Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 64 / No. 22
June 12, 2015

Health Effects of Cut Gas Lines and Other Petroleum Product Release Incidents — Seven States, 2010–2012

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Large mass casualty gas explosions and catastrophic oil spills are widely reported and receive considerable regulatory attention. Smaller, less catastrophic petroleum product releases are less likely to receive publicity, although study of these incidents might help focus and prioritize prevention efforts. To describe the causes and health impacts of petroleum product release incidents (including gas explosions and oil spills), the Agency for Toxic Substances and Disease Registry (ATSDR) analyzed 2010–2012 data from the National Toxic Substance Incidents Program (NTSIP). A total of 1,369 petroleum product release incidents were reported from seven states, resulting in 512 injuries and 36 deaths. Approximately one fourth of the incidents were associated with utilities, and approximately one fifth were associated with private vehicles or residences. Approximately 10% of petroleum product releases resulted from inadvertent damage to utility lines. Understanding the characteristics of acute petroleum product releases can aid the public and utility workers in the development of preventive strategies and reduce the morbidity and mortality associated with such releases.

Petroleum is refined to produce gasoline, heating oil, propane, and other fuels (*1*). If not managed properly, these products can adversely affect humans, wildlife, and the environment (*2*). Adverse health effects can include skin irritation, eye irritation, dizziness, headache, nausea and, and in extreme cases, death (*2*). Because petroleum is widely used, unintentional acute releases can occur almost anywhere.

In 2010, ATSDR established NTSIP to collect information useful for reducing morbidity and mortality associated with acute toxic substance releases.* State NTSIP partners collect information pertaining to acute petroleum and nonpetroleum releases and the public health effects of those releases and enter it into a web-based application. Acute nonpetroleum releases include but are not limited to any substance that, after release into the environment and upon exposure, ingestion, or inhalation, could cause morbidity or mortality. Nonpetroleum releases include chemical, biologic, radiologic and medical materials (*3*). However, NTSIP limits collection of information regarding releases of petroleum to those that result in an injury or a public health action (e.g., evacuation, shelter-in-place, alternative water usage, ban on fishing, health advisory, health investigation, prohibition against livestock or produce consumption, water intake shutdown or environmental sampling, and well survey). Additionally, NTSIP excludes petroleum-related incidents for which the only source of petroleum was the fuel tank of a vehicle involved in a crash.

Continuing Education examination available at http://www.cdc.gov/mmwr/cme/conted_info.html#weekly.

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

U.S. Department of Health and Human Services
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During 2010–2012, seven states contributed data to NTSIP: Louisiana, New York, North Carolina, Oregon, Tennessee, Utah, and Wisconsin. To identify petroleum releases, ATSDR first searched the NTSIP system for "petroleum incidents" by searching on the chemical name variable for petroleum products listed in the 2010 NTSIP training manual (*3*). ATSDR then reviewed the comments and synopsis fields of the identified records to confirm that they described petroleum incidents. Descriptive statistical analyses comparing petroleum and nonpetroleum incidents were then performed.

NTSIP recorded 8,684 single-substance incidents during 2010–2012, of which 1,369 (15.8%) were petroleum-related. Of the 1,369 NTSIP petroleum-related incidents, 259 (18.9%) incidents included injuries (Table 1). In addition, 512 (15.1%) of the 3,399 persons injured in all NTSIP incidents were injured in petroleum incidents. The most commonly reported contributing factors for petroleum incidents were equipment failure (51.7%) and human error (40.2%). The remaining contributing factors were weather (4.3%), intentional or illegal acts (2.2%), and other factors (1.6%). Among the 1,369 petroleum incidents, 1,170 (85.5%) occurred in fixed facilities.

The utilities industry accounted for the greatest number of petroleum-release incidents (327 [23.9%]) (Table 2); most of these incidents (253 [77.4%]) were related to natural gas distribution. Of the utility releases, 131 (40.1%) involved lines damaged or cut because of errors by contractors, construction workers, or residents. A total of 14 (4.3%) of the 327 utility releases resulted in injuries, with a total of 27 persons injured (Table 2).

The second most commonly reported type of petroleum releases (296 [21.6%]) occurred in private vehicles and residences. These incidents were the most likely (105 [40.5%]) to result in injury and caused injuries to 236 persons (46.1%) (Table 2). Of the 105 petroleum-release incidents with injured persons, 59 (56.2%) incidents involved explosion or fire or both.

For both petroleum and nonpetroleum incidents, most injuries were to members of the general public, followed by employees (Table 3). Petroleum incidents resulted in a higher percentage of persons admitted to the hospital and deaths compared with nonpetroleum incidents (Table 3). The most commonly reported injuries for petroleum incidents were burns (32.5%) and trauma (24.6%). Petroleum incidents were less likely than nonpetroleum incidents to result in persons requiring decontamination (10.4% compared with 21.9%) (Table 3).

Illustrative Case Reports

Incident A. While a subcontractor was installing cable lines, he hit a 2-inch (51 mm) natural gas line. Natural gas leaked into the sewer system and into a townhouse, which exploded. One member of the public, two utility workers, and two firefighters were injured in the explosion. They had burns, trauma, and shortness of breath. All injured persons were treated at the hospital, but none were admitted. The gas was turned off, and hundreds of neighbors were evacuated for 24 hours.

Incident B. A neighbor smelled natural gas and called utilities. Utility personnel investigated, but did not find a gas leak.

The *MMWR* series of publications is published by the Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Report title]. MMWR Morb Mortal Wkly Rep 2015;64:[inclusive page numbers].

Later, a nearby house exploded, injuring three members of the public. Two persons were admitted and treated at a hospital for burns. The third person died in the explosion. The area was evacuated for 6 days, affecting approximately 20 persons. The American Red Cross responded to provide assistance.

Discussion

Petroleum release incidents have the potential to cause mass casualties and environmental contamination. In 2010, two incidents of acute, unintentional releases of petroleum products received prominent attention in the news media (*4*–*7*). One was a Pacific Gas and Electric gas line explosion in San Bruno, California. A 30-inch natural gas pipeline ruptured after reports from residents in the neighborhood stating they smelled gas. This release led to an explosion that left 35 homes burned, eight persons dead, and 30 more injured (*6*). The second incident was in Enbridge, Michigan, were a ruptured pipeline released more than 800,000 gallons of crude oil into the Kalamazoo River (*5*), resulting in serious environmental impacts and various adverse health effects (e.g., headache, nausea, and respiratory symptoms) in nearby residents (*7*).

NTSIP data from seven states for 2010–2012 indicate that petroleum incidents accounted for 15.8% of all toxic substance releases, and most of the petroleum incidents involved utilities. Nearly half of the utility incidents involved homeowners or construction contractors damaging or cutting lines. Petroleum releases caused by cut lines can be prevented if the public and construction professionals follow one simple precaution: call 811. Many underground utility pipes and conduits, but not all, are marked by signs above ground signaling their location. Each state has different rules and regulations governing digging, and some rules are more stringent than others. The telephone

TABLE 1. Number and percentage of reported petroleum release incidents compared with nonpetroleum and all reported single-substance incidents, by selected characteristics — National Toxic Substance Incidents Program (NTSIP) 2010–2012

	Petroleum incidents		Nonpetroleum incidents		All reported NTSIP incidents	
Characteristic	**No.**	**(%*)**	**No.**	**(%*)**	**No.**	**(%*)**
Incidents	1,369	—	7,315	—	8.684	—
Evacuations ordered	719	(52.5)	764	(10.5)	1,483	(17.2)
No. of evacuees	33,541	—	24,261	—	57,802	—
Incidents with injuries	259	(18.9)	1,114	(15.3)	1,373	(15.9)
No. of Injured persons	512	—	2,887	—	3,399	—
Shelter-in-place ordered	52	(3.8)	99	(1.3)	151	(1.7)

*Percentages calculated using the number of incidents in each column as denominators.

TABLE 2. Number and percentage of reported petroleum release incidents and injured persons, by type of industry or location — National Toxic Substance Incidents Program, 2010–2012

Industry or location	No. of incidents	(%)	No. of incidents with injuries	(%)	No. of injured persons	(%)
Utilities	327	(23.9)	14	(5.4)	27	(5.3)
Private residence, vehicle	296	(21.6)	105	(40.5)	236	(46.1)
Real estate	133	(9.7)	20	(7.7)	33	(6.4)
Educational services	86	(6.3)	4	(1.5)	4	(0.8)
Unknown	84	(6.1)	15	(5.8)	19	(3.7)
Transportation and warehousing	75	(5.5)	22	(8.5)	35	(6.8)
Retail trade	61	(4.5)	10	(3.9)	23	(4.5)
Manufacturing: paper, printing, chemicals, petroleum, leather, lumber, stone	52	(3.8)	8	(3.1)	23	(4.5)
Construction	36	(2.6)	6	(2.3)	8	(1.6)
Accommodation and food services	35	(2.6)	10	(3.9)	16	(3.1)
Health care and social assistance	33	(2.4)	5	(1.9)	12	(2.3)
Wholesale trade	31	(2.3)	11	(4.2)	15	(2.9)
Public administration	21	(1.5)	6	(2.3)	12	(2.3)
Arts, entertainment, and recreation	20	(1.5)	7	(2.7)	20	(3.9)
Administrative and support, waste management and remediation services	18	(1.3)	2	(0.8)	4	(0.8)
Mining	13	(0.9)	4	(1.5)	5	(1.0)
Other*	48	(3.5)	10	(3.9)	20	(3.9)
Total	**1,369**	**(100.0)**	**259**	**(99.9†)**	**512**	**(99.9†)**

* Includes Manufacturing: food, textile, metal, electric, transport, professional, and apparel; Professional: scientific and technical services; Agriculture: forestry, fishing, and hunting; Information; Finance and Insurance; Management of companies and enterprise; and Other services.
† Percentages do not equal 100 because of rounding.

