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Acute Kidney Injury Associated with Synthetic Cannabinoid Use — Multiple States, 2012

In March 2012, the Wyoming Department of Health was notified by Natrona County public health officials regarding three patients hospitalized for unexplained acute kidney injury (AKI), all of whom reported recent use of synthetic cannabinoids (SCs), sometimes referred to as "synthetic marijuana." SCs are designer drugs of abuse typically dissolved in a solvent, applied to dried plant material, and smoked as an alternative to marijuana. AKI has not been reported previously in users of SCs and might be associated with 1) a previously unrecognized toxicity, 2) a contaminant or a known nephrotoxin present in a single batch of drug, or 3) a new SC compound entering the market. After the Wyoming Department of Health launched an investigation and issued an alert, a total of 16 cases of AKI after SC use were reported in six states. Review of medical records, follow-up interviews with several patients, and laboratory analysis of product samples and clinical specimens were performed. The results of the investigation determined that no single SC brand or compound explained all 16 cases. Toxicologic analysis of product samples and clinical specimens (available from seven cases) identified a fluorinated SC previously unreported in synthetic marijuana products: (1-(5-fluoropentyl)-1H-indol-3-yl) (2,2,3,3-tetramethylcyclopropyl) methanone, also known as XLR-11, in four of five product samples and four of six patients' clinical specimens. Public health practitioners, poison center staff members, and clinicians should be aware of the potential for renal or other unusual toxicities in users of SC products and should ask about SC use in cases of unexplained AKI.

Epidemiologic Findings

The first three patients (Table 1, cases 1–3) reported smoking SCs in the days or hours before symptom onset. Public health staff members interviewed the three and reviewed their medical records. The patients were young, previously healthy males who reported smoking either a blueberry-flavored SC product (one patient) or an unspecified SC product (two patients). They experienced severe nausea, vomiting, and flank or abdominal pain and went to emergency departments during February 26–29. Local law enforcement officials were notified and released a media advisory warning of illness associated with SC use.

The Wyoming Department of Health launched an investigation to identify other cases and determine the cause of illness. A case initially was defined as nausea, vomiting, abdominal or back pain, and AKI (i.e., serum creatinine concentration above the facility's reference range) in a patient reporting SC use and illness onset during February 1–March 1. Hospital staff members from two regional medical facilities conducted retrospective reviews of emergency department and hospital admission records. The Wyoming Department of Health issued a health alert on March 1 to all licensed health-care providers, hospitals, emergency departments, and urgent-care centers in Wyoming, describing the possible association between AKI and SC use and requesting that potential cases be reported.

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On March 21, the Wyoming state epidemiologist contacted CDC regarding the first three cases. On March 24, a fourth Wyoming patient became ill after smoking either a blueberry-flavored or bubblegum-flavored SC product and was found to meet the case definition (Table 1, case 4).

A collaboration among several state public health officials, poison center toxicologists, forensic laboratory scientists, individual clinicians, and the Arkansas K2 Research Consortium, identified an additional 12 cases of SC-associated AKI in Oregon (six cases), New York (two), Oklahoma (two), Rhode Island (one), and Kansas (one) in hospitalized patients who had serum creatinine concentration above the facility's reference range after smoking an SC product during March 16–December 3. CDC medical toxicologists reviewed clinical and laboratory data from all 16 cases (Table 1).

All 16 patients initially visited emergency departments and subsequently were hospitalized. The 16 patients included 15 males aged 15–33 years (median: 18.5 years) and one female aged 15 years; all but one had nausea and vomiting. Twelve patients reported abdominal, flank, and/or back pain. None reported preexisting renal dysfunction or use of medication that might have caused renal problems. The highest serum creatinine concentrations (creatinine peak) among the 16 patients ranged from 3.3 to 21.0 mg/dL (median: 6.7 mg/dL; normal 0.6–1.3 mg/dL) and occurred 1–6 days after symptom onset (median: 3 days). Urinalysis for 15 patients showed variable results: proteinuria (eight patients), casts (five), white blood cells (nine), and red blood cells (eight). Twelve patients underwent renal ultrasonograpy, nine of whom had a nonspecific increase in renal cortical echogenicity; none had hydronephrosis.

