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Vaccine-Associated Paralytic Poliomyelitis and BCG-osis in an Immigrant Child with Severe Combined Immunodeficiency Syndrome — Texas, 2013

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Poliovirus transmission has been eliminated in most of the world through the use of inactivated poliovirus vaccine (IPV) and live, attenuated oral poliovirus vaccine (OPV). In the United States, use of OPV was discontinued by the year 2000 because of the potential for vaccine-associated paralytic polio (VAPP); an average of eight cases were reported each year in the United States during 1980–2000 (*1*). Polio eradication efforts in other parts of the world continue to rely on OPV to take advantage of transmission of poliovirus vaccine strains to unvaccinated persons in the population, lower cost, and ease of administration. In 2013, an infant aged 7 months who recently immigrated to the United States from India was referred to a hospital in San Antonio, Texas. The infant had fever, an enlarging skin lesion in the deltoid region with axillary lymphadenopathy, decreased activity, and inability to bear weight on the left leg, progressing to paralysis of the left leg over a 6-week period. Recognition of lymphopenia on complete blood count led to immune evaluation, which revealed the presence of severe combined immunodeficiency syndrome (SCIDS), an inherited disorder. A history of OPV and bacille Calmette-Guérin (BCG) vaccination in India led to the diagnoses of VAPP and BCG-osis, which were confirmed microbiologically. This report demonstrates the importance of obtaining a comprehensive clinical history in a child who has recently immigrated to the United States, with recognition that differing vaccine practices in other countries might require additional consideration of potential etiologies.

The last outbreak of polio caused by importation of wild poliovirus in the United States occurred in 1979 in an unvaccinated community (*2*). The last endemically acquired case of VAPP in the United States occurred in the same community in 1999 (*2*). In 2005, an unvaccinated U.S. resident was infected with polio vaccine virus in Costa Rica and subsequently developed VAPP (*2*). A case of immunodeficiency-associated vaccine-derived poliovirus (iVDPV) infection, without paralysis, was diagnosed in an unvaccinated child with SCIDS in 2005, but the source of the virus could not be definitively identified (*3*). A woman in Minnesota aged 44 years with long-standing common variable immunodeficiency died after developing VAPP in 2009 (*4*). She was probably infected when her child received OPV approximately 12 years earlier. Case reports and cohort studies from several countries other than the United States demonstrate the continued occurrence of iVDPVs and the need for ongoing surveillance (*5*).

BCG, a live vaccine strain of *Mycobacterium bovis*, is commonly used to prevent the spread and disease burden of tuberculosis (TB) but is not used in the United States because of the low prevalence of TB in the general population and the fact that BCG vaccination complicates the interpretation of

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TB skin tests. However, OPV and BCG vaccine recipients who are in the United States as visitors or immigrants might present their health care providers with complex medical issues related to vaccines other than those recommended by CDC and the American Academy of Pediatrics.

A boy from India aged 7 months was brought to a community hospital emergency department in San Antonio, Texas, in early July 2013. His parents reported that he had a 6-week history of intermittent fever associated with a draining skin lesion over the left deltoid at the site of BCG vaccination. The child was diagnosed with acute lymphadenitis, prescribed trimethoprim/sulfamethoxazole, and sent home.

The child again was brought to the emergency department with increased irritability and decreased movement of the left leg, and was admitted to the hospital for further evaluation. The child appeared tired and anxious but was responsive to touch. The physical examination was negative for meningeal signs, no evidence of respiratory distress was found. A firm, mobile, tender, 2x2-cm mass was palpated under the left axilla. The child did not move his left leg spontaneously or in response to pain. Deep tendon reflexes were absent in the left leg and diminished in the right. Decreased anal sphincter tone was noted. The rest of the physical examination was noted as normal for age.

Laboratory, imaging, and microbiologic studies were conducted (Table). Immunology evaluation revealed immunoglobulin (Ig) M and IgA levels to be extremely low, and IgG level low, reflecting waning maternal antibody. B and T cells were absent; however, NK cells were present. Magnetic resonance imaging revealed abnormal signals in the cervical and lower thoracic spinal cord and the cauda equine, suggesting the presence of an encephalitic or postinfectious demyelinating process. Viral cultures from stool specimens grew an enterovirus, which was confirmed by polymerase chain reaction.

With the history of two additional OPV vaccinations during national immunization days in India, a diagnosis of VAPP was considered. The stool culture was subsequently identified as iVDPV type 1 (iVDPV1). The nonrecombinant iVDPV1 isolates had 10- 12 nucleotide substitutions from Sabin 1 vaccine virus in the 906- nucleotide VP1 capsid protein coding region. This result is consistent with initiation of a period of prolonged virus replication after receipt of the first OPV dose, based on the rate of evolution of approximately 1% per year (*6*), although other potential sources of secondary exposure are possible. The sequences had one amino acid substitution in neutralizing antigenic site 1 and one amino acid substitution in neutralizing antigenic site 3a, compared with Sabin 1 virus. An axillary lymph node biopsy showed evidence of acute and chronic inflammation with the presence of macrophages. Blood culture identified *M. bovis*, confirming a diagnosis of BCG-osis (disseminated BCG infection). Genetic studies eventually confirmed the diagnosis of RAG-1 deficient SCIDS with homozygous mutation. Family history revealed the child's older sibling died in infancy after rotavirus vaccination.