TABLE 3. Number and percentage of persons injured from reported petroleum and nonpetroleum release incidents, by selected characteristics — National Toxic Substance Incidents Program, 2010–2012

	Petroleum		Nonpetroleum	
Characteristic	**No.**	**(%)**	**No.**	**(%)**
General public	277	(54.1)	1,290	(44.7)
Employee	159	(31.0)	1,089	(37.7)
Firefighter	63	(12.3)	168	(5.8)
Police officer	7	(1.4)	38	(1.3)
Unknown responder	2	(0.4)	13	(0.4)
Missing	4	(0.8)	8	(0.3)
Student	0	—	267	(9.3)
Hospital personnel	0	—	9	(0.3)
Employee response team	0	—	3	(0.1)
EMT personnel	0	—	2	(0.1)
Total	**512**	**(100.0)**	**2,887**	**(100.0)**
Injured person disposition				
Treated at hospital (not admitted))	217	(42.4)	1,760	(61.0)
Treated at hospital (admitted)	139	(27.1)	342	(11.8)
Treated on scene (First aid)	99	(19.3)	444	(15.4)
Died	36	(7.0)	109	(3.8)
On scene or on arrival at hospital	26	(72.2)	87	(79.8)
After arrival at hospital	10	(27.8)	22	(20.2)
Treated at hospital (admission unknown)	15	(2.9)	53	(1.8)
Observation at hospital, no treatment	2	(0.4)	53	(1.8)
Injury reported by official	1	(0.2)	69	(2.4)
See private physician in ≤24 hrs	0	—	26	(0.9)
Missing	3	(0.6)	31	(1.0)
Injury type*				
Burns	176	(32.5)	323	(8.4)
Thermal	137	(77.8)	84	(16.0)
Chemical	14	(8.0)	181	(56.0)
Both thermal and chemical	18	(10.2)	45	(13.9)
Unknown	7	(4.0)	13	(4.0)
Trauma	133	(24.6)	206	(5.3)
Nonchemical	98	(73.7)	121	(58.7)
Chemical	16	(12.0)	56	(27.2)
Both nonchemical and chemical	9	(6.8)	16	(7.8)
Unknown	10	(7.5)	13	(6.3)
Dizziness	82	(15.2)	873	(22.3)
Respiratory irritation	51	(9.4)	1,044	(26.7)
Headache	37	(6.8)	380	(9.7)
Other†	62	(11.5)	1,081	(27.7)
Total	**541**	**(100.0)**	**3,907**	**(100.0)**
Persons decontaminated				
Yes	53	(10.4)	630	(21.8)
No	451	(88.1)	2,202	(76.3)
Unknown	8	(1.6)	55	(1.9)

Abbreviation: EMT = emergency management technician.
* Some persons had multiple injuries.
† Other injuries included gastrointestinal, heat stress, eye irritation, heart problems, short of breath, and skin irritation.

number 811 has been nationally designated to eliminate confusion over multiple "Call Before You Dig" numbers across the country. Dialing 811 connects callers with local centers that notify the appropriate local utilities, who then send crews to the requested site to mark the approximate location of underground lines at no charge (*8*).

Private vehicles and residences had the second greatest number of total petroleum release incidents, the greatest number of incidents involving injured persons, and the greatest total of injured persons. Many of these incidents were attributable to propane tank explosions, natural gas leaks, and gasoline misuse (e.g., using gasoline with charcoal grills and fireplaces).

The findings in this report are subject to at least three limitations. First, NTSIP data only include petroleum incidents that result in an injury or public health action; therefore, petroleum incident data are skewed toward higher percentages with injuries and evacuations. Second, because home incidents with no injury or public health action are not included in NTSIP, these data do not include all home incidents. Finally, with only seven

What is already known on this topic?

Most petroleum products are highly flammable, and many can explode. Unintentional releases of petroleum products can cause significant morbidity, mortality, environmental damage, and financial loss.

What is added by this report?

During 2010–2012, a total of 1,369 unintentional petroleum product release incidents were reported by seven states to the National Toxic Substance Incidents Program. The incidents resulted in injuries to 512 persons and 36 deaths. Forty-six percent of the incidents were related to utilities, private residences, or private vehicles. The greatest number of petroleum release incidents resulted from cut utility lines or gas leaks, and burns were the most common type of injury.

What are the implications for public health practice?

The most common causes of petroleum release incidents are preventable. Contractors, construction workers, homeowners, and renters need to understand the potential health and environmental consequences of damaging gas lines when digging. Additionally, members of the public need to be made more aware of how to recognize gas leaks and of what can happen if they misuse petroleum products.

states participating in NTSIP, no generalizations can be made regarding other states or data nationally.

Because of the danger posed by petroleum incidents and their continuing occurrence, strategies to prevent releases are needed. Based on the NTSIP data, a comprehensive approach to construction worker training regarding ruptured line prevention might reduce petroleum release incidents and their health consequences. In addition, education is needed to inform the public regarding the safe use of petroleum products and the need to be able to recognize a gas leak and know what steps to take to prevent explosions and fires.

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Serogroup B Meningococcal Disease Outbreak and Carriage Evaluation at a College — Rhode Island, 2015

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On February 2, 2015, the Rhode Island Department of Health was notified of a case of meningococcal disease in a male undergraduate student at Providence College. Three days later, a second case was reported in a male undergraduate with no contact with the first student, indicating an attack rate of 44 cases per 100,000 students, nearly 500 times higher than the national incidence of 0.15 cases per 100,000 among persons aged 17–22 years (Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC, unpublished data, 2013). Both cases were caused by a rare outbreak strain of *Neisseria meningitidis* serogroup B (ST-9069); neither case was fatal. In response to the outbreak, potential contacts received antibiotic chemoprophylaxis, and a mass vaccination campaign with a recently licensed serogroup B meningococcal (MenB) vaccine was implemented. In collaboration with CDC, the first phase of a meningococcal carriage evaluation was undertaken.

Meningococcal disease is uncommon in the United States but can infect otherwise healthy persons. *N. meningitidis* serogroup B accounts for approximately half of all meningococcal cases among persons aged 17–22 years in the U.S. (Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC, unpublished data, 2013) and caused four recent outbreaks in college settings (*1*,*2*). *N. meningitidis* is transmitted through direct contact with large-droplet respiratory tract secretions from persons with meningococcal disease or asymptomatic nasopharyngeal carriage (*3*). Two MenB vaccines, MenB-FHbp (Trumenba, Wyeth Pharmaceuticals, Inc.) and MenB-4C (Bexsero, Novartis Vaccines) were recently licensed in the United States.* Although there are no current recommendations for general use of MenB vaccines, the Advisory Committee on Immunization Practices recommends use of MenB vaccines in persons aged ≥10 years at increased risk for serogroup B meningococcal disease, including in outbreak settings (*4*). CDC's interim guidance suggests consideration of vaccination during outbreaks in which two or more primary cases of *N. meningitidis* serogroup B are reported in organizations of <5,000 persons within a 6-month period (*5*).

*Additional information available at http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm431370.htm.

As part of the outbreak response, ciprofloxacin chemoprophylaxis (*3*) was provided to 71 persons who were potentially exposed to oral secretions from either of the two students. Additionally, the school provided education to students on signs and symptoms of meningococcal disease and safe hygiene practices to prevent transmission. Molecular testing on the outbreak strain detected the gene coding for FHbp B24 (*6*), predicting cross-protection with both MenB vaccines (*7*).

During 2 vaccination days (February 8 and 11), the first of 3 doses of MenB-FHbp was offered to eligible persons affiliated with Providence College: 1) all undergraduate students; 2) graduate students or staff aged <25 years who lived or worked on campus, 3) persons in an intimate physical relationship with an undergraduate, and 4) asplenic persons or persons with an immunocompromising condition known to place them at risk for meningococcal disease. Persons who declined vaccination were required to sign opt-out forms. Among 3,745 eligible persons, 3,525 (94%) received the first dose. No further college-associated cases were identified as of June 8, 2015.