Six of eight patients with a renal biopsy demonstrated acute tubular injury, and three of eight patients demonstrated features of acute interstitial nephritis. Kidney function recovery was apparent within 3 days of creatinine peak in most patients. However, five of the 16 patients required hemodialysis, and four patients received corticosteroids; none died. Other infectious, autoimmune, pharmacologic, or other toxic causes of AKI were not found.

Toxicologic Analysis

Of the 16 cases, toxicologic analysis of implicated SC products and clinical specimens was possible in seven (Table 2). No single SC product explained all of the cases. Two SC products recovered by law enforcement officials in Wyoming and epidemiologically linked to cases 1–3 were tested by the Arkansas K2 Research Consortium laboratory (Arkansas K2) and the University of California–San Francisco Clinical and Environmental Toxicology Laboratory (UCSF). Gas chromatography/mass spectrometry (Arkansas K2) and liquid chromatography/time-of-flight mass spectrometry (UCSF) analysis revealed that both products contained 3-(1-naphthoyl) indole, a precursor to several aminoalkylindole synthetic cannabinoids. One of the two product samples also contained the potent synthetic cannabinoid AM2201, which has been linked to human disease and death, but not to AKI.

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TABLE 1. Demographic and clinical characteristics and implicated product in 16 cases associated with synthetic cannabinoid use — multiple states, 2012

Case no.	State	Patient age (yrs)	Chief symptom at presentation	Peak creatinine (mg/dL)	Urine microscopy results*	Renal ultrasound results	Implicated product
1	Wyoming	19	Nausea and vomiting, abdominal pain	5.2	WBCs, RBCs, RBC/ granular casts	Within normal limits	Synthetic cannabinoid, not otherwise specified
2	Wyoming	15	Nausea and vomiting, abdominal pain	6.8	WBCs, RBCs, RBC/ granular casts, eosinophils	Increased cortical echogenicity bilaterally	Synthetic cannabinoid, not otherwise specified
3	Wyoming	21	Nausea and vomiting, flank pain	6.3	WBCs, RBCs, epithelial casts, granular casts	Not available	Blueberry-flavored
4	Wyoming	18	Nausea and vomiting, flank pain	4.1	Hyaline casts, WBCs	No increased cortical echogenicity or hydronephrosis	Blueberry-flavored or bubblegum-flavored
5	Rhode Island	25	Nausea and vomiting, anuria	21.0	RBCs, proteinuria, eosinophils	Not performed	Synthetic cannabinoid, not otherwise specified
6	New York	30	Nausea and vomiting	9.0	WBCs, RBCs, RBC/ hyaline casts,	Not performed	Phantom Wicked Dreams
7	Oregon	18	Nausea and vomiting, abdominal pain pain	6.6	WBCs, protein 30	Increased cortical echogenicity, no hydronephrosis	"Synthetic marijuana"
8	New York	33	Nausea and vomiting	3.3	Not available	Not performed	Spice Gold
9	Oregon	27	Flank pain	4.7	Small blood, protein 30	Normal echogenicity, no hydronephrosis	Mad Monkey or Clown Loyal
10	Washington/ Oregon	15	Nausea and vomiting, abdominal pain / back pain	9.1	Protein trace	Increased cortical echogenicity, no hydronephrosis	Synthetic cannabinoid, not otherwise specified
11	Kansas	26	Nausea and vomiting, abdominal pain / back pain	7.7	Within normal limits	Increased cortical echogenicity	Mr. Happy
12	Oregon	17	Nausea and vomiting, flank pain	10.6	WBCs, RBCs, protein 2+, eosinophils 1+	Increased cortical echogenicity, no hydronephrosis	Clown Loyal
13	Oregon	18	Nausea and vomiting, abdominal pain pain	9.6	Protein 2+, blood 3+, no RBCs	Increased cortical echogenicity, no hydronephrosis	Lava
14	Oregon	18	Nausea and vomiting, abdominal pain pain	5.5	Protein 1+	Increased cortical echogenicity, no hydronephrosis	Lava
15	Oklahoma	15	Nausea and vomiting, abdominal pain pain	11.5	WBCs, RBCs	Increased cortical echogenicity, bilateral symmetrical enlargement	Flame 2.0
16	Oklahoma	15†	Nausea and vomiting	6.2	WBC, protein 1+	Increased cortical echogenicity	Flame 2.0

Abbreviations: WBCs = white blood cells; RBCs = red blood cells.
* Elevated levels listed if above the reporting laboratory's reference range.
† Female patient; all others are male.