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TABLE. Laboratory, imaging, and microbiologic study results for a male patient aged 7 months recently immigrated from India who was brought to a hospital emergency department — San Antonio, Texas, July 2013

Type of study	Results
Laboratory	
CBC	ALC-216 cells/mm^3
Lymphocyte subsets	CD3 = 6 cells/mm^3; CD4 = 2; CD8 = 0; CD19 = 1; CD16/56 = 189
HIV 1/2	Negative
Immunoglobulins	IgA undetectable; IgM undetectable; IgG 140 mg/dL
CSF	83 WBCs/mm^3; 50% PMNs; 42% MNCs; 2% lymphocytes; protein = 48 mg/dL; glucose = 49 mg/dL
Imaging	
Chest radiograph	Normal
Brain and spine MRI	8-mm lesion in right cerebral peduncle; prominent abnormal T2 weighted signal at cord T11 level on the left; additional abnormal signal and contrast enhancement of several nerve roots
Chest, abdomen, pelvis CT	Enlarged lymph nodes: left supraclavicular, left axilla, retroperitoneal
Microbiology	
Blood	No bacterial growth at 48 hrs; later positive for AFB identified as *Mycobacterium bovis*/BCG
CSF	Negative bacterial meningitis screen and Gram stain; negative fungal smear and culture; negative PCR for HSV-1, HSV-2, and CMV
Stool	Enterovirus isolated; identified as iVDPV1
Lymph node FNA	AFB stain positive; identified as *M. bovis*/BCG

Abbreviations: CBC = complete blood count; ALC = absolute lymphocyte count; HIV = human immunodeficiency virus; IgA = immunoglobulin A; IgM = immunoglobulin M; CSF = cerebrospinal fluid; WBCs = white blood cells; PMNs = polymorphonuclear neutrophils; MNCs = mononuclear cells; MRI = magnetic resonance imaging; CT = computed tomography; AFB = acid-fast bacilli; BCG = bacille Calmette-Guérin; PCR = polymerase chain reaction; HSV = herpes simplex virus; CMV = cytomegalovirus; iVDPV1 = immunodeficiency-associated vaccine-derived poliovirus type 1; FNA = fine-needle aspiration.

Parental consanguinity and recurrent pregnancy losses in the mother were also reported. Chromosome microarray yielded homozygosity for >10% of the genome. The child progressed to respiratory distress during further observation. After consultation with multiple specialist physicians and with ethics committee review, the family chose to withdraw support, and the child died shortly thereafter.

Discussion

Live, attenuated vaccines have had substantial impact in reducing or eliminating endemic infectious diseases but their administration is not without some risk. Live viral vaccines are contraindicated in persons with immune deficiencies, and this is part of the rationale for newborn screening for SCIDS. VDPVs can emerge to cause polio outbreaks in areas with low OPV coverage and can replicate for years in persons who are immunodeficient (*7*).

When these risks outweigh those of endemic disease, replacement of OPV by IPV is appropriate, as occurred in the United States after 1999. As the incidence of polio declines worldwide, similar considerations might apply in other countries. In one prospective study of 942 children and adults from Sri Lanka with symptoms suggestive of underlying immune disease, five patients were identified as having stool shedding of all three types of vaccine-strain poliovirus (*8*). Three of the five patients had been identified as having SCIDS, and none survived the first year of life. In a study involving patients from Tunisia with primary immunodeficiencies, polioviruses were detected in six patients, and all isolates were vaccine-related (*9*).

Use of OPV in India and Nigeria has led to decline in poliovirus transmission, which contributes to interruption of wild poliovirus globally, but the risk associated with OPV is VAPP. According to the National Polio Surveillance Project, a collaboration between India and the World Health Organization, five cases of VDPV infection were reported in India in 2013 (*10*). All cases were attributed to immunodeficiencies, but the case described in this report is the first in which SCIDS was confirmed by molecular genetic analysis. Similarly, although the use of BCG in countries with high prevalence of TB helps to prevent tuberculous meningitis and miliary disease, and is a highly cost-effective intervention against severe childhood TB infection, its use is not recommended in the United States because of low risk for infection with TB and the fact that BCG vaccination complicates the interpretation of TB skin tests.*

International travel carries a small risk for importation of live, attenuated vaccine organisms into the United States with attendant clinical consequences. Because vaccine schedules vary based on different public health considerations in different parts of the world, it is imperative that U.S. pediatricians be thorough and careful to know the immunization and family history of foreign-born children. In doing so, vaccine-related diseases, such as polio, can be considered in the differential diagnosis, and appropriate diagnostic specimens can be collected. By being vigilant, vaccine-associated diseases can be diagnosed early, the spread of disease can be prevented by immunization of exposed persons in the community and among contacts, and appropriate treatment can be given in a timely manner to minimize suffering and reduce morbidity and mortality.

* Additional information available at http://www.cdc.gov/tb.

What is already known on this topic?

Routine use of oral poliovirus vaccine was discontinued in the United States in the late 1990s, when the number of vaccine-associated paralytic polio cases exceeded the number of endemic cases. Endemic polio has not been eliminated worldwide. Thus, some countries continue to administer oral poliovirus vaccine.

What is added by this report?

In 2013, an immigrant to the United States, aged 7 months, was diagnosed with severe combined immune deficiency, paralytic poliomyelitis caused by a Sabine vaccine strain type 1 virus, and disseminated bacille Calmette-Guérin (BCG) infection (BCG-osis). The infant had been vaccinated with oral poliovirus vaccine and BCG in India.

What are the implications for public health practice?

Primary health care providers in the United States should recognize the potential for live viral vaccine diseases, such as vaccine-associated paralytic poliomyelitis and BCG-osis, in foreign-born children recently arrived from abroad. By being vigilant, vaccine-associated diseases can be diagnosed early, the spread of disease can be prevented by immunization of exposed persons in the community and among contacts, and appropriate treatment can be given in a timely manner to minimize suffering and reduce morbidity and mortality.

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Racial Disparities in Access to Maternity Care Practices That Support Breastfeeding — United States, 2011

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Despite the well documented health benefits of breastfeeding (*1*), initiation of breastfeeding and breastfeeding duration rates among black infants in the United States are approximately 16% lower than among whites (*2*). Although many factors play a role in a woman's ability to breastfeed, experiences during the childbirth hospitalization are critical for establishing breastfeeding (*3*). To analyze whether the implementation by maternity facilities of practices that support breastfeeding varied depending on the racial composition of the area surrounding the facility, CDC linked data from its 2011 Maternity Practices in Infant Nutrition and Care (mPINC) survey to U.S. Census data on the percentage of blacks living within the zip code area of each facility. The results of that analysis indicated that facilities in zip code areas where the percentage of black residents was >12.2% (the national average during 2007–2011) were less likely than facilities in zip code areas where the percentage was ≤12.2% to meet five of 10 mPINC indicators for recommended practices supportive of breastfeeding and more likely to implement one practice; differences for the other four practices were not statistically significant. Comparing facilities in areas with >12.2% black residents with facilities in areas with ≤12.2% black residents, the largest differences were in the percentage of facilities that implemented recommended practices related to early initiation of breastfeeding (46.0% compared with 59.9%), limited use of breastfeeding supplements (13.1% compared with 25.8%), and rooming-in (27.7% compared with 39.4%). These findings suggest there are racial disparities in access to maternity care practices known to support breastfeeding.