An evaluation to assess the prevalence of nasopharyngeal carriage of *N. meningitidis* among students and the impact of MenB vaccination on carriage was conducted during February 16–20. Undergraduate students and graduate students who lived on campus were eligible to participate. After obtaining informed consent, an oropharyngeal swab and a short questionnaire assessing risk factors for meningococcal disease and carriage were collected from each participant. Specimens were tested using bacterial culture, real-time polymerase chain reaction, and molecular methods. Log-linear binomial regression models were used to calculate prevalence ratios (PRs) and 95% confidence intervals (CIs).

Of 717 participants in the carriage evaluation, 470 (66%) were female, 655 (91%) lived on campus, and 701 (98%) had received the first MenB-FHbp vaccine dose. Preliminary data indicate that 176 (25%) were carriers of *N. meningitidis*. Among 31 (4%) participants with serogroup B carriage, none carried the outbreak strain. Eight (1%) participants carried serogroup C, one (<1%) carried serogroup X, four (1%) carried serogroup Y, and 132 (18%) carried nongroupable *N. meningitidis*. Males (PR = 1.5, CI = 1.2–2.0), smokers (PR = 1.5, CI = 1.1–2.0), and persons who reported visiting

bars or nightclubs or attending parties one or more times per week (PR = 2.7, CI = 1.8–4.2) had increased carriage prevalences, whereas recent antibiotic use was associated with decreased carriage (PR = 0.4, CI = 0.2–0.7).

The baseline carriage prevalence of *N. meningitidis* among Providence College students is comparable to prevalences of up to 34% previously observed among university students in the United Kingdom (*8*) but is higher than previous U.S. estimates of 1%–8% among the general population (*9,10*). No carriage of the outbreak strain was detected. There are several possible explanations for this finding. First, the outbreak strain ST-9069 might have a lower propensity for developing a carrier state. Second, the well-targeted chemoprophylaxis strategy, the vaccination campaign, or both, might have eradicated ST-9069 carriage on the campus before the carriage evaluation. Third, our sample size might not have been large enough to detect a very low prevalence of the outbreak strain. A second carriage evaluation was conducted in April; laboratory testing is ongoing, and a third evaluation is planned for the fall of 2015. These additional evaluations will permit assessment of the impact of the MenB vaccination campaign on carriage over time among Providence College students, and might inform recommendations for other college populations.

Acknowledgments

The Rhode Island Meningococcal Carriage Evaluation Team: Conrad P. Quinn, Leonard Mayer, Tami Skoff, Amanda Faulkner, Amy Blain, Christine Miner, Adria Lee, Anna Acosta, Sarah Meyer, How-Yi Chang, and Marsenia Harrison.

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Use of Serogroup B Meningococcal Vaccines in Persons Aged ≥10 Years at Increased Risk for Serogroup B Meningococcal Disease: Recommendations of the Advisory Committee on Immunization Practices, 2015

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In October 2014, the Food and Drug Administration (FDA) licensed the first serogroup B meningococcal (MenB) vaccine (MenB-FHbp [Trumenba, Wyeth Pharmaceuticals, Inc.]) as a 3-dose series. In January 2015, FDA licensed a second MenB vaccine (MenB-4C [Bexsero, Novartis Vaccines]) as a 2-dose series. Both vaccines were approved for use in persons aged 10–25 years. Following outbreaks of serogroup B meningococcal disease on two college campuses in 2013, both MenB vaccines were granted Breakthrough Therapy designations, which expedites drug development and review by FDA, and were licensed based on accelerated approval regulations (*1*). On February 26, 2015, the Advisory Committee on Immunization Practices (ACIP) recommended use of MenB vaccines among certain groups of persons aged ≥10 years who are at increased risk for serogroup B meningococcal disease. This report summarizes information on MenB administration and provides recommendations and guidance for use of these vaccines among persons aged ≥10 years in certain groups who are at increased risk for serogroup B meningococcal disease, and reviews the evidence considered by ACIP to make these recommendations. Recommendations for broader use of MenB vaccines in adolescents and college students will be considered separately by ACIP.

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

Methods

The ACIP Meningococcal Vaccines Work Group reviewed safety and immunogenicity data from seven clinical trials of MenB-4C (*2–7*) (Novartis, unpublished data) and nine clinical trials of MenB-FHbp (*8–13*) (Pfizer, unpublished data) during its monthly teleconferences. The Work Group also evaluated published peer-reviewed literature and unpublished data on meningococcal disease epidemiology in the United States. A summary of the data reviewed and Work Group discussions was presented to ACIP, and recommendations for use of MenB vaccines among persons aged ≥10 years at increased risk for serogroup B meningococcal disease were approved by ACIP at its February 26, 2015, meeting (meeting minutes are available at http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html).

The type and quality of evidence supporting the use of MenB vaccines in persons aged ≥10 years at increased risk for serogroup B meningococcal disease was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework (*14*), and determined to be type 2 (moderate level of evidence) for use in outbreak settings, and type 3 (low level of evidence) for use in persons at increased risk for serogroup B meningococcal disease. The recommendation was designated Category A (recommended for all persons in an age-based or risk-factor–based group) (*15*).

Persons at Increased Risk for Meningococcal Disease

Persons who have persistent deficiencies (e.g., genetic deficiencies) in the complement pathway (e.g., C3, properdin, Factor D, Factor H, or C5-C9) have up to a 10,000-fold increased risk for meningococcal disease and can experience recurrent disease (*16,17*). Persons receiving eculizumab (Soliris, Alexion Pharmaceuticals) for treatment of atypical hemolytic uremic syndrome or paroxysmal nocturnal hemoglobinuria also are at increased risk because the drug binds to C5 and inhibits the terminal complement pathway (information available at http://soliris.net/sites/default/files/assets/soliris_pi.pdf). Similarly, persons with functional or anatomic asplenia (including persons with sickle cell disease) appear to be at increased risk for meningococcal disease, and have a higher mortality rate (40%–70%) from the disease than healthy

populations (*18*). Among microbiologists who routinely work with *Neisseria meningitidis* isolates, the attack rate of laboratory-acquired meningococcal infection has been estimated at 13 per 100,000 persons, which is many fold higher than the rate for adults in the general population (*19*). In the United States, 97%–98% of all cases of meningococcal disease are sporadic; however, outbreaks continue to occur. Recently, outbreaks of serogroup B meningococcal disease have been reported from several college campuses. Data from four college campus outbreaks (March 2013–May 2015) showed a 200 to 1,400–fold increase in risk for meningococcal disease among students at these colleges during the outbreak period compared with the general population in this age group (Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, CDC, unpublished data, 2015).

MenB Vaccine Immunogenicity and Safety

Because of the low incidence of serogroup B meningococcal disease, vaccine efficacy estimates were based on demonstration of immune response, as measured by serum bactericidal activity using human complement (hSBA), against a small number of serogroup B strains. In studies supporting U.S. licensure, immunogenicity was assessed by the proportion of subjects who achieved a ≥4-fold increase in hSBA titer for each of the strains tested, and the proportion of subjects who achieved a titer greater than or equal to the lower limit of quantification of the assay for all strains (composite response) (*20*,*21*). The lower limit of quantification was defined as the lowest amount of the antibody in a sample that can be reliably quantified.

MenB-4C Vaccine

MenB-4C consists of three recombinant proteins (Neisserial adhesin A [NadA], factor H binding protein [FHbp] fusion protein, and Neisserial Heparin Binding Antigen [NHBA] fusion protein), and outer membrane vesicles (OMVs) containing outer membrane protein PorA serosubtype P1.4. MenB-4C is licensed as a 2-dose series, with doses administered at least 1 month apart, although in some studies, MenB-4C doses were administered up to 6 months apart.

In persons aged ≥10 years, safety and immunogenicity of MenB-4C were evaluated in seven clinical trials: six randomized controlled trials and one immunogenicity extension study (*2*–*7*) (Novartis, unpublished data). In one randomized controlled trial conducted in the United Kingdom, a subset of enrolled subjects (university students aged 18–24 years) received 2 doses of MenB-4C vaccine 1 month apart. One month following the second dose, 88% (95% confidence interval [CI] = 82%–93%) of subjects had a composite hSBA response to all three test strains; 66% (CI = 58%–72%) of the subjects had a composite hSBA response to all three test strains at 11 months after the second dose (*20*). In a randomized controlled trial conducted in Australia and Canada, persons aged 11–17 years received 2 doses of MenB-4C 1 month apart. One month following the second dose, 63% (CI = 57%–68%) of subjects had a composite hSBA response to all three test strains (*20*).

In an open-label study conducted in Germany and Italy, antibody responses to MenB-4C were assessed in laboratory workers aged 18–50 years who were routinely exposed to *Neisseria meningitidis.* Among the subjects, 83% (CI = 69%–92%) achieved an hSBA titer ≥1:8 against at least one of the three test strains 1 month after the second dose of MenB-4C (*3*).

In three clinical trials for which a control group was available, serious adverse events were assessed in 2,716 participants who received at least 1 dose of MenB-4C and for whom safety data were collected through 6 months postvaccination (*2*,*4*,*6*). Five serious adverse events were considered by the study investigator to be related (or possibly related) to the vaccine.* Rates of serious adverse events were similar in the vaccine and the control groups. In addition, information about serious adverse events was collected during three prelicensure vaccination campaigns in response to three outbreaks of serogroup B meningococcal disease (at two universities in the United States and in one region in Canada). A total of 59,091 participants in the vaccination campaigns received at least 1 dose of MenB-4C. Three serious adverse events were considered by the study investigator to be related (or possibly related) to the vaccine†; all resolved with no sequelae (CDC and Novartis, unpublished data). No deaths were considered to be related to MenB-4C in the clinical trials or campaigns. The most common solicited adverse reactions observed in the 7 days after receipt of MenB-4C in the clinical trials were pain at the injection site, myalgia, erythema, fatigue, headache, induration, nausea, and arthralgia (*9*,*20*).

Safety and immunogenicity data regarding MenB-4C when co-administered with vaccines routinely administered to U.S. adolescents are not available.

MenB-FHbp Vaccine

MenB-FHbp consists of two purified recombinant FHbp antigens. One antigen from each FHbp subfamily (A and B) is included in the vaccine. MenB-FHbp is licensed as a 3-dose series, with the second and third doses administered 2 and 6 months after the first dose.

* The administration of the investigational vaccine and a serious adverse event were considered reasonably related in time and the serious adverse event could not be explained by causes other than exposure to the investigational vaccine. The reported serious adverse events included tremor (one), dyspnea (one), acute thyroiditis (one), and juvenile arthritis (two).

† The reported serious adverse events included rhabdomyolysis (one), anaphylaxis (one) and fever (one).

Safety and immunogenicity of MenB-FHbp in persons aged ≥10 years were evaluated in nine clinical trials: six randomized controlled trials and three open label studies (*8–13*) (Pfizer, unpublished data). In a multicenter trial conducted in the United States, persons aged 11–17 years were randomly assigned to one of three groups. Group 1 received MenB-FHbp and quadrivalent human papillomavirus vaccine (4vHPV, [Gardasil Merck and Co.]), group 2 received MenB-FHbp and saline, and group 3 received 4vHPV and saline.

One month following the third dose, 81% (CI = 78.0%–83.7%) of subjects in group 1 and 83.9% (CI = 81.1%–86.4%) of subjects in group 2 had a composite hSBA response to all four test strains (*13*,*21*). After the second of 3 doses, approximately 50% of the subjects in each study group had a composite hSBA response to all test strains. In studies conducted among European persons aged 11–18 years, the hSBA responses in subjects who received MenB-FHbp according to the same schedule were similar to hSBA antibody responses in subjects in the U.S. study (*9*,*21*).

In one open label study, immunogenicity was assessed among a small number of meningococcal laboratory workers who received the vaccine. Among the subjects, 50% achieved a titer greater than or equal to the lower limit of quantification to all four test strains (Pfizer, unpublished data).

Concomitant administration of MenB-FHbp with vaccines routinely administered to U.S. adolescents has been evaluated in three trials. Subjects received MenB-FHbp co-administered with 4vHPV (Gardasil, Merck and Co.), MenACWY (Menactra, Sanofi Pasteur), Tdap (Adacel, Sanofi Pasteur) or dTaP/IPV (Repevax, Sanofi Pasteur) vaccines. Except for the antibody response to HPV type 18, no immunologic interference was observed for serogroup B or concomitant vaccine antigens (HPV types 6, 11, 16, MenACWY, tetanus, diphtheria, pertussis and IPV antigens) when MenB-FHbp was administered concomitantly (*11*,*13*) (Pfizer, unpublished data). For HPV type 18, noninferiority criteria (lower bound of the CI of the geometric mean titer ratio >0.67) were not met for the geometric mean titer ratio at 1 month after the third 4vHPV vaccination (lower bound of the CI for the geometric mean titer ratio was 0.62); however, ≥99% of subjects achieved seroconversion for all four HPV antigens.

In four clinical trials (*9*,*11–13*) a total of 2,557 subjects received at least 1 dose of MenB-FHbp; four subjects reported seven serious adverse events that were considered by the study investigator to be related (or possibly related) to the vaccine.[§] All vaccine-related serious adverse events resolved without sequelae. No increased risk for any specific serious adverse event considered to be clinically significant was identified in any of the studies. No deaths were considered to be related to MenB-FHbp. The most common solicited adverse reactions observed in the 7 days after receipt of MenB-FHbp in the clinical trials were pain at the injection site, fatigue, headache, myalgia, and chills (*21*).

Rationale for Recommendations

Certain groups of persons known to be at increased risk for meningococcal disease are recommended to be routinely vaccinated with a quadrivalent meningococcal conjugate vaccine (MenACWY), which protects against serogroups A, C, W, and Y (*16*). Many of these groups are also at increased risk for serogroup B meningococcal disease. Available immunogenicity and safety data support the use of MenB vaccines in groups at increased risk for serogroup B meningococcal disease.

Both MenB vaccines are approved for use in persons aged 10–25 years; however, because there are no theoretical differences in safety for persons aged >25 years compared with those aged 10–25 years, ACIP supported routine use of MenB vaccines in persons aged ≥10 years who are at increased risk for serogroup B meningococcal disease. These recommendations do not apply to children aged <10 years.

Recommendations

Certain persons aged ≥10 years who are at increased risk for meningococcal disease should receive MenB vaccine. These persons include:

- Persons with persistent complement component deficiencies.[¶]
- Persons with anatomic or functional asplenia.[**]
- Microbiologists routinely exposed to isolates of *Neisseria meningitidis*.
- Persons identified as at increased risk because of a serogroup B meningococcal disease outbreak.

Certain other groups are included in the MenACWY recommendations for persons at increased risk, but are not included in this recommendation. MenB vaccines are not licensed for children aged <10 years and are not currently recommended for children aged 2 months–9 years who are at increased risk for serogroup B meningococcal disease. MenB vaccine is not recommended for persons who travel to or reside in countries where meningococcal disease is hyperendemic or epidemic because the risk for meningococcal disease in these countries generally is not caused by serogroup B. The vaccine is not currently recommended for routine use in first-year

[§] The reported serious adverse events included pyrexia (one), vomiting (one), vertigo (one), chills (one), headache (one), anaphylaxis (one) and neutropenia (one).

[¶] Including inherited or chronic deficiencies in C3, C5-9, properdin, factor D, factor H, or who are taking eculizumab (Soliris).

[**] Including sickle cell disease.

What is currently recommended?

The Advisory Committee on Immunization Practices recommends routine vaccination with quadrivalent meningococcal conjugate vaccine (MenACWY) of certain groups of persons at increased risk for meningococcal disease: persons who have persistent complement component deficiencies; persons who have anatomic or functional asplenia; microbiologists who routinely are exposed to isolates of *Neisseria meningitidis;* persons identified to be at increased risk because of a meningococcal disease outbreak attributable to serogroup A, C, W, or Y; military recruits; first-year college students living in residence halls; and persons who travel to or reside in areas in which meningococcal disease is hyperendemic or epidemic.

Why are the recommendations being modified now?

Two serogroup B meningococcal (MenB) vaccines were recently licensed by the Food and Drug Administration and approved for use in persons aged 10–25 years. The evidence supporting the use of MenB vaccines in persons at increased risk for serogroup B meningococcal disease was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation framework and determined to be type 2 (moderate level of evidence) for use in outbreak settings and type 3 (low level of evidence) for use in persons at increased risk for serogroup B meningococcal disease. The recommendation was designated as Category A (recommended for all persons in an age- or risk-factor–based group).

What are the new recommendations?

Certain persons aged ≥10 years at increased risk for meningococcal disease should receive MenB vaccine. These persons include those with persistent complement component deficiencies; persons with anatomic or functional asplenia; microbiologists routinely exposed to isolates of *Neisseria meningitidis;* and persons identified to be at increased risk because of a serogroup B meningococcal disease outbreak.

college students living in residence halls, military recruits, or all adolescents. Recommendations for broader use of MenB vaccines in adolescents and college students will be considered separately by the ACIP.

MenB vaccine should be administered as either a 2-dose series of MenB-4C or a 3-dose series of MenB-FHbp. The same vaccine product should be used for all doses. Based on available data and expert opinion, MenB-4C or MenB-FHbp may be administered concomitantly with MenACWY vaccines, but at a different anatomic site, if feasible.

Precautions and Contraindications

Before administering MenB vaccines, providers should consult the package insert for precautions, warnings, and contraindications (*20,21*). Adverse events occurring after administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reports can be submitted to VAERS online, by fax, or by mail. Additional information about VAERS is available by telephone (1–800–822–7967) or online (http://vaers.hhs.gov).

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Acknowledgments

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Progress Toward Measles Elimination — South-East Asia Region, 2003–2013

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In 2013, the 66th session of the Regional Committee of the World Health Organization (WHO) South-East Asia Region* adopted the goal of measles elimination and rubella and congenital rubella syndrome control† by 2020 after rigorous prior consultations (*1*–*3*). The recommended strategies include 1) achieving and maintaining ≥95% coverage with 2 doses of measles- and rubella-containing vaccine in every district through routine or supplementary immunization activities (SIAs)§; 2) developing and sustaining a sensitive and timely case-based measles surveillance system that meets recommended performance indicators¶; 3) developing and maintaining an accredited measles laboratory network; and 4) achieving timely identification, investigation, and response to measles outbreaks. This report updates previous reports and summarizes progress toward measles elimination in the South-East Asia Region during 2003–2013 (*4*). Within the region, coverage with the first dose of a measles-containing vaccine (MCV1) increased from 67% to 78%; an estimated 286 million children (95% of the target population) were vaccinated in SIAs; measles incidence decreased 73%, from 59 to 16 cases per million population; and estimated measles deaths decreased 63%. To achieve measles elimination in the region, additional efforts are needed in countries with <95% 2-dose routine MCV coverage, particularly in India and Indonesia, to strengthen routine immunization services, conduct periodic high-quality SIAs, and strengthen measles case-based surveillance and laboratory diagnosis of measles.

Immunization Activities

MCV1 was introduced in all 11 countries in the South-East Asia region before 2003. During 2003–2013, MCV1 was administered at age 9 months in all countries except Sri Lanka, where the age of administration was increased from 9 to 12 months in 2011 (Table 1). During 2003–2013, the number of countries in the region with a routine second dose of MCV (MCV2) increased from two to nine. The recommended age for administration for MCV2 varied by country and ranged from 15 months to 7 years. Countries report national and subnational coverage with MCV1 and MCV2 delivered through the routine immunization program to WHO and the United Nations Children's Fund (UNICEF), which use data from administrative records (vaccine doses administered divided by the target population) and surveys reported by member states each year to estimate MCV1 and MCV2 coverage (*5*). Estimated MCV1 coverage increased in the region from 67% in 2003 to 78% in 2013; four countries reported ≥95% MCV1 coverage nationwide and in all districts in 2013 (Table 1, Figure). Estimated MCV2 coverage increased from 6% in 2003 to 53% in 2013; in 2013, estimated MCV2 coverage in three countries was ≥95%. During 2003–2013, measles SIAs were conducted in all countries except Thailand and reached 286 million children (95% of target population) (Table 2). Of the 39 SIAs, 16 (41%) achieved ≥95% administrative coverage.

Surveillance Activities

By 2013, measles surveillance with laboratory confirmation of suspected cases was implemented in all countries in the region. Bangladesh, Nepal, and Myanmar reported case-based measles surveillance data monthly to the WHO South-East Asia Regional Office, whereas other countries in the region reported aggregate measles surveillance data monthly (*6*). Five countries (Bangladesh, India, Indonesia, Myanmar, and Nepal) used the WHO-supported network of surveillance medical officers initially established for polio eradication to conduct measles surveillance (*3*). A measles-rubella laboratory network was established in the region by 2003, as an integral part of

* The WHO South-East Asia Region consists of 11 countries: Bangladesh, Bhutan, North Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste.

† Measles elimination is defined as the absence of endemic measles cases for a period of ≥12 months in the presence of adequate surveillance. One indicator of measles elimination is a sustained measles incidence of <1 case per 1 million population. Rubella /congenital rubella syndrome control is defined as 95% reduction in disease incidence from the 2013 level.

§ SIAs generally are carried out using two target age ranges. An initial, nationwide catch-up SIA targets all children aged 9 months–14 years, with the goal of eliminating susceptibility to measles in the general population. Periodic follow-up SIAs then target all children born since the last SIA. Follow-up SIAs generally are conducted nationwide every 2–4 years and target children aged 9–59 months; their goal is to eliminate any measles susceptibility that has developed in recent birth cohorts and to protect children who did not respond to the first measles vaccination.

¶ These indicators include 1) ≥2 discarded nonmeasles nonrubella cases per 100,000 population at the national level per year (such cases are defined as suspected cases that have been investigated and discarded as nonmeasles and nonrubella cases using laboratory testing in a proficient laboratory or epidemiologic linkage to a laboratory-confirmed outbreak of another communicable disease that is neither measles nor rubella); 2) ≥2 discarded nonmeasles nonrubella cases per 100,000 per year in ≥80% of subnational administrative units; 3) ≥80% of suspected measles cases tested for measles immunoglobulin M antibodies; 4) ≥80% of suspected cases have an adequate investigation conducted within 48 hours of notification; 5) ≥80% of laboratory-confirmed chains of transmission have adequate samples collected for detecting measles or rubella virus and tested in an accredited laboratory; and 6) an annualized incidence rate of zero for confirmed endemic measles cases.

TABLE 1. Estimated coverage* with the first and second dose of measles-containing vaccine (MCV), vaccination schedule,† number of reported measles cases,§ and measles cases per 1 million population,¶ by country — World Health Organization (WHO) South-East Asia Region, 2003 and 2013

	2003						2013						2003–2013	
	WHO/UNICEF estimated coverage* (%)		MCV schedule†		No. of reported measles cases (JRF)§	Measles incidence per million population¶	WHO/UNICEF estimated coverage* (%)		MCV schedule†		No. of reported measles cases (JRF)§	Measles incidence per million population¶	% change in MCV1 coverage	% change in measles incidence per million population
Country	MCV1 (%)	MCV2 (%)	MCV1	MCV2			MCV1 (%)	MCV2 (%)	MCV-1	MCV2				
Bangladesh	76	—**	M-9 mos	—**	4,067	30.6	93	81	MR-9 mos	M-15 mos	237	1.5	22	-95
Bhutan	88	—**	M-9 mos	—**	0	00.0	94	89	MR-9 mos	M-24 mos	0	0.0	7	0
North Korea	95	—**	M-9 mos	—**	0	00.0	99	99	M-9 mos	M-15 mos	0	0.0	4	0
India	62	—**	M-9 mos	—**	47,147	44.0	74	42	M-9 mos	M-16–24 mos	13,822	11.1	19	-75
Indonesia	74	21††	M-9 mos	M-7 yrs††	24,457	114.4	84	79	M-9 mos	M-6yrs§§	8,419	33.9	14	-70
Maldives	96	—**	M-9 mos	—**	75	267.3	99	99	M-9 mos	MMR-18 mos	0	—	3	-100
Myanmar	80	—**	M-9 mos	—**	830	15.6	86	80	M-9 mos	M-18 mos	1,010	16.2	8	4
Nepal	75	—**	M-9 mos	—**	13,344	537.8	88	—**	MR-9 mos	—**	1,861	68.3	17	-87
Sri Lanka	99	90	M-9–12 mos¶¶	MR-3 yrs	65	3.4	99	99	MMR-1 yrs	MMR-3 yrs	2,107	102.9	0	2,947
Thailand	96	92	M-9 mos	MMR-6 yrs	4,519	71.8	99	94	MMR-9 mos	MMR-7 yrs	2,641	40.7	3	-43
Timor-Leste	55	—**	M-9 mos	—**	94	110.6	70	—**	M-9 mos	—**	4	3.4	27	-97
Region overall	**67**	**6**			**94,598**	**58.9**	**78**	**53**			**30,101**	**16.2**	**16**	**-72**

Abbreviations: M = measles; MR = measles-rubella; MMR = measles-mumps-rubella; UNICEF = United Nations Children's Fund; JRF = Joint Reporting Form.
* Data were from WHO and UNICEF estimates, 2013 revision (as of July 2014). Data available at http://www.who.int/immunization/monitoring_surveillance/data/en.
† As reported to WHO/UNICEF on JRFs for the year.
§ JRF was submitted to WHO and UNICEF by member states with the official immunization data and reports the number of measles cases in the country for the year.
¶ Measles incidence was calculated based on the reported measles cases and population by member states through WHO/UNICEF JRF.
** MCV2 was not introduced in routine immunization.
†† Subnational introduction in schools of West Java at age 7 years.
§§ In a few selected provinces in Indonesia, MCV2 was given at age 24 months.
¶¶ Changed in 2011 from age 9 months to 9–12 months.

the WHO Global Measles and Rubella Laboratory Network. By 2013, this regional laboratory network had expanded to include 34 proficient laboratories** with one regional reference laboratory in Thailand. All countries in the region except Timor-Leste had at least one proficient laboratory, including India (nine laboratories), Indonesia (four), and Thailand (13). In addition, Bangladesh, Bhutan, Nepal, Sri Lanka, and Thailand had also started sentinel surveillance for congenital rubella syndrome.

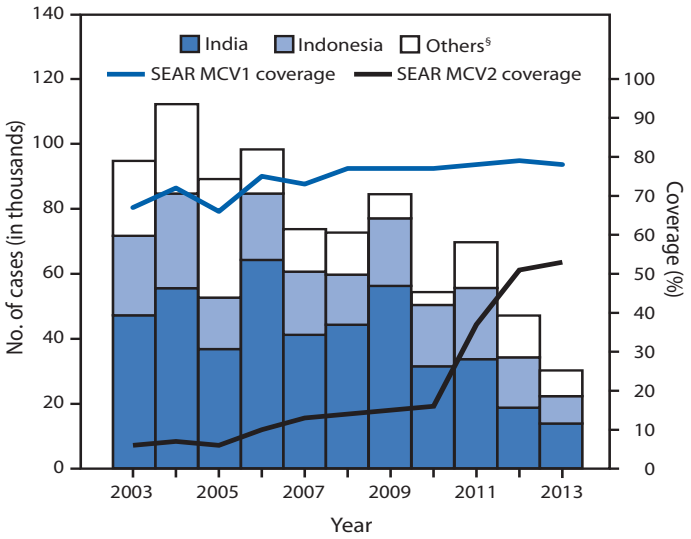
During 2003–2013, a total of 5,680 suspected measles outbreaks were reported in countries in the region, 5,166 (91%) of which were fully investigated.†† Among those investigated, 2,530 (49%) were laboratory-confirmed measles outbreaks, 1,437 (28%) were laboratory-confirmed rubella outbreaks, and 532 (10%) were laboratory-confirmed mixed measles and rubella outbreaks.

Measles Incidence and Measles Virus Genotypes

From 2003 to 2013, annual measles incidence in the region decreased 73%, from 59 to 16 cases per million population. Five countries reported measles incidence of <5 cases per million in 2013, including three (Bhutan, North Korea, and

** A laboratory that has met defined criteria outlined in the report, "Framework for verifying elimination of measles and rubella" (Wkly Epidemiol Rec 2013;88:89–100, available at http://www.who.int/wer/2013/wer8809/en).
†† A house-to-house survey is conducted in the affected area; ≥5 suspected cases serologically tested for measles/rubella immunoglobulin M; and a case investigation form or line list with basic epidemiologic data is completed.

FIGURE. Number of reported measles cases* and estimated percentage of children who received their first and second dose of measles-containing vaccine (MCV),† by country — World Health Organization (WHO) South-East Asia Region (SEAR), 2003–2013



Abbreviations : MCV1 = first dose of MCV in routine immunization; MCV2 = second dose of MCV in routine immunization.
* Cases of measles reported to WHO and the United Nations Children's Fund (UNICEF) through the Joint Reporting Form from WHO-SEAR.
† Data are from WHO and UNICEF estimates for SEAR, available at http://www.who.int/immunization/monitoring_surveillance/data/subject/en.
§ Others include Bangladesh, Bhutan, North Korea, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste.

TABLE 2. Measles supplementary immunization activities (SIAs),* by country, target age group, type of SIA, and number and percentage of targeted children vaccinated — World Health Organization (WHO) South-East Asia Region, 2003–2013†

Country	Year	Vaccine type	SIA type	Extent of SIA	Target age group	Target population	Administrative coverage (%)
Bangladesh	2005	M	Catch-up	Pilot	9 mos–10 yrs	1,481,321	93
	2006	M	Catch-up	National	9 mos–10 yrs	34,199,590	>100§
	2010	M	Follow-up	National	9 mos–5 yrs	18,136,066	100
Bhutan	2006	MR	Catch-up	National	9 mos–14 yrs (males) and 15–44 yrs (females)	338,040	98
North Korea	2007	M	Catch-up	National	6 mos–45 yrs	16,123,376	100
India	2010	M	Catch-up	Subnational	9 mos–10 yrs	10,469,901	90
	2011	M	Catch-up	Subnational	9 mos–10 yrs	34,127,013	90
	2012	M	Catch-up	Subnational	9 mos–10 yrs	50,134,186	90
	2013	M	Catch-up	Subnational	9 mos–10 yrs	36,012,805	93
Indonesia	2003	M	Catch-up	Subnational	6–12 yrs	1,030,445	95
	2004	M	Catch-up	Subnational	6–12 yrs	2,180,918	94
	2005	M	Catch-up	Subnational	6 mos–15 yrs	5,515,324	94
	2006	M	Catch-up	Subnational	6–12 yrs	3,161,323	96
	2006	M	Catch-up	Subnational	6 mos–5 yrs	3,978,096	93
	2007	M	Follow-up	Subnational	6 mos–5 yrs	14,913,092	91
	2007	M	Catch-up	Subnational	6 mos–12 yrs	5,473,025	>100§
	2008	M	Follow-up	Subnational	1–3 yrs	11,203	78
	2009	M	Follow-up	Subnational	9 mos–5 yrs	2,124,572	92
	2010	M	Follow-up	Subnational	9 mos–5 yrs	3,619,024	91
	2011	M	Follow-up	Subnational	9 mos–5 yrs	11,989,559	95
Maldives	2005	MR	Catch-up	National	6–25 yrs (males) and 6–35 yrs (females)	144,997	85
	2006	MR	Catch-up	National	6–25 yrs (males) and 6–35 yrs (females)	144,997	85
	2007	MMR	Catch-up	National	4–6 yrs	29,529	56
Myanmar	2003	M	Follow-up	National	9 mos–5 yrs	2,502,969	90
	2004	M	Follow-up	National	9 mos–5 yrs	1,679,487	65
	2007	M	Follow-up	National	9 mos–5 yrs	6,056,000	94
	2012	M	Follow-up	National	9 mos–5 yrs	6,432,064	97
Nepal	2004	M	Catch-up	National	9 mos–15 yrs	5,344,765	>100§
	2005	M	Catch-up	National	9 mos–15 yrs	4,326,348	>100§
	2008	M	Follow-up	National	9 mos–59 mos	199,751	97
	2008	M	Follow-up	National	9 mos–59 mos	3,903,515	93
	2012	MR	Catch-up	National	9 mos–14 yrs	9,579,306	>100§
Sri Lanka	2003	M	Catch-up	National	10–15 yrs	1,987,847	95
	2004	MR	Catch-up	National	16–20 yrs	1,890,326	72
	2013	M	Catch-up	National	6 mos–12m	176,587	98
Timor-Leste	2003	M	Catch-up	National	9 mos–5 yrs	128,318	99
	2006	M	Catch-up	National	6 mos–14 yrs	390,687	40
	2009	M	Follow-up	National	9 mos–5 yrs	167,136	76
	2011	M	Catch-up	National	6 mos–14 yrs	494,427	92
Total						**300,597,935**	

Abbreviations: MCV = measles-containing vaccine; M = measles; MR = measles-rubella; MMR = measles-mumps-rubella.

* SIAs generally are carried out using two target age ranges. An initial, nationwide catch-up SIA targets all children aged 9 months–14 years, with the goal of eliminating susceptibility to measles in the general population. Periodic follow-up SIAs then target all children born since the last SIA. Follow-up SIAs generally are conducted nationwide every 2–4 years and target children aged 9–59 months; their goal is to eliminate any measles susceptibility that has developed in recent birth cohorts and to protect children who did not respond to the first measles vaccination.

† Data available at http://www.who.int/immunization/monitoring_surveillance/data/en.

§ Values >100% indicate that the intervention reached more persons than the estimated target population.

Maldives) that reported zero cases (Table 1, Figure). In 2013, a total of 248 laboratory-confirmed measles outbreaks and 14 laboratory-confirmed mixed measles and rubella outbreaks were reported in the region. A total of 10,108 confirmed measles cases (laboratory-confirmed and epidemiologically linked) were reported in these outbreaks. The largest proportion of cases (35%) occurred in children aged 1–4 years, followed by children aged 5–9 years (30%), children aged <1 year and persons aged ≥15 years (13% each), and children aged 10–14 years (9%). Of these cases, 68% were in unvaccinated persons. The highest percentage of unvaccinated persons (87%) was in the <1 year age group, followed by the ≥15 years (82%), 10–14 years (71%), 5–9 years (62%) and 1–4 years (61%) age groups.

During 2003–2013, among isolates from patients, measles virus genotypes detected and reported in the region included

D4, D7, and D8 in India; D8, D9, G2, and G3 in Indonesia; D5 in Maldives: D5 and D9 in Myanmar; D4 and D8 in Nepal; D8 in Sri Lanka; and D5, D8, D9, and G2 in Thailand.

Discussion

During 2003–2013, substantial progress was made toward measles control in the South-East Asia Region: through implementation of the regional measles mortality reduction strategies, measles incidence decreased 73% and estimated measles deaths decreased 63% (*1*,*3*,*7*). By 2008, the goal of reducing measles-related deaths by 90% by 2010 from the 2000 baseline was achieved by all countries in the region except India (*8*,*9*). After increases in MCV1 and MCV2 coverage and implementation of SIAs, Bhutan, North Korea, and Maldives reported no laboratory-confirmed measles cases in 2013 and might have interrupted endemic measles virus transmission. This apparent success will only be confirmed once the regional verification commission is established and a formal evaluation is conducted, but it indicates that measles elimination in this region is feasible when the current tools and strategies are optimally implemented.

In September 2013, after an extensive review of the progress made and the biologic, programmatic, and financial feasibility of measles and rubella elimination, the 66th session of the Regional Committee of the South-East Asia Region adopted the goal of measles elimination and rubella/congenital rubella syndrome control in the South-East Asia Region by 2020 (*1*,*3*), resulting in all six WHO regions now having a measles elimination goal. However, challenges exist to achieving measles elimination in the South-East Asia Region. In 2013, routine MCV1 coverage was <95% nationally for seven of the 11 countries in the region. Of the estimated 21.5 million infants worldwide who did not receive MCV1, almost one third were in India (6.4 million) and Indonesia (0.7 million) (*7*). In addition, more than half of the SIAs implemented in the region during 2003–2013 did not achieve the target of ≥95% coverage. Information on measles genotypes circulating before measles elimination activities started is important to distinguish indigenous circulating viruses from imported ones, which is required to confirm measles elimination in the region.

The findings in this report are subject to at least two limitations. First, vaccination coverage estimates are derived from administrative data and can be inaccurate because of errors in estimates of target populations or errors in recording doses administered. Second, surveillance data might significantly underestimate actual disease incidence, because not all patients seek care, and not all those who seek care are reported. However, the data on coverage, incidence, and estimated deaths all indicate that measles-associated morbidity and mortality declined considerably in this region during 2003–2013.

What is already known on this topic?

During 1999–2002, coverage with the first dose of measles-containing vaccine in the World Health Organization's South-East Asia Region increased from 58% to 70%, Sri Lanka and Thailand added a second routine dose of measles-containing vaccine, and 16 million children were vaccinated against measles during supplementary immunization activities (SIAs).

What is added by this report?

During 2003–2013, estimated coverage with the first and second doses of measles-containing vaccine increased from 67% to 78% and from 6% to 53%, respectively, and measles SIAs reached 286 million children. Measles incidence declined by 73%, and estimated measles deaths decreased by 63%. The region adopted the goals of measles elimination and rubella and congenital rubella syndrome control by 2020. All countries in the region conduct some form of case-based measles surveillance, and some countries have implemented sentinel surveillance for congenital rubella syndrome.

What are the implications for public health practice?

To achieve regional measles elimination by 2020, the following are needed: strengthening routine immunization to achieve ≥95% coverage with 2 doses of measles-containing vaccine; optimizing the timing of measles vaccine doses; conducting high-quality SIAs; enhancing surveillance and building on existing laboratory networks; and seeking opportunities for collaboration with other programs.

The adoption of a measles elimination goal in the South-East Asia Region is an opportunity to reenergize efforts and maintain momentum in the region to 1) strengthen routine immunization and achieve ≥95% coverage with MCV2; 2) optimize the timing of MCV1 and MCV2 doses, based on measles epidemiology in each country[§§]; 3) conduct high-quality SIAs; 4) enhance surveillance and build on existing laboratory networks to perform case-based surveillance; and 5) seek opportunities to collaborate with other programs, including use of the measles elimination platform to integrate rubella and congenital rubella syndrome control efforts. As of 2015, all 11 countries in the South-East Asia Region had either developed or were drafting national plans based on the strategies outlined in the Global Measles and Rubella Strategic Plan and the Regional Committee resolution (*1*,*10*). With 35 million surviving infants in the region (26% of the global total), the measles elimination goal is a significant opportunity to further decrease measles-related deaths and illness globally by 2020 (*7*).

[§§] WHO recommendations on optimal age for administration of first and second MCV doses and interval between doses depends on rate of measles transmission in country and capacity of the health systems. Additional information available at http://www.who.int/wer/2009/wer8435.pdf?ua=1.

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Notes from the Field

Increase in Reported Adverse Health Effects Related to Synthetic Cannabinoid Use — United States, January–May 2015

Royal Law, MPH[1]; Josh Schier, MD[1]; Colleen Martin, MSPH[1]; Arthur Chang, MD[1]; Amy Wolkin, DrPH[1] (Author affiliations at end of text)

On April 6, 2015, CDC received notification of an increase in telephone calls to U.S. poison centers related to synthetic cannabinoid use. Monthly calls to all poison centers are tracked by the National Poison Data System, which reported that adverse health effects or concerns about possible adverse health effects related to synthetic cannabinoid use increased 330% from 349 in January 2015 to 1,501 in April 2015. Synthetic cannabinoids include various psychoactive chemicals or a mixture of such chemicals that are sprayed onto plant material, which is then often smoked or ingested to achieve a "high." These products are sold under a variety of names (e.g., synthetic marijuana, spice, K2, black mamba, and crazy clown) and can be sold in retail outlets as herbal products. Law enforcement agencies have regulated a number of these substances; however, manufacturers of synthetic cannabinoids frequently change the formulation to avoid detection and regulation. After the initial notification, CDC analyzed information from the National Poison Data System on reported adverse health effects related to synthetic cannabinoid use for the period January–May 2015.

During the 2015 study period, poison centers reported 3,572 calls related to synthetic cannabinoid use, a 229% increase from the 1,085 calls during the same January–May period in 2014 (Figure). The number of calls spiked notably in mid-April before decreasing nearly to 2014 levels by the end of May (Figure). Most calls concerned use among males (2,882 [80.7%]). Among 3,442 (96.4%) calls where age of the user was recorded, the median age was 26 years (range = 7 months–72 years).

The most commonly reported adverse health effects were agitation (1,262 [35.3%]), tachycardia (1,035 [29.0%]), drowsiness or lethargy (939 [26.3%]), vomiting (585 [16.4%]), and confusion (506, [4.2%]). Among 2,961 calls for which a medical outcome was reported, 335 (11.3%) callers had a major adverse effect (signs or symptoms that are life-threatening or result in substantial residual disability or disfigurement); 1,407 (47.5%) had a moderate effect (signs or symptoms that are not life-threatening and do not result in residual disability or disfigurement, but usually require some form of treatment). A total of 1,095 (37.0%) had a minor effect (signs or symptoms that are minimally bothersome and generally resolve rapidly with no residual disability or disfigurement), and 109 (3.7%) had no effect (*1*). A total of 15 (0.5%) deaths were reported.

Inhalation by smoking was the most common means of consumption (2,870 [80.3%]), followed by ingestion (698 [19.5%]). Most reported use was intentional (3,310 [92.7%]). Among 626 calls reporting use of synthetic cannabinoids with multiple substances, the most commonly reported other substances included alcohol (144 [23.0%]), plant-derived marijuana (103 [16.5%]), and benzodiazepines (69 [11.0%]). Only one of the deaths included reports of multiple substance use.

Calls indicating severe medical outcomes (major effect and death) were compared with calls indicating less severe outcomes (moderate effect, minor effect, and no effect). Results of a chi-square test demonstrated a significant association between sex and degree of severity. Males were significantly more likely to have a severe outcome (88.6%) than a less severe outcome (80.1%) ($p<0.001$). A significant association also was found between age group and severity ($p<0.001$); pairwise comparisons (adjusted by the stepdown Bonferroni procedure) indicated that persons aged 30–39 years and aged >40 years were significantly more likely than those aged 10–19 years to report a severe outcome ($p = 0.001$ and $p<0.001$, respectively).

The findings in this report are subject to at least two limitations. First, in some states, poison centers acted as central reporting centers for hospitals that evaluated persons experiencing a health effect associated with synthetic cannabinoid use. Situations in which a poison center was not contacted were not recorded, thus possibly underestimating the number of persons who were evaluated after synthetic cannabinoid use. Second, calls involving multiple substances were included in the analysis; therefore, adverse health effects might have resulted from use of other substances or a combination of substances.

The increasing number of synthetic cannabinoid variants available, higher toxicity of new variants, and the potentially increased use as indicated by calls to poison centers (*2*–*3*) might suggest that synthetic cannabinoids pose an emerging public health threat. Multiple other recent outbreaks (*2*–*4*) suggest a need for greater public health surveillance and awareness, targeted public health messaging, and enhanced efforts to remove these products from the market.

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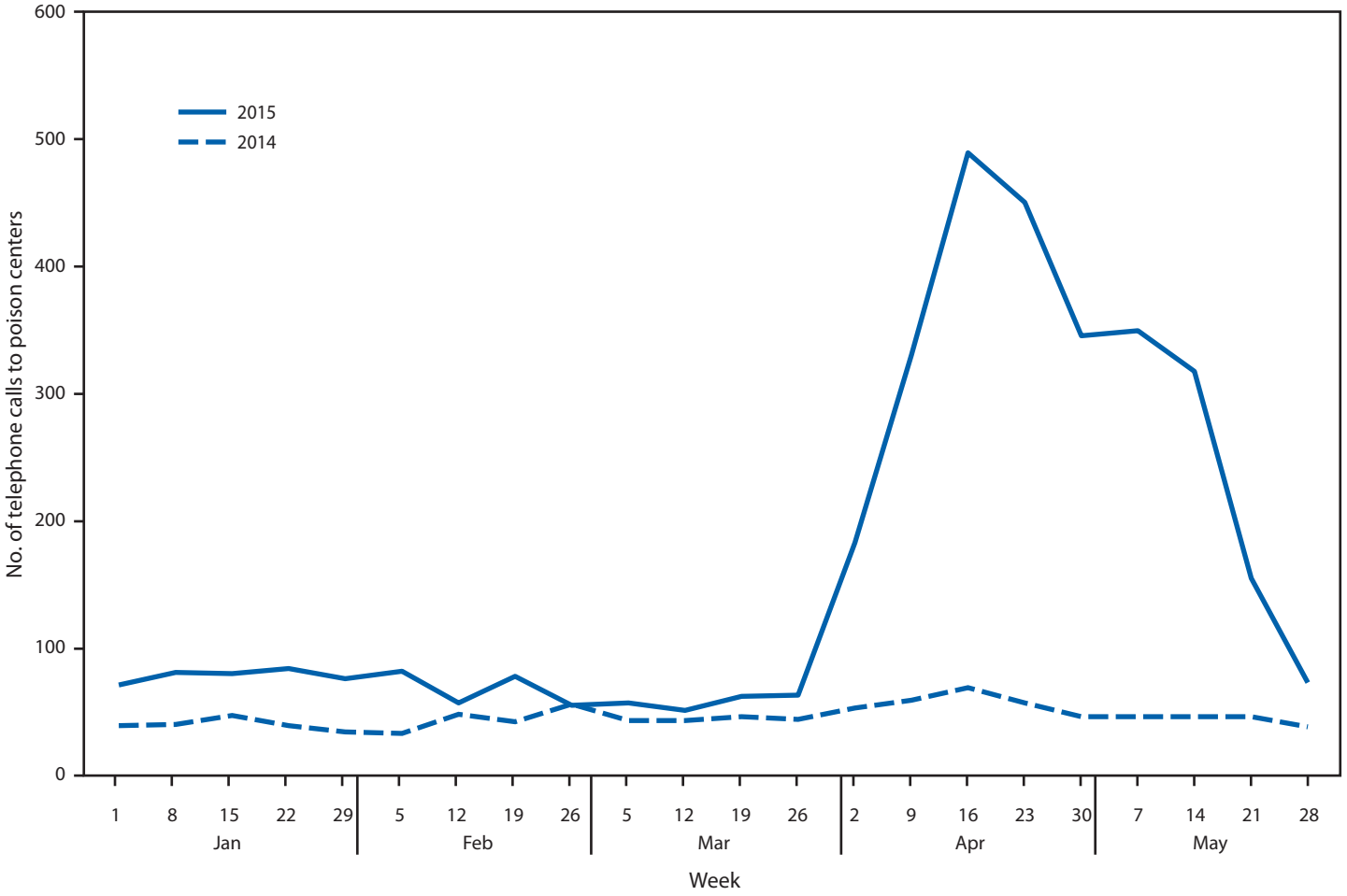
FIGURE. Number of telephone calls to poison centers reporting adverse health effects related to synthetic cannabinoid use, by week — National Poison Data System, United States, January–May 2014 and 2015



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Notice to Readers

Updated 'N' Indicators for the National Notifiable Diseases Surveillance System for 2014–2015

CDC's National Notifiable Diseases Surveillance System (NNDSS) maintains and annually updates information about which Nationally Notifiable Infectious Conditions (NNICs) are considered "reportable" (i.e., by health care providers, hospitals, laboratories, or other public health reporters) in each of the different reporting jurisdictions. NNICs designated "not reportable" are indicated with an "N"; those conditions that are reportable are recorded with either the number of cases or with a "—" (i.e., a dash symbol) to indicate that no cases were reported for that NNIC. These designations are used in the annual *MMWR* Summary of Notifiable Diseases — United States and in the weekly *MMWR* Notifiable Diseases and Mortality Tables I and II of provisional NNDSS data.

NNDSS staff within the Division of Health Informatics and Surveillance performed assessments with each reporting jurisdiction to ascertain the reportable disease status of each NNIC for the years 2013–2015. The assessment results for 2013 and 2014 were used to populate the "N" indicators for NNDSS data in the *MMWR* Summary of Notifiable Diseases — United States, 2013 and the NNDSS weekly provisional *MMWR* Notifiable Diseases and Mortality Tables I and II for 2014, respectively. Assessment results for 2015 are being used to populate the "N" indicators in the *MMWR* weekly provisional tables for 2015.

When the data for a specified year are reconciled and finalized, NNDSS reporting exceptions ("N" indicators) are summarized by NNIC and reporting jurisdiction in a report that can be found under the Downloads and Resources tab at http://wwwn.cdc.gov/nndss/.

Errata

Vol. 64, No. 18

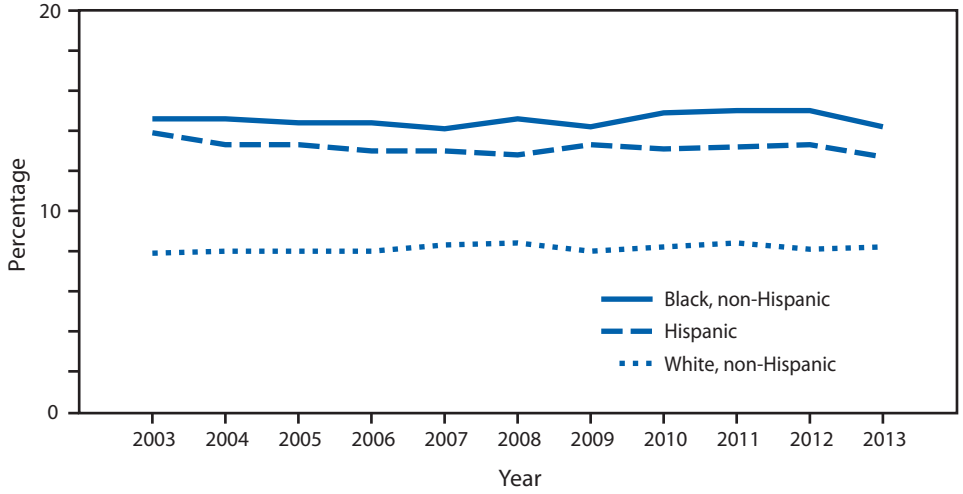
In the report, "Norovirus Outbreak Associated with a Natural Lake Used for Recreation — Oregon, 2014," on pages 485–6, an error occurred in the fifth sentence of the first paragraph of the report. That sentence should read, "Analyses from a retrospective cohort study revealed that swimming at Blue Lake during July 12–13 was significantly associated with illness during July 13–14 (adjusted relative risk = 2.3; 95% confidence interval [CI] = 1.1–**4.9**)."

In the report, "Initiation of a Ring Approach to Infection Prevention and Control at Non-Ebola Health Care Facilities — Liberia, January–February 2015," on page 505, an error occurred in the fifth sentence of the second paragraph. That sentence should read, "For three **of six** patients with available data, a fever (defined as a temperature >100.4°F [>38°C] taken with an infrared thermometer) was not recorded on arrival at the HCF."

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted* Percentage of Persons Who Reported Fair or Poor Health,† by Race and Hispanic Origin — National Health Interview Survey, United States,§ 2003–2013



* Estimates are age-adjusted to the 2000 projected U.S. standard population using six age groups (in years): <18, 18–44, 45–54, 55–64, 65–74, ≥75.
† Respondents were asked "Would you say (person's) health in general is excellent, very good, good, fair, or poor?" Responses of fair or poor were combined into one measure.
§ Estimates are based on household interviews of a sample of the noninstitutionalized U.S. civilian population.

During 2003–2013, non-Hispanic black and Hispanic persons were more likely than non-Hispanic white persons to report fair or poor health. Fair or poor health status ranged between 14%–15% for non-Hispanic black persons and 13%–14% for Hispanic persons, and was 8% for non-Hispanic white persons, with no significant changes during the decade in the percentage of those reporting fair or poor health within each of the three groups.

Source: National Center for Health Statistics, *Health, United States, 2014, With Special Feature: Adults Aged 55–64* (Table 50). Available at http://www.cdc.gov/nchs/hus.htm.

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ISSN: 0149-2195