TABLE 2. Results of toxicologic analysis of implicated products and/or clinical specimens from seven patients with acute kidney injury associated with synthetic cannabinoid use — multiple states, 2012

Case no.	State	Implicated product	Synthetic cannabinoids identified from product samples	Clinical specimen type	Days after last use	Synthetic cannabinoids identified from clinical specimens
4	Wyoming	Blueberry-flavored or bubblegum-flavored	XLR-11 and indole precursor	Urine	2	XLR-11 N-pentanoic acid metabolite (400 ng/mL)
				Blood	3	Not detected
6	New York	Phantom Wicked Dreams	Not performed	Blood	2	XLR-11 N-pentanoic acid metabolite (42 ng/mL)
				Blood	3	Not detected
11	Kansas	Mr. Happy	XLR-11 (69 mg/g)	Serum	0	XLR-11 (35 ng/mL); N-pentanoic acid metabolite (102 ng/mL); UR-144 (6 ng/mL)
			UR-144 (61 mg/g)	Urine	0	XLR-11 N-pentanoic acid metabolite (529 ng/mL)
12	Oregon	Clown Loyal	XLR-11 (92.1 mg/g)	Serum	9	Not detected
13	Oregon	Lava	XLR-11 (1.7 mg/g)	Serum	2	XLR-11 (33 ng/mL); N-pentanoic acid metabolite (38 ng/mL)
				Serum	4	Not detected
14	Oregon	Lava	XLR-11 (1.7 mg/g)	Serum	2	Serum insufficient
				Urine	4	Not detected
15	Oklahoma	Flame 2.0	Not detected			Not performed

Standardized liquid chromatography–time of flight mass spectrometry methods validated for trace level analysis of synthetic cannabinoid parent compounds and metabolites were used for all clinical assays (UCSF). A sample of the product smoked by the patient in case 4 contained 3-(1-naphthoyl) indole and XLR-11, a previously undescribed fluorinated-derivative of the SC compound UR-144 currently in circulation. A urine specimen collected from the same patient was positive for the XLR-11 N-pentanoic acid metabolite. A blood specimen from the patient in case 6, who smoked "Phantom Wicked Dreams," contained the N-pentanoic acid metabolite of XLR-11. In case 11, analysis of the SC product "Mr. Happy" and a serum specimen revealed the SCs XLR-11 and UR-144; a urine specimen contained the N-pentanoic acid metabolite of XLR-11. In case 12, samples of "Clown Loyal" were found to contain XLR-11. In cases 13 and 14, analysis of "Lava" and associated clinical specimens identified XLR-11 and the N-pentanoic acid metabolite of XLR-11. In case 15, analysis of "Flame 2.0" was negative for XLR-11. For nine of the 16 cases, neither product samples nor clinical specimens were available for analysis.

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What is already known on this topic?

Synthetic cannabinoids (SCs) are psychoactive chemicals dissolved in solvent, applied to plant material, and smoked as a drug of abuse. They are sold in "head shops" and tobacco and convenience stores under labels such as "synthetic marijuana," "herbal incense," "potpourri," and "spice." Most reports of adverse events related to SCs have been neurologic, cardiovascular, or sympathomimetic.

What is added by this report?

Sixteen cases of acute kidney injury following exposure to SCs were identified in six states with illness onset during March 16–December 7, 2012. Patients ranged in age from 15 to 33 years; 15 were male, and none reported a history of kidney disease. Gas and liquid chromatography and mass spectrometry identified a new SC, XLR-11, associated with some of these cases.

What are the implications for public health practice?

Novel drugs of abuse are emerging continuously. SCs often are packaged in colorful wrappers bearing labels such as "not for human consumption" or "incense," although health professionals and legal authorities know these products are smoked like marijuana. Law enforcement officials, public health officials, clinicians, scientists, and the members of the public should be aware of the potential for adverse health effects posed by SCs.

Editorial Note

Synthetic cannabinoid compounds originally were developed to facilitate study of cannabinoid receptor pharmacology, but in recent years have emerged as drugs of abuse. In 2005, SC products marketed as "Spice" first emerged in European countries, before appearing in the United States in 2009, where they were marketed initially as "K2." Today, SC products are distributed worldwide under countless trade names and packaged in colorful wrappers designed to appeal to teens, young adults, and first-time drug users (*1*). Products often are packaged with disingenuous labels such as "not for human consumption" or "incense," but health professionals and legal authorities are keenly aware that these products are smoked like marijuana. Despite federal and state regulations to prohibit SC sale and distribution, illicit use continues, and reports of illness are increasing (*1–4*).

The expectation of a more intense high than that induced by marijuana, easy access, affordability, and avoidance of detection by many commonly used urine drug tests all contribute to the growing abuse of SCs, especially among male adolescents (*1,5*). The increasing use of SCs by young persons, coupled with mounting evidence of adverse health effects, has led to state and federal legislation (*3,6*). However, full recognition of the potential dangers of SCs is not widespread among users or sellers, and SC products remain available on the Internet and at many convenience stores. Further, differences in state drug enforcement statutes have led to different laws and approaches to drug enforcement (*7*).

Although related to delta-9-tetrahydrocannabinol, the active ingredient in marijuana, SCs are two to three times more likely to be associated with sympathomimetic effects (i.e., tachycardia and hypertension), and approximately five times more likely to be associated with hallucinations (*8*). In addition, an increase in the occurrence of seizures has been reported with SC use (*9*). This report describes unanticipated AKI with SC abuse. Given the rapidity with which new SC compounds enter the marketplace and their increasing use in the past 3 years, outbreaks of unexpected toxicity associated with their use are likely to increase.

Management of suspected SC toxicity is symptomatic and supportive; no antidote exists. All of the patients in this report recovered creatinine clearance during their hospital stay, although the length of time was variable; one patient was discharged before his creatinine normalized. However, a risk for long-term kidney sequelae might exist. Recent studies suggest an increased risk for chronic and end-stage renal disease following AKI of various etiologies, despite initial recovery (*10*). Physicians caring for otherwise healthy adolescents and young adults with unexplained AKI should inquire about SC use, and cases of suspected SC poisoning should be reported to both the regional poison center and the appropriate state health department. Regional poison centers can be reached by telephone at 1-800-222-1222, from anywhere in the United States.

In this report, the product used by five of the 16 patients, including two patients (cases 13 and 14) who used the same product, contained a novel fluorinated SC (XLR-11). In addition, XLR-11 and/or XLR-11 metabolites were found in five of the seven cases for whom clinical specimens were available. XLR-11 emerged on the SC market in the first half of 2012; therefore, experience with this fluorinated compound has been limited. The consistent finding of XLR-11 in product samples and clinical specimens has alternative explanations. XLR-11, a metabolite, or a contaminant associated with it might be responsible for AKI in these patients, or its presence might simply reflect the widespread use of this particular compound in SC products during the study period rather than a causal association with AKI. Health-care providers should be aware of renal and other unexpected toxicities from use of SC products, especially with newer SC compounds.

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Completeness of Reporting of Chronic Hepatitis B and C Virus Infections — Michigan, 1995–2008

Chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infections are leading causes of death from cirrhosis and hepatocellular carcinoma in the United States (*1*). Because underreporting has complicated the understanding of disease burden, in 2010 the Institute of Medicine requested that CDC perform a comprehensive evaluation of national viral hepatitis surveillance (*1*). Hepatitis surveillance data rely on local and state estimates, and a better understanding of reporting at these levels can inform strategies to improve national data quality. As an initial assessment, CDC partnered with the Michigan Department of Community Health (MDCH) and an urban health-care system in southeastern Michigan to evaluate the completeness of reporting (including case status, demographic, and risk factor information) of cases of chronic HBV and HCV infection among persons who were enrolled in a multicenter chronic hepatitis cohort study (*2*) to the MDCH viral hepatitis registry. This report summarizes the results of that assessment. Among clinically confirmed chronic hepatitis infections, 82% of HBV infections and 65% of HCV infections were reported. Completeness of reporting of chronic HBV and HCV infections was significantly improved for those with more recent clinical diagnoses, but reporting still remained incomplete. The completeness of reporting varied significantly by demographic characteristics of patients with HCV infection. Few reports of either HBV or HCV infection included risk factors. Improving surveillance of chronic hepatitis in Michigan will require exploration of more efficient methods for the transfer of laboratory and clinical data and evaluation of the most appropriate sources for risk factor information to aid in the prevention of viral hepatitis transmission. Similar collaborations with health-care institutions that use electronic *International Classification of Diseases, Ninth Revision* (ICD-9) codes and laboratory data can provide local and state health departments with insight into the challenges to case reporting in their jurisdictions.

Reporting of chronic HBV and HCV infections became mandatory in Michigan in 2004 and 2000, respectively. In 2004, electronic dual reporting of both infections by laboratories and by health-care providers began with the launch of the Michigan Disease Surveillance System (MDSS). As part of an ongoing, multicenter, chronic hepatitis cohort study, investigators compiled clinical data from patients suspected to have chronic HBV or chronic HCV infection at any time during 2006–2008 and who resided in Michigan and sought care within the health-care network, which was comprised of several hospitals and clinics serving approximately 1 million Michigan residents (*2*). As of 2011, this health-care network had been documented by MDCH as a reporting institution for approximately 8% of all state reports of chronic HBV infection and 6% of all reports of chronic HCV infection since the advent of MDSS. According to U.S. Census data, the health-care network's patient population has a higher representation of blacks (37% versus 25%), females (57% versus 51%), persons aged ≥65 years (20% versus 13%), and persons aged <17 years (24% versus 20%) than the surrounding regional population.

Clinically confirmed cases of chronic HBV and chronic HCV infection were identified in the cohort study by methods that have been described previously (*2*) (Box). To evaluate the completeness of reporting of chronic HBV and HCV infections, all clinically confirmed cohort cases found in the health-care system during the study period of 2006–2008 were matched to cases reported to MDSS by first name, last name, and date of birth, using probabilistic record-linkage software. The year of initial diagnosis (i.e., the year of the first written diagnosis or laboratory evidence of infection) among cohort cases found in the health-care system ranged from 1995 to 2008.

Cases from the cohort study that matched in MDSS were queried for case classification in MDSS (acute, chronic, or both) and for the presence of age, sex, and risk factor data in MDSS. For cohort patients coinfected with HBV and HCV who met confirmation criteria for only one infection, only the diagnosis meeting definitive inclusion criteria was considered a case. Age, sex, and year of initial diagnosis were examined for their association with completeness of reporting. Differences between the proportions of confirmed cases reported, by age, sex, and race/ethnicity, were tested for statistical significance by chi-square test. Year-to-year differences in the proportions of cases reported were assessed for trend using the Cochrane-Armitage trend test and year of initial diagnosis.

In the cohort of 4,393 persons, 14% had HBV infections, 85% had HCV infections, and 1% had coinfections, yielding a total of 670 HBV and 3,796 HCV infection cases. Of the HBV infection cases, 597 (89%) met clinical confirmation criteria for chronic HBV infection (29 by physician diagnosis alone and 568 by laboratory criteria with or without a physician diagnosis). Of the HCV infection cases, 3,036 (80%) met clinical confirmation criteria for chronic HCV infection (115 by physician diagnosis alone and 2,921 by laboratory criteria with or without a physician diagnosis). A total of 490 (82%) of the 597 confirmed cases with chronic HBV infection were matched to MDSS, and 1,967 (65%) of the 3,037 confirmed cases with chronic HCV infection were

BOX. Criteria for identifying clinically confirmed cases of HBV and HCV infection in a cohort study — Michigan, 2006–2008

Confirmed chronic HBV infection if either of the following criteria are met*

Criteria 1

Specialist and primary-care provider documentation criteria

Written/dictated description in a progress note by a specialist (hepatologist, gastroenterologist, or infectious disease specialist) or patient's primary-care provider† that describes patient as having chronic HBV infection, being a HBV carrier, or having nonreplicating HBV.

Criteria 2

Laboratory criteria

Any two of the following test results at least 6 months apart: HBsAg positive, HBV DNA positive, or HBeAg positive. (Any combination of these tests performed ≥6 months apart is acceptable.)

Confirmed chronic HCV infection if either of the following criteria are met§

Criteria 1

Specialist and primary-care provider documentation criteria

Written/dictated description in a progress note by a specialist (hepatologist, gastroenterologist, or infectious disease specialist) or patient's primary-care provider† that describes patient as having chronic HCV infection.

Criteria 2

Laboratory criteria

Has any of the following test results:

- Anti-HCV (hepatitis C antibody) positive by enzyme immunoassay (EIA or ELISA)
- HCV RIBA (recombinant immunoblot assay) positive
- HCV RNA detectable
- Report of HCV genotype

AND followed ≥6 months later by either of the following:

- HCV RNA detectable
- Report of HCV genotype

Criteria 3

Combination clinical and laboratory criteria

Patient has not presented with acute hepatitis (a discrete onset of any sign or symptom consistent with acute viral hepatitis [e.g., anorexia, abdominal discomfort, nausea, or vomiting, and either 1) jaundice or dark urine, or 2) serum ALT levels >400 IU/L])

AND has either of the following:

- HCV RNA detectable
- Report of HCV genotype

Source: Moorman AC, Gordon SC, Rupp LB, et al. Baseline characteristics and mortality among people in care for chronic viral hepatitis: the chronic hepatitis cohort study. Clin Infect Dis 2013;56:40–50.

Abbreviations: HBV = hepatitis B virus; HCV = hepatitis C virus; HBsAg = hepatitis B surface antigen; HBeAg = hepatitis B e antigen; ICD-9 = *International Classification of Diseases, Ninth Revision*; EIA = enzyme immunoassay; ELISA = enzyme-linked immunosorbent assay; RIBA = recombinant immunoblot assay; ALT = alanine aminotransferase.

* Patients who are confirmed per these criteria to have had chronic HBV infection at any point, but who later cleared the disease (spontaneously or as a result of treatment), belong in the cohort and should be classified as having a confirmed case of HBV infection.

† This must be a textual description within a progress note, with or without an ICD-9 code. The primary-care provider should appear to have an informed, confident basis for the diagnosis based on serologic results and/or patient history, or the citation of outside laboratory studies that corroborate the diagnosis.

§ Patients who are confirmed via these criteria to have had chronic HCV infection, but who have been successfully treated and have cleared HCV RNA, belong in the cohort and should be classified as having a confirmed case of HCV infection.

matched. Of the cases matched to MDSS, sex was reported in 99.6% (488 of 490) of HBV infection cases and 99.0% (1,947 of 1,967) of HCV cases. Race/ethnicity was reported for 75.1% and 66.7% of cases, respectively. Risk factor data were reported for <5% of HCV infection cases because of inadequate health department resources for case follow-up. HBV infection risk factor data were not recorded because of the absence of risk factor–related questions in case questionnaires. Of the 597 chronic HBV infections, 463 (78%) were appropriately classified as chronic in MDSS. Of the 3,036 chronic HCV infections, 1,918 (64%) were appropriately classified as chronic in MDSS (Table 1).

Completeness of reporting of chronic HBV and HCV infection consistently improved over time and varied significantly by the year of diagnosis, with more complete reporting among cases with more recent diagnoses (p<0.001). Reporting of confirmed cases of HCV infection varied significantly by age group (p=0.001), sex (p=0.049), and race/ethnicity (p=0.024); reporting of these cases was more complete among persons aged 0–30 years, among males, and among non-Hispanic whites and Asians/Pacific Islanders (Table 2).

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TABLE 1. Completeness of reporting for clinically confirmed cases of HBV and HCV infection,* and corresponding case classification of the reported cases in the Michigan Disease Surveillance System — Michigan, 1995–2008

Clinical classification	Reported cases and classification								Unreported	
	Total		Acute		Chronic		Both		Total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Confirmed HBV	**490/597**	**(82)**	27/597	(6)	400/597	(67)	63/597	(11)	**107/597**	**(18)**
Confirmed HCV	**1,967/3,036**	**(65)**	49/3,036	(2)	1,870/3,036	(62)	48/3,036	(2)	**1,069/3,036**	**(35)**

Abbreviations: HBV = hepatitis B virus; HCV = hepatitis C virus.

* Confirmed cases were considered to be cases identified in the cohort study by published methods (Moorman AC, Gordon SC, Rupp LB, et al. Baseline characteristics and mortality among people in care for chronic viral hepatitis: the chronic hepatitis cohort study. Clin Infect Dis 2013;56:40–50). Cases were confirmed by a combination of written diagnoses by health-care providers, *International Classification of Diseases, Ninth Revision* coding, and laboratory data consistent with a chronic HBV and a chronic HCV diagnosis. Reported cases were considered to be the clinically confirmed cases that were successfully matched to and identified in the Michigan Diseases Surveillance System.

TABLE 2. Completeness of reporting for confirmed cases of chronic HBV and HCV infection,* by selected characteristics — Michigan, 1995–2008

Characteristic	Confirmed HBV (N = 597)			Confirmed HCV (N = 3,036)		
	No. reported (n = 490)	(%)	p-value	No. reported (n = 1,967)	(%)	p-value
Age group (yrs)			**0.419**			**0.001**
0–30	66/85	(78)		60/80	(75)	
31–44	201/241	(83)		303/486	(62)	
45–54	128/150	(85)		989/1489	(66)	
55–64	64/80	(80)		481/735	(65)	
≥65	31/41	(76)		134/246	(54)	
Sex			**0.963**			**0.049**
Female	182/222	(82)		727/1161	(63)	
Male	308/375	(82)		1240/1875	(66)	
Race/Ethnicity			**0.548**			**0.024**
White, non-Hispanic	162/191	(85)		832/1242	(67)	
Hispanic	2/2	(100)		19/30	(63)	
Black, non-Hispanic	160/203	(79)		928/1496	(62)	
Asian/Pacific Islander	96/115	(83)		53/73	(73)	
Other/Unknown	70/86	(81)		135/195	(69)	
Year of first diagnosis†			**<0.001**			**<0.001**
1995–1996	41/65	(66)		99/178	(56)	
1997–1998	21/26	(78)		130/260	(50)	
1999–2000	25/34	(71)		159/321	(50)	
2001–2002	44/61	(73)		198/329	(60)	
2003–2004	53/65	(84)		221/380	(58)	
2005–2006	188/222	(84)		691/955	(72)	
2007–2008	118/123	(94)		469/613	(77)	

Abbreviations: HBV = hepatitis B virus; HCV = hepatitis C virus.

* Confirmed cases were considered to be cases identified in the cohort study by published methods (Moorman AC, Gordon SC, Rupp LB, et al. Baseline characteristics and mortality among people in care for chronic viral hepatitis: the chronic hepatitis cohort study. Clin Infect Dis 2013;56:40–50). Cases were confirmed by a combination of written diagnoses by health-care providers, *International Classification of Diseases, Ninth Revision* coding, and laboratory data consistent with a chronic HBV and a chronic HCV diagnosis. Reported cases were considered to be the clinically confirmed cases that were successfully matched to and identified in the Michigan Diseases Surveillance System.

† One case of chronic HBV infection from the cohort was missing data on year of first diagnosis.

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Editorial Note

This initial evaluation of viral hepatitis surveillance in Michigan showed that reporting of chronic HBV and HCV infections was incomplete. However, reporting has improved over time, with more recently diagnosed cases significantly more likely to be reported and included in state surveillance data, particularly after dual reporting by laboratories and health-care providers began in 2004. Incomplete reporting and demographic disparities in reporting of chronic HCV infections should be considered when using surveillance data to estimate actual disease burden. Information on risk factors for infection, which could inform prevention efforts, were seldom reported because of the constrained resources for case follow-up of HCV infections and the absence of risk factor–related questions in HBV case forms.

Case reporting of notifiable infectious conditions is intended to describe disease burden, facilitate case management, ascertain risk factors to prevent transmission, identify and curtail outbreaks, and monitor implementation and impact of public health recommendations (*3*). Several challenges complicate chronic hepatitis surveillance efforts. The number of cases eligible for reporting is large, and data management is burdened by the reporting of numerous laboratory tests meeting the case definition per individual case (*4*). A previous comprehensive evaluation of viral hepatitis surveillance programs underscored the need for additional resources to achieve better investigation and case management of reported chronic viral hepatitis infections (*5*). Because of the challenges of case reporting, few states reported chronic HBV cases (11 through passive surveillance and eight through active surveillance) and chronic HCV cases (eight through passive surveillance and eight through active surveillance) to CDC in 2010 (*6*).

Chronic viral hepatitis cases might not be reported for several reasons. First, many cases, particularly before 2008, were reported to health departments by fax, which has made the completeness subject to the limitations of manual entry of cases by health departments. Second, older cases might have been diagnosed before mandatory reporting was implemented. Third,

What is already known on this topic?

There are many challenges to surveillance of chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infections, including the large number of cases eligible for reporting and the multiple laboratory tests required for each identified case. In 2010, the Institute of Medicine requested that CDC perform a comprehensive evaluation of the national viral hepatitis surveillance system.

What is added by this report?

In partnership with the Michigan Department of Community Health (MDCH) and an urban health-care system in southeastern Michigan, CDC evaluated the completeness of reporting of cases of chronic HBV and HCV infection among persons enrolled in a chronic hepatitis cohort study to MDCH's viral hepatitis registry. Overall, 82% of chronic HBV infection cases and 65% of chronic HCV infection cases were reported; recently diagnosed cases were more likely to be reported. Basic demographic data were included for most reported cases, but risk factor data rarely were reported.

What are the implications for public health practice?

In Michigan, reporting of chronic viral hepatitis is improving since the adoption of a dual laboratory and health-care provider-based electronic reporting system, but still remains incomplete. As a specific response to the Institute of Medicine report and action plan, this evaluation serves as a model for evaluating viral hepatitis surveillance in other states. Improving surveillance of chronic hepatitis will require electronic transfer of laboratory and clinical data and alternate sources to obtain other information, such as risk factor data, necessary for prevention and case management.

cases are often diagnosed at outside institutions and referred to the health-care system; in the transfer of care, case reports might not have been made by the diagnosing institution.

The findings in this report are subject to at least four limitations. First, the matching of actual cases with MDSS is subject to potential misclassification of clinically confirmed cases by study investigators. Second, detection of cases in MDSS is subject to the limitations of matching, and at least some cases might be missed by changes in names or changes in residence. Third, reporting at the participating health-care system's facilities might not be representative of reporting at other clinical-care or testing centers. Finally, in some cases, the year of diagnosis might be different from the year of the report, so the observed trends in reporting should be interpreted with caution.

This evaluation was possible because the state health department and hospital officials were willing to take a critical look at reporting for purposes of quality improvement. As an important response to the Institute of Medicine report and action plan (*1*), this evaluation serves as a model for similar efforts in other states and, in fact, will be replicated in other states with facilities participating in the cohort study.

The improvements in reporting of chronic HBV and HCV infections in Michigan coincide with improvements statewide in automated laboratory reporting, and a more detailed investigation of the association between the two factors is warranted. The persisting gaps in reporting highlight the need for more efficient means of transferring and interpreting reportable data. In previous studies, electronic reporting has been shown to improve the reporting of notifiable diseases, including hepatitis (*7*–*8*), and might be a method for improving the quality of reporting. For example, investigators at the U.S. Department of Veterans Affairs found that ICD-9 codes for HCV infections were highly predictive of actual HCV infection in their administrative databases (*9*).

Given the complexity of chronic hepatitis surveillance and the limited resources available, public health authorities should explore new strategies to improve reporting, such as wider adoption of electronic reporting. This report offers a roadmap for using large datasets from clinical institutions to provide state and local health departments with insight into the disease burden represented by chronic viral hepatitis case reports. The findings suggest the need for exploration of additional data sources for risk factor information, especially because data in chronic viral hepatitis case reports might not reflect the current risk for secondary transmission. Such a critical evaluation of surveillance data can help inform efforts to improve linkages to care and to prevent viral hepatitis transmission.

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CDC Grand Rounds: The Growing Threat of Multidrug-Resistant Gonorrhea

Although gonorrhea has afflicted humans for centuries, and the causative bacterium, *Neisseria gonorrhoeae*, was identified more than a century ago, gonorrhea remains a public health problem in the United States. Gonorrhea is the second most commonly reported notifiable infection in the United States; >300,000 cases were reported in 2011 (*1*). In the United States, health inequities persist; the incidence of reported gonorrhea among blacks is 17 times the rate among whites, likely because of structural socioeconomic factors (*1,2*).

Infection with *N. gonorrhoeae* is spread through sexual contact and, depending on the anatomic site of exposure, can cause acute urethritis, cervicitis, proctitis, or pharyngitis. However, most cases of gonorrhea are asymptomatic, particularly cervical, pharyngeal, and rectal infections. Untreated or inadequately treated gonorrhea can facilitate human immunodeficiency virus (HIV) transmission and cause serious reproductive complications in women, such as pelvic inflammatory disease, ectopic pregnancy, and infertility. Other severe complications, including disseminated gonococcal infection and neonatal conjunctivitis and blindness, still occur in resource-limited settings, but are now rare in the United States. Empiric antimicrobial therapy is used for treatment of gonorrhea. