WPV1 genotypes and one WPV3 genotype in the African Region: West Africa-B1 (WEAF-B1) type 1 genotype was detected in Nigeria, Niger, and Chad; WEAF-B2 type 1 genotype and WEAF-B type 3 genotype only were detected in Nigeria. In the WHO Eastern Mediterranean Region, South Asia (SOAS) type 1 and SOAS type 3 genotypes were detected in 2012. When genomic sequencing detects >1.5% nucleotide sequence divergence from previously identified PV isolates, this highlights quality gaps in AFP surveillance. Sequence analysis indicated that chains of WPV transmission had been missed by AFP surveillance during 2012 in Afghanistan, Chad, Nigeria, Pakistan, and Niger; chains of VDPV transmission also were missed in Nigeria and Somalia.

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Editorial Note

Notable gains in interrupting WPV transmission have occurred since GPEI was declared a programmatic emergency in January 2012; the number of countries with WPV transmission decreased from 16 in 2011 to five in 2012, and reported WPV cases decreased from 650 to 223, with WPV transmission now primarily in localized "sanctuaries." AFP surveillance

⁹ Discrete geographic locations with large numbers of missed children where the virus has ample opportunity to circulate.

TABLE 2. Number of poliovirus (PV) isolates from stool specimens of persons with acute flaccid paralysis and timing of results, by World Health
Organization (WHO) region, 2011 and 2012*

		20	011			2012						
	No. of –	No. of PV isolates			isolation re	% ITD results within 60	No. of –	No. of PV isolates			% PV isolation - results on	% ITD results within 60
WHO region	specimens	Wild	Sabin [†]	cVDPV§	time [¶]	days**	specimens	Wild	Sabin [†]	cVDPV§	time [¶]	days**
African	36,942	1,035	2,476	46	91	86	39,710	221	2,629	43	95	93
Americas	1,762	0	36	1	61	_	1,926	0	31	0	77	100
Eastern Mediterranean	23,011	512	807	17	98	97	26,626	174	930	71	94	99
European	3,270	0	77	7	96	78	3,167	0	66	2	96	88
South-East Asia	127,543	2	4,907	15	97	98	129,106	0	3,470	1	98	100
Western Pacific	14,453	21	266	7	97	86	15,094	0	223	8	98	84
Total	206,981	1,570	8,569	93	90	74	215,629	395	7,349	125	93	94

Abbreviations: cVDPV = circulating vaccine-derived poliovirus; ITD = intratypic differentiation.

* Data as of February 13, 2013 (Uzbekistan excluded, no data provided).

⁺ Either concordant Sabin-like results in ITD test and VDPV screening, or <1% sequence difference compared with Sabin vaccine virus (<0.6% for PV type 2).

⁵ For PV types 1 and 3, 10 or more VP1 nucleotide differences from the respective PV; for PV type 2, six or more VP1 nucleotide differences from Sabin type 2 PV. [¶] Results reported within 14 days for laboratories in the following WHO regions: African, Americas, Eastern Mediterranean, and South-East Asia, and Western Pacific

(not including China). Results reported within 28 days for the European Region and China.

** Results reported within 60 days of paralysis onset for all WHO regions except Eastern Mediterranean Region, which reported within 45 days of paralysis onset.

[§] Demonstrating <6 nucleotide changes from Sabin OPV strains for PV type 2, and <10 changes from Sabin OPV strains for PV types 1 and 3.</p>

What is already known on this topic?

Progress of the Global Polio Eradication Initiative (GPEI) is monitored through surveillance of acute flaccid paralysis (AFP) cases, laboratory surveillance to test stool specimens for polio viruses (PVs), typing and sequencing tests to track PV transmission, and environmental surveillance of sewage samples of PV at selected sites. Standardized indicators enable monitoring of progress over time and comparison between countries.

What is added by this report?

Progress has been made since polio eradication was declared a global public health programmatic emergency in 2012. During 2011–2012, wild poliovirus (WPV) case numbers and the number of countries with WPV transmission decreased. However, in 2012, only 63% of countries with WPV circulation met national AFP surveillance indicator targets, compared with 62% in 2011. During 2011–2012, the number of countries with PV transmission with \geq 80% of their populations living in areas meeting surveillance indicators increased from seven of 19 (37%) to nine of 19 (47%).

What are the implications for public health importance?