The mPINC survey is a biennial census of maternity facilities (hospitals and free-standing birth centers) in the United States and its territories (*4*). The survey is sent to the person at each facility most knowledgeable about the facility's maternity care practices and policies. A total of 2,727 facilities participated in the 2011 mPINC survey (response rate = 83%). These data were analyzed for 10 mPINC indicators for recommended maternity care practices* from the World Health Organization/United Nations Children's Fund's *Ten Steps to Successful Breastfeeding* (*5*). The *Ten Steps* are evidence-based practices shown to increase breastfeeding exclusivity and duration, and are the basis for the Baby-Friendly Hospital Initiative.†

To estimate the prevalence of facilities with recommended maternity care practices by the percentage of black residents in their area, zip code level data for the category "non-Hispanic black or African American alone" were obtained for the period 2007–2011 from the U.S. Census Bureau's American Community Survey (ACS). ACS is a continuous nationwide survey that collects detailed information on demographic, social, economic, and housing characteristics; these data are only available by zip code as 5-year estimates (*6*). ACS and mPINC data were linked by zip codes; of the 2,727 facilities that participated in the 2011 mPINC survey, 84 (3%) facilities were missing zip code level racial data in ACS, resulting in a final analytic sample of 2,643 facilities. Facilities were divided into two categories: 1) those in zip code areas where the percentage of black residents was >12.2% (the national average during 2007–2011) (*6*) and 2) those in zip code areas where the percentage was ≤12.2%. The z-test was used to compare data from the two categories and determine whether differences in implementation of recommended maternity care practices were statistically significant ($p<0.05$). No other racial or ethnic groups were examined.

* The 10 mPINC indicators for recommended maternity care practices from the *Ten Steps* were as follows: 1) Model breastfeeding policy: hospital has a written breastfeeding policy that includes 10 model policy elements; 2) Staff competency assessment: nurses/birth attendants are assessed for competency in basic breastfeeding management and support at least once per year; 3) Prenatal breastfeeding education: breastfeeding education is included as a routine element of prenatal classes; 4) Early initiation of breastfeeding: ≥90% of healthy, full-term, breastfed infants initiate breastfeeding within 1 hour of uncomplicated vaginal birth; 5) Teach breastfeeding techniques: ≥90% of mothers who are breastfeeding or intend to breastfeed are taught breastfeeding techniques (e.g., positioning and how to express milk); 6) Limited use of breastfeeding supplements: <10% of healthy, full-term, breastfed infants are supplemented with formula, glucose water, or water; 7) Rooming-in: ≥90% of healthy, full-term infants, regardless of feeding method, remain with their mother for at least 23 hours per day during the hospital stay; 8) Teach feeding cues: ≥90% of mothers are taught to recognize and respond to infant feeding cues instead of feeding on a set schedule; 9) Limited use of pacifiers: <10% of healthy, full-term, breastfed infants are given pacifiers by maternity care staff members; and 10) Post-discharge support: hospital routinely provides three modes of post-discharge support to breastfeeding mothers (physical contact, active reaching out, and referrals).

† Additional information available at http://www.babyfriendlyusa.org/about-us/baby-friendly-hospital-initiative/the-ten-steps.

In 2011, three of the 10 mPINC indicators for recommended practices were met by >75% of the 2,643 facilities surveyed. The three were providing prenatal breastfeeding education (92.7%), teaching breastfeeding techniques (90.7%), and teaching mothers how to recognize and respond to infant feeding cues (84.7%) (Table).

Facilities in zip code areas with >12.2% black residents were significantly more likely to assess staff competency than facilities in zip code areas with ≤12.2% black residents (59.4% compared with 53.2%) (Table). However, facilities in zip code areas with >12.2% black residents were significantly less likely than facilities in zip code areas with ≤12.2% black residents to meet five of the nine other mPINC indicators for recommended practices: early initiation of breastfeeding (46.0% compared with 59.9%), limited use of breastfeeding supplements (13.1% compared with 25.8%), rooming-in (27.7% compared with 39.4%), limited use of pacifiers, (30.5% compared with 37.9%), and post-discharge support (23.9% compared with 29.9%) (Table).

Discussion

In 2011, implementation of 10 recommended maternity care practices supportive of breastfeeding among 2,643 maternity facilities varied widely, ranging from 18.9% to 92.7%, and was <50% for five practices. For half of the 10 practices, implementation was significantly lower among facilities in zip code areas with a higher percentage of black residents. These findings are important because research has shown that U.S. residents usually are admitted to hospitals within a relatively short distance of where they live, although persons living in rural areas might

TABLE. Prevalence of facilities meeting indicators for recommended maternity care practices,* by racial composition† of the zip code areas where the facilities were located — Maternity Practices in Infant Nutrition and Care Survey (mPINC), United States, 2011

mPINC indicators for recommended maternity care practices	Total facilities surveyed (N = 2,643§)	Percentage of black residents in the facility zip code area				
		≤12.2% (n = 2,030§)	>12.2% (n = 613§)	Percentage-point difference	Standard error of the difference	p-value
	%	%	%			
Model breastfeeding policy: hospital has a written breastfeeding policy that includes 10 model policy elements.	18.9	18.5	20.3	-1.8	1.87	0.33
Staff competency assessment: nurses/birth attendants are assessed for competency in basic breastfeeding management and support at least once per year.	54.6	53.2	59.4	-6.2	2.28	0.01¶
Prenatal breastfeeding education: breastfeeding education is included as a routine element of prenatal classes.	92.7	92.9	91.8	1.1	1.25	0.38
Early initiation of breastfeeding: ≥90% of healthy, full-term, breastfed infants initiate breastfeeding within 1 hour of uncomplicated vaginal birth.	56.7	59.9	46.0	13.9	2.31	<0.01¶
Teach breastfeeding techniques: ≥90% of mothers who are breastfeeding or intend to breastfeed are taught breastfeeding techniques (e.g., positioning and how to express milk).	90.7	91.2	89.2	2.0	1.41	0.16
Limited use of breastfeeding supplements: <10% of healthy, full-term, breastfed infants are supplemented with formula, glucose water, or water.	22.8	25.8	13.1	12.7	1.69	<0.01¶
Rooming-in: ≥90% of healthy, full-term infants, regardless of feeding method, remain with their mother for at least 23 hours per day during the hospital stay.	36.7	39.4	27.7	11.7	2.12	<0.01¶
Teach feeding cues: ≥90% of mothers are taught to recognize and respond to infant feeding cues instead of feeding on a set schedule.	84.7	85.1	83.2	1.9	1.71	0.26
Limited use of pacifiers: <10% of healthy, full-term, breastfed infants are given pacifiers by maternity care staff members.	36.2	37.9	30.5	7.4	2.16	<0.01¶
Post-discharge support: hospital routinely provides three modes of post-discharge support to breastfeeding mothers (physical contact, active reaching out, and referrals).	28.5	29.9	23.9	6.0	2.00	<0.01¶

* mPINC indicators for recommended maternity care practices are from *Ten Steps to Successful Breastfeeding*, available at http://www.babyfriendlyusa.org/about-us/babyfriendly-hospital-initiative/the-ten-steps.

† Zip code areas in which the percentage of "non-Hispanic black or African American" residents was >12.2% (the national average during 2007–2011), compared with ≤12.2%, according to data from the U.S. Census Bureau's American Community Survey.

§ Number of respondents varied slightly from the total for each of the prevalence estimates.

¶ Statistically significant percentage-point difference by z-test.

What is already known on this topic?

Breastfeeding has many health benefits for infants, yet there are persistent gaps in breastfeeding rates between black and white infants in the United States. Maternity care practices experienced during the hospital stay have a major impact on the establishment of breastfeeding.

What is added by this report?

Facilities located in zip code areas with higher percentages of blacks were less likely to meet five indicators for recommended maternity care practices supportive of breastfeeding and more likely to meet one indicator, than facilities in areas with a lower percentage of blacks. The largest differences were for indicators related to early initiation of breastfeeding, limited use of breastfeeding supplements, and rooming-in.

What are the implications for public health practice?

Interventions are needed to ensure that all maternity care facilities are implementing the recommended policies and practices known to be important for the establishment of breastfeeding. Facilities located in areas with higher percentages of blacks might need additional support.

travel farther than those in cities (*7*). Therefore, women living in zip code areas with a higher percentage of blacks might have less access to facilities implementing recommended maternity care practices, which might contribute to lower breastfeeding rates among blacks compared with other racial groups.

The reasons for the differences in maternity care practices by racial composition of the areas are not clear. Further research is needed on barriers to implementing recommended practices in these areas, on whether poorer maternity care practices are linked to lower breastfeeding rates in these areas, and on evaluating other factors that might be contributing to these disparities.

This is the first report based on national data showing that practices at maternity facilities vary with the racial composition of the zip code area in which the facility is located. However, similar findings were observed in a previous study in North Carolina that assessed whether there were differences in breastfeeding support services available through the Supplemental Nutrition Program for Women, Infants, and Children (WIC) program based on the county level racial/ethnic composition of the WIC sites. It was found not only that breastfeeding initiation by WIC site was negatively associated with the percentage of black clients, but also that WIC sites with higher percentages of black clients were less likely to offer clinic-based breastfeeding support services (*8*).

In a review of U.S.-based randomized trials evaluating breastfeeding interventions targeting minorities, interventions to change hospital or WIC policies, including enhanced practices and services, were among the public health approaches found to successfully improve breastfeeding outcomes among minority women (*9*). CDC currently is funding a project that addresses the need for quality improvement in maternity care practices. In June 2012, CDC awarded a 3-year cooperative agreement to the National Initiative for Children's Healthcare Quality to assist 89 hospitals, mostly located in states that have lower breastfeeding rates and that serve low-income and minority women, with improving maternity care practices to support breastfeeding and to move toward the Baby-Friendly designation. Detailed descriptions of the cooperative agreement program have been published (*2,10*).

The findings in this report are subject to at least four limitations. First, one mPINC indicator for each of the *Ten Steps* was selected; these indicators are consistent with the *Ten Steps*,[§] but might not encompass all aspects of each step. Second, although the mPINC survey was sent to the person identified as the most knowledgeable about the facility's policies and practices and facilities were encouraged to get input from key staff members as needed, responses might not accurately reflect actual practices. Third, the racial composition of the patients served at each facility is not collected in the mPINC survey. However, because most U.S. residents are admitted to hospitals close to where they live and most hospital service areas have only one local hospital, the data in this report for zip code areas are likely reasonable estimates for the racial composition of hospital patients, assuming overall hospital admission patterns (*7*) apply to births. Finally, only facilities with zip code level race data were included in this analysis. Excluded facilities might have had different percentages of blacks and maternity care practices. However, only 3% of facilities were excluded, which is not likely to have affected results.

The findings suggest that the implementation of maternity care practices supportive of breastfeeding vary based on the racial composition of the area, which means women living in areas with higher percentages of blacks might have less access to these services. Although the reasons for these disparities are unclear, the results might provide some insight into why there has been a persistent gap in breastfeeding initiation and duration rates between black and white infants in the United States. All facilities, regardless of the racial/ethnic composition of the populations they serve, can support the breastfeeding decisions of their patients by implementing evidence-based policies and practices shown to be critical for establishing breastfeeding, so that more infants are able to reap the numerous health benefits of breastfeeding.

[§] Additional information available at https://www.babyfriendlyusa.org/get-started/the-guidelines-evaluation-criteria.

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Update on Recommendations for Use of Herpes Zoster Vaccine

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Herpes zoster vaccine (Zostavax [Merck & Co., Inc.]) was licensed in 2006 and recommended by the Advisory Committee on Immunization Practices (ACIP) in 2008 for prevention of herpes zoster (shingles) and its complications among adults aged ≥60 years (*1*). The Food and Drug Administration (FDA) approved the use of Zostavax in 2011 for adults aged 50 through 59 years based on a large study of safety and efficacy in this age group (*2*). ACIP initially considered the use of herpes zoster vaccine among adults aged 50 through 59 years in June 2011, but declined to recommend the vaccine in this age group, citing shortages of Zostavax and limited data on long-term protection afforded by herpes zoster vaccine (*2*). In October 2013, ACIP reviewed the epidemiology of herpes zoster and its complications, herpes zoster vaccine supply, short-term vaccine efficacy in adults aged 50 through 59 years, short- and long- term vaccine efficacy and effectiveness in adults aged ≥60 years, an updated cost-effectiveness analysis, and deliberations of the ACIP herpes zoster work group, all of which are summarized in this report. No vote was taken, and ACIP maintained its current recommendation that herpes zoster vaccine be routinely recommended for adults aged ≥60 years. Meeting minutes are available at http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html.

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 Obstetrics and Gynecology (ACOG). Recommendations for routine use of vaccines in adults are harmonized with recommendations of AAFP, ACOG, and the American College of Physicians (ACP). 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.*

Herpes Zoster Vaccine Background

The burden of herpes zoster increases as persons age, with steep increases occurring after age 50 years. Not only does the risk of herpes zoster itself increase with age, but among persons who experience herpes zoster, older persons are much more likely to experience postherpetic neuralgia (PHN) (*3*), non-pain complications (*3*), hospitalizations (*4*), and interference with activities of daily living (*5*). Because persons aged 50 years can expect to live an additional 32 years and persons aged 60 years, another 23 years (*6*), vaccination must offer durable effectiveness to protect against this increasing burden of disease.

Merck is the only U.S. supplier of varicella zoster virus (VZV)-containing vaccines (Zostavax; varicella vaccine [Varivax]; and combined measles, mumps, rubella, and varicella vaccine [MMR-V, ProQuad]). Beginning in 2007, Merck experienced production shortfalls of the bulk product used to manufacture VZV-based vaccines, leading to intermittent delays in filling of Zostavax orders. As a result of increased production capacity and reliability, by January 2012, Merck had resumed routine supply of varicella-containing vaccines, and Zostavax returned to normal shipping (*7*). As of August 2014, no subsequent supply disruptions have been reported.

Studies of Efficacy and Duration of Protection

One randomized, placebo-controlled trial has evaluated short-term efficacy of herpes zoster vaccine administered to adults aged 50 through 59 years. This study of 22,439 adults in this age group showed a vaccine efficacy of 69.8% (95% confidence interval [CI] = 54.1%–80.6%) for the prevention of herpes zoster over a mean follow up period of 1.3 years (*8*). Efficacy for prevention of PHN and long-term vaccine efficacy in this age group were not studied.

Two studies have evaluated the short-term efficacy of the zoster vaccine in adults aged ≥60 years. The shingles prevention study (SPS) (*9*), a randomized controlled trial, followed 38,546 subjects for up to 4.9 years after vaccination (median = 3.1 years) and found a vaccine efficacy of 51.3% (CI = 44.2%–57.6%) for prevention of herpes zoster and 66.5% (CI = 47.5%–79.2%) for prevention of PHN. The short-term persistence substudy (STPS) (*10*) followed a subset of 14,270 SPS subjects primarily 4 to 7 years after vaccination and found a vaccine efficacy of 39.6% (CI = 18.2%–55.5%) for prevention of herpes zoster and 60.1% (CI = -9.8%–86.7%) for prevention of PHN. The point estimates for vaccine efficacy for prevention of herpes zoster by year after vaccination

from the combined SPS and STPS studies decreased from 62.0% (CI = 49.6%–71.6%) in the first year after vaccination to 43.1% (CI = 5.1%–66.5%) in year 5. The 95% CIs around the point estimates for years 6 (30.6%) and 7 (52.8%) included zero; therefore vaccine protection could not be demonstrated after year 5. Vaccine efficacy for prevention of PHN decreased from 83.4% (CI = 56.7%–95.0%) in year 1 to 69.8 (CI = 27.3%–89.1%) in year 2. Estimates for years 3 through 7 after vaccination were not statistically significantly different from zero, although point estimates were generally higher compared with estimates of vaccine efficacy against herpes zoster.

The long-term persistence study (*11*) continued to follow 6,687 vaccinated subjects from STPS primarily from year 7 through year 10 after vaccination. By the end of the STPS, subjects in the placebo group had been vaccinated; therefore, no concurrent control group was available for comparison. Instead, a statistical model estimated herpes zoster and PHN incidence in a comparable unvaccinated group using historical SPS control subjects. The model estimated a vaccine effectiveness of 21.1% (CI = 10.9%–30.4%) for prevention of herpes zoster and 35.4% (CI = 8.8%–55.8%) for prevention of PHN over years 7 to 10 combined. Methodologic challenges in reliance on herpes zoster incidence in historical controls for calculation of vaccine effectiveness against herpes zoster include the fact that several studies (*3,12–14*) have shown increases in herpes zoster incidence over time. The lack of a concurrent control group seriously diminishes the strength of evidence for duration of vaccine protection from years 7 through 10. In addition, although some vaccine protection is demonstrated during the combined years 7–10 using this methodology, there is a high degree of uncertainty about trends in vaccine effectiveness over this time frame. For these reasons, effectiveness of herpes zoster vaccine administered to persons aged ≥60 years for preventing herpes zoster beyond 5 years remains uncertain.

ACIP Review

At the October 2013 meeting, ACIP reviewed results from an updated cost-effectiveness analysis comparing health outcomes, health care resource utilization, costs, and quality-adjusted life years (QALYs) related to herpes zoster, PHN, and non-pain complications among unvaccinated persons and persons vaccinated at either age 50, 60, or 70 years (*15*). The model assumed waning of vaccine protection against herpes zoster to zero over 10 years for all ages, based on SPS, STPS, and long-term persistence study data. Projecting outcomes from ages 50 to 99 years, vaccination at age 60 years would prevent the most shingles cases (26,147 cases per 1 million persons) followed by vaccination at age 70 years and then age 50 years (preventing 21,269 and 19,795 cases, respectively). However, vaccination at age 70 years would prevent the most cases of PHN (6,439 cases per 1 million persons), followed by age 60 years and then age 50 years (preventing 2,698 and 941 PHN cases, respectively). From a societal perspective, vaccinating at age 70, 60, and 50 years would cost $37,000, $86,000, and $287,000 per QALY saved, respectively. The high cost per QALY saved with vaccination at age 50 years results from limited impact on prevention of PHN and other complications from ages 50 through 59 years and no remaining vaccine protection after age 60 when risk for PHN and other complications increases sharply. Results were robust in sensitivity analyses in which various more optimistic and pessimistic assumptions were made regarding waning of vaccine protection.

Because the protection offered by the herpes zoster vaccine wanes within the first 5 years after vaccination, and duration of protection beyond 5 years is uncertain, it is unknown to what extent persons vaccinated before age 60 years will be protected as they age and their risk for herpes zoster and its complications increases. Because duration of protection offered by the vaccine is uncertain, the need for revaccination is not clear. Assuming waning of vaccination protection according to currently available studies, the cost-effectiveness model projects a substantially greater reduction of disease burden, health care utilization, and costs with vaccination of older adults who have higher incidence of herpes zoster and related complications. Considering that the burden of herpes zoster and its complications increases with age and that the duration of vaccine protection in persons aged ≥60 years is uncertain, ACIP maintained its current recommendation that herpes zoster vaccine be routinely recommended for adults aged ≥60 years.

What recommendations are being reviewed?

Since 2008, the Advisory Committee on Immunization Practices (ACIP) has recommended routine vaccination of all persons aged ≥60 years with 1 dose of herpes zoster vaccine.

Why are the recommendations being reviewed now?

After approval by the Food and Drug Administration for use of zoster vaccine in adults aged 50 through 59 years in 2011, ACIP initially considered use of the vaccine among adults in this age group, but declined to change its recommendations at that time, citing shortages of Zostavax and limited data on long-term protection afforded by herpes zoster vaccine. A new review was conducted because the manufacturer has resumed routine supply of Zostavax and additional data on long-term protection have become available.

What is currently recommended?

Considering that the burden of herpes zoster and its complications increases with age and that the duration of vaccine protection in persons aged ≥60 years is uncertain, ACIP's recommendation remains unchanged; herpes zoster vaccine is routinely recommended only for adults aged ≥60 years.

With FDA approval, Zostavax is available in the United States and indicated for use among adults aged ≥50 years. Vaccination providers considering the use of Zostavax among certain persons aged 50 through 59 years despite the absence of an ACIP recommendation should discuss the risks and benefits of vaccination with their patients. Although the vaccine has short-term efficacy, there have been no long-term studies of vaccine protection in this age group. In adults vaccinated at age ≥60 years, vaccine efficacy wanes within the first 5 years after vaccination, and protection beyond 5 years is uncertain; therefore, adults receiving the vaccine before age 60 years might not be protected when their risks for herpes zoster and its complications are highest. CDC is actively monitoring postmarketing data on duration of vaccine protection in adults vaccinated at age ≥60 years. As additional data become available, ACIP will reevaluate the optimal age for vaccination and the need for revaccination to maintain protection against herpes zoster and its complications.

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Acknowledgments

Members of ACIP Herpes Zoster Work Group (Jeffrey S. Duchin, MD, Chair). Members of ACIP. Member roster for July 2013–June 2014 is available at http://www.cdc.gov/vaccines/acip/committee/members-archive.html.

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Closure of Varicella-Zoster Virus–Containing Vaccines Pregnancy Registry — United States, 2013

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Vaccines that contain live attenuated varicella-zoster virus (VZV) (Varivax, ProQuad, and Zostavax [all products of Merck & Co., Inc.]) are contraindicated during pregnancy (*1,2*). To monitor the pregnancy outcomes of women inadvertently vaccinated with VZV-containing vaccines immediately before or during pregnancy, Merck and CDC established the Merck/CDC Pregnancy Registry for VZV-Containing Vaccines in 1995 (*3*). This report updates previously published summaries of registry data (*4,5*), provides the rationale for the closure of the registry, and describes plans for continued monitoring of the safety of these vaccines when inadvertently administered to pregnant women or immediately before pregnancy. From inception of the registry in 1995 through March 2012, no cases of congenital varicella syndrome and no increased prevalence of other birth defects have been detected among women vaccinated within 3 months before or during pregnancy. Although a small risk for congenital varicella syndrome cannot be ruled out, the number of exposures being registered each year (approximately two varicella-susceptible women exposed during the high-risk period for congenital varicella syndrome) is now too low to improve on the current estimate of the risk.

Congenital varicella syndrome is characterized by cutaneous scarring and/or limb hypoplasia; other associated anomalies include microcephaly, muscular atrophy, ocular or neurologic abnormalities, and low birth weight. Because exposure to wild-type VZV in utero might result in congenital varicella syndrome, vaccines that contain live, attenuated VZV are contraindicated during pregnancy. To monitor the pregnancy outcomes of women inadvertently vaccinated with VZV-containing vaccines immediately before or during pregnancy, Merck, in collaboration with CDC, established a registry in 1995, when Varivax, indicated for prevention of varicella (chickenpox) in persons aged ≥12 months, was licensed in the United States (*1,3*). Reports of exposure to ProQuad, which is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella among children aged 12 months through 12 years, and Zostavax, which is licensed for the prevention of herpes zoster (shingles) among persons aged ≥50 years, were added to the registry in 2006, upon licensure of those vaccines. Detailed methods for the pregnancy registry have been described previously (*4,5*).

From March 1995 to March 2012, the registry received 860 prospective reports (received before the outcome of pregnancy was known) and 68 retrospective reports (received after the outcome of pregnancy was known) of women who inadvertently received Varivax within 3 months before pregnancy or at any time during pregnancy, and whose pregnancy outcomes were known, available for analysis, and considered complete. No defects consistent with congenital varicella syndrome were reported among the live-born infants or any of the conceptuses lost because of spontaneous abortion or elective termination for which information was available. Based on the 95 live-born infants of varicella-susceptible women exposed during the high-risk period for congenital varicella syndrome (first and second trimester of pregnancy) who were reported prospectively to the registry, the 95% confidence interval for risk for congenital varicella syndrome ranged from 0% to 3.8%. The overall prevalence for major birth defects in the registry was 2.2% among live-born infants (95% confidence interval = 1.3–3.5), similar to the prevalence in the general population (*6*). These data are reassuring regarding the safety of Varivax inadvertently administered during pregnancy; however, the number of women enrolled is insufficient to exclude a theoretical risk for congenital varicella syndrome lower than the risk estimated after infection with wild-type VZV (approximately 1% of live births when infection is contracted during the first two trimesters of pregnancy) (*7*). No informative data on outcomes after exposures to ProQuad or Zostavax during pregnancy were obtained. Neither vaccine is licensed for the age groups that include women of traditional childbearing ages. Only nine reports of exposure to these vaccines were received by the registry since 2006. The annual reports with detailed data are available to health care providers from the manufacturer upon request (telephone, 1-800-986-8999).

As a result of sustained high coverage with varicella vaccine in childhood, and because VZV-containing vaccines are contraindicated during pregnancy, the number of vaccine administrations (inadvertent) immediately before and during pregnancy, and thus registry enrollments, have declined. The number of varicella-susceptible women exposed during the high risk-period for congenital varicella syndrome decreased to a yearly average of two during 2009–2012. To lower the estimate of the theoretical risk for congenital varicella syndrome

among varicella-susceptible women exposed to Varivax during the high-risk period from the current 95% confidence interval upper bound estimate of 3.8% to 1.0% (the risk after infection with wild-type VZV), an additional 271 exposed susceptible women would need to be enrolled. At the observed average rate of annual enrollment, that number would not be reached until the year 2147.

The low rate of exposure of varicella-susceptible women of childbearing age to VZV-containing vaccines, in addition to the rarity of the outcome, contribute to the low feasibility that the registry will provide more robust data on the risk for congenital varicella syndrome within a reasonable timeframe. For this reason, the Food and Drug Administration, in support of the closure of the registry, approved the revision of information in the product labels regarding the registry (*8*). New patient enrollment was discontinued as of October 16, 2013. Follow-up of patients enrolled before this date will continue until after their estimated date of delivery (after July 2014), and final data will be analyzed for a summary report.

Because a theoretical risk for congenital varicella syndrome cannot be ruled out, pregnant women should not be vaccinated with Varivax, ProQuad, or Zostavax. The Advisory Committee on Immunization Practices also recommends that women should be counseled to avoid becoming pregnant for 1 month after each dose of a VZV-containing vaccine, considering the biologic plausibility of vaccine virus replication (*1,2*).

Merck will continue to monitor pregnancy outcomes after inadvertent exposures to VZV-containing vaccines during pregnancy or within 3 months before conception. CDC and the Food and Drug Administration will continue to monitor adverse events after vaccination with VZV-containing vaccines through the Vaccine Adverse Event Reporting System (VAERS). New cases of exposure immediately before or during pregnancy or other adverse events after vaccination with Varivax, ProQuad, or Zostavax, should be reported to Merck (telephone, 1-877-888-4231) and to VAERS (https://vaers.hhs.gov/index). Laboratory testing and strain identification for VZV for any suspected pregnancy-related vaccine adverse event will continue to be provided, if requested, by CDC (additional information available at http://www.cdc.gov/chickenpox/lab-testing/collecting-specimens.html) and through Merck's VZV-identification program (telephone, 1-877-888-4231).

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Notes from the Field

Atypical Pneumonia in Three Members of an Extended Family — South Carolina and North Carolina, July–August 2013

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On August 5, 2013, the South Carolina Department of Health and Environmental Control was notified of a case of acute respiratory failure in a previously healthy woman. A family interview revealed the patient's uncle and cousin had also been hospitalized with similar symptoms in North Carolina. The South Carolina Department of Health and Environmental Control and the North Carolina Division of Public Health collaborated to identify the cause of the respiratory illness cluster and to prevent additional illnesses.

The index patient (patient 1) was a woman aged 19 years and a resident of South Carolina. She was a smoker with no known prior medical conditions. During late July 2013, she experienced fever, shortness of breath, cough, and diarrhea and was hospitalized after 2 days of worsening respiratory symptoms. Chest radiographs from admission revealed diffuse bilateral infiltrates. Total white blood cell count was 25,000 with a neutrophil predominance. She subsequently experienced respiratory failure and required mechanical ventilation for 13 days. She received antibiotic treatment, including levofloxacin, azithromycin, cefepime, and vancomycin, and was discharged after a 17-day hospitalization. She recovered fully. No etiology was identified by laboratory testing, including bacterial cultures of blood and respiratory specimens, *Legionella* urinary antigen assay, and multiplex polymerase chain reaction (PCR) testing for influenza A and B, parainfluenza virus (PIV) 1–4, rhinovirus, adenovirus, human metapneumovirus, and respiratory syncytial virus (RSV).

Family interviews revealed that an uncle and cousin, both North Carolina residents, had experienced similar symptoms during the weeks before and after the index patient's illness onset. Patient 2, aged 55 years, was the index patient's uncle. He was a long-distance truck driver with a history of diabetes and obesity. He had experienced shortness of breath, cough, and fever in late June 2013, approximately 1 month before the index patient's illness onset. After 5 days of worsening respiratory symptoms, he was hospitalized with bilateral pneumonia and progressive respiratory failure, for which he required mechanical ventilation. *Legionella* urinary antigen and bacterial cultures of respiratory specimens were negative. Chest radiographs revealed bilateral infiltrates. He received a single dose of ceftriaxone 4 days before hospitalization, and levofloxacin and piperacillin/tazobactam during a 14-day hospitalization. He recovered fully.

Patient 3, a cousin of the index patient and daughter of patient 2, was aged 26 years and had multiple risk factors for respiratory illness, including asthma, smoking, and pregnancy (33 weeks). She visited her father frequently during his hospitalization in late June. Four days before the index patient's illness onset, patient 3 and the index patient traveled together by car for approximately 1 hour to attend the funeral of another family member who had died of unrelated causes. Two days after the index patient's illness onset, patient 3 experienced shortness of breath, wheezing, and cough. Four days after these symptoms developed, patient 3 was hospitalized for progressive respiratory distress and placed on mechanical ventilation for respiratory failure. Chest radiographs revealed diffuse bilateral opacities. *Legionella* urinary antigen, bacterial cultures of respiratory specimens, and molecular testing for adenovirus, influenza types A and B, PIV1-3, and RSV were all negative. Patient 3 was prescribed azithromycin 1 day before hospitalization and received azithromycin and ceftriaxone during an 11-day hospitalization. She ultimately required mechanical ventilation for 6 days before making a complete recovery.

Patient 3's infant was delivered prematurely by emergency Cesarean section at the time of her hospital admission. Upon delivery, the infant received a diagnosis of respiratory distress syndrome and possible sepsis; however, the complete blood count and C-reactive protein were not indicative of a bacterial infection. A blood culture was not performed. Ampicillin and gentamicin were administered during the infant's 18-day hospitalization. He recovered fully.

As part of the public health investigation, upper airway aspirates and nasopharyngeal swabs from patients 1 and 3 were collected and submitted to CDC's Pneumonia Response and Surveillance Laboratory for additional testing; respiratory specimens from patient 2 were unavailable. All specimens were tested by using a multiplex real-time PCR assay for simultaneous detection of *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Legionella* species, and human nucleic acid control. *M. pneumoniae* was identified in both oropharyngeal and nasopharyngeal aspirates collected from patient 3 at 2 days and 8 days after her symptom onset. High-resolution melt analysis was used to determine susceptibility of the *M. pneumoniae* strain to macrolides on the basis of detection of a single nucleotide polymorphism within the 23S rRNA

locus that confers resistance to this class of antibiotics. A profile consistent with macrolide sensitivity was observed in the *M. pneumoniae*–positive specimen. Further characterization by using multiple locus variable number tandem repeat analysis revealed a commonly observed strain type (3/5/6/2) in this patient. No respiratory pathogens were identified in specimens obtained from patient 1, which were collected 10 days after her symptom onset.

Although *M. pneumoniae* was only identified in clinical specimens from one patient in this cluster, the epidemiologic and clinical information collected during this investigation indicates that the organism was the likely cause of this cluster of atypical pneumonia. Pneumonia caused by *M. pneumoniae* typically has an incubation period of 1–3 weeks (*1*). All three patients had bilateral pulmonary infiltrates, lack of positive laboratory tests for other etiologies, and multiple opportunities for person-to-person spread within the family network. Two additional members of the extended family also experienced mild upper respiratory symptoms, including rhinorrhea and cough, in late July and early August 2013; however, neither sought medical care, and laboratory testing was not performed.

M. pneumoniae is a frequent cause of community-acquired pneumonia, and outbreaks of mild-to-moderate disease are common (*2,3*). Extrapulmonary manifestations of *M. pneumoniae* infection can contribute to severe disease and death (*4*). This disease cluster is remarkable because of the severity of illness, including the requirement for mechanical ventilation for all three patients. Risk factors for severe *M. pneumoniae* disease are not well-defined. However, conditions that compromise cardiopulmonary function (e.g., conditions present among the patients described) likely contributed (*5–7*). Testing for atypical bacterial respiratory pathogens (e.g., *M. pneumoniae*) should be considered when investigating clusters of community-acquired pneumonia, including clusters of severe disease. Increased awareness and availability of diagnostic tests at state and local public health laboratories might lead to improved understanding of the actual burden of this pathogen in the United States and its contributory role in outbreaks of severe respiratory illness.

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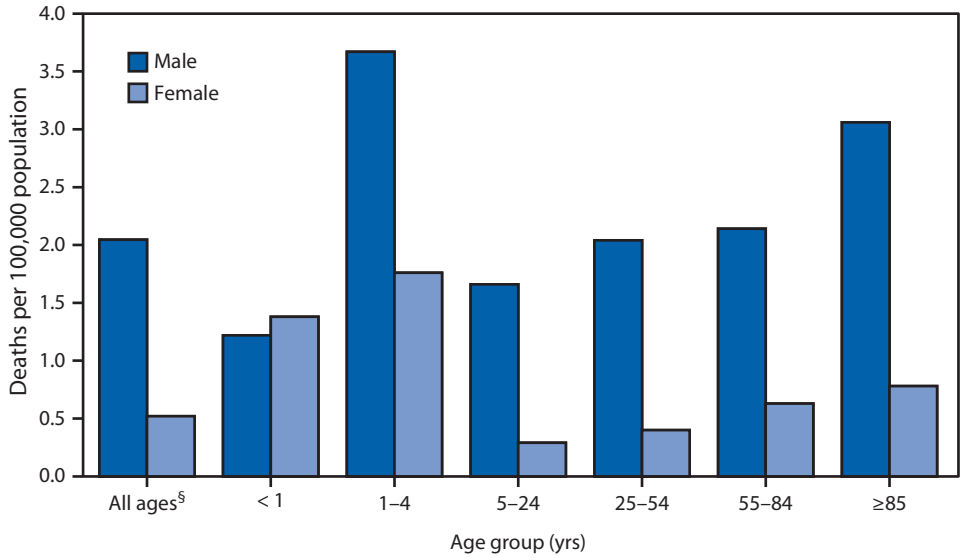
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Death Rates from Unintentional Drowning,* by Age Group and Sex — United States,† 2011



* Unintentional drowning as the underlying cause of death includes codes for accidental drowning and submersion (W65-74), watercraft causing drowning and submersion (V90), and water-transport–related drowning and submersion without accident to watercraft (V92) in the *International Classification of Diseases, 10th Revision*.
† U.S. residents only.
§ Includes decedents whose ages were not reported.

A total of 3,961 deaths from unintentional drowning were reported in the United States in 2011. In that year, the overall death rate for males was 2.05 per 100,000 population, almost four times the rate for females (0.52). In each age group except for infants (i.e., those aged <1 year) , the drowning death rate was higher for males. Males aged 1–4 years had the highest rate (3.67); for males and females, death rates increased with age after age 5–24 years.

Source: National Vital Statistics System. Mortality public use data files, 1999–2010. Available at http://www.cdc.gov/nchs/data_access/vitalstatsonline.htm.

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