PV transmission can be undetected in areas where gaps in AFP surveillance quality exist, and this trend has been confirmed through laboratory analysis and environmental surveillance. Improving sensitivity for PV detection will involve expanding environmental surveillance activities and strengthening AFP performance, particularly at the subnational level, with ongoing supervision and monitoring of active surveillance at the health facility level.

performance indicators met certification-level quality in the majority of countries with PV circulation during 2011–2012 including polio-endemic countries, and improved during this period in Angola, CAR, and DRC; however, critical surveillance gaps remain in parts of Cameroon, Chad, and Niger that border areas of Nigeria with ongoing WPV transmission, and at subnational levels in multiple countries.

Environmental sampling continues to complement AFP surveillance in determining areas where PV circulates. GPEI plans to expand environmental surveillance in areas at highest risk for WPV transmission or cVDPV emergence, with consideration of site feasibility and laboratory capacity (2). Strengthening AFP surveillance becomes increasingly important to detect low-level WPV circulation in its last remaining foci of transmission to target intensified activities, promptly detect any new outbreaks, and eventually achieve, document, certify, and maintain regional polio-free status.

Regional certification of polio-free status only occurs when all member states demonstrate the absence of WPV transmission for 3 consecutive years with surveillance meeting performance targets. Global certification occurs only when all regions are certified poliofree, maintain certification-standard surveillance, and implement posteradication containment measures (2). The detection of PV in some countries (e.g., Afghanistan, Nigeria, Pakistan, and Somalia) that is highly diverged from previously identified PV isolates indicates that WPV or VDPV transmission remained undetected by AFP surveillance even when AFP performance indicators were met at the state/provincial level (6). For these reasons, increased emphasis will be placed on activities to ensure that AFP surveillance performance is maintained and improved at all administrative levels throughout each country in 2013. This can be accomplished by 1) tracking implementation of recommendations after surveillance reviews, 2) continuous monitoring of indicators at all administrative levels, 3) retraining staff, 4) improving timely collection and appropriate transportation of stool specimens, and 5) enhancing supervision. Ongoing supervision of active surveillance at health facilities also is needed to ensure optimal surveillance performance, with special attention to populations with a high risk for undetected PV transmission (e.g., mobile and displaced populations). In countries with large populations (e.g., Nigeria and Pakistan), surveillance performance needs to be closely monitored at lower administrative levels (e.g., districts).

The *GPEI Polio Eradication and Endgame Strategic Plan for* 2013–2018^{**} includes specific efforts to 1) interrupt all PV transmission, 2) certify polio eradication, 3) withdraw OPV, and 4) strengthen routine immunization and surveillance systems as part of the legacy of GPEI. The strategic plan will be submitted to the World Health Assembly in May 2013 to reinvigorate the commitment of countries and other GPEI partners toward polio eradication.

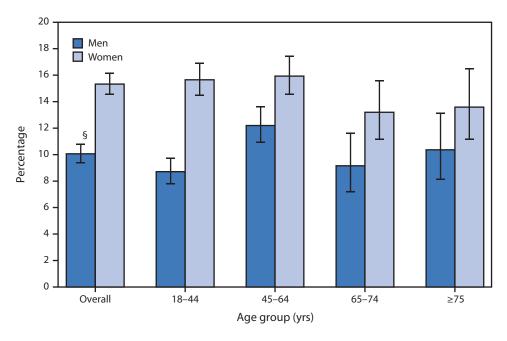
** Current draft available at http://www.polioeradication.org/resourcelibrary/ strategyandwork.aspx.

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FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Adults Who Often Felt Very Tired or Exhausted in the Past 3 Months,* by Sex and Age Group — National Health Interview Survey, United States, 2010–2011[†]



* Based on responses to the following: "In the past 3 months, how often did you feel very tired or exhausted? Would you say never, some days, most days, or every day?" Persons reporting feelings of tiredness or exhaustion on most days or every day were categorized as often feeling very tired or exhausted. Unknowns were not included in the denominators when calculating percentages.

⁺ Estimates are based on household interviews of a sample of the U.S. civilian, noninstitutionalized population. § 95% confidence interval.

During 2010–2011, women (15.3%) were more likely than men (10.1%) to often feel very tired or exhausted. Among adults aged 18–44 years, women were nearly twice as likely as men (15.7% versus 8.7%) to often feel very tired or exhausted. In addition, a difference was observed among women and men aged 45–64 years (15.9% versus 12.2%), but no differences by sex were observed among persons aged 64–74 years or those aged \geq 75 years.

Source: National Health Interview Survey, 2010 Quality of Life and 2011 Functioning and Disability supplements. Data were from a subset of the adults randomly selected for the Sample Adult Component of the National Health Interview Survey questionnaire. Additional information available at http://www.cdc.gov/nchs/nhis.htm.

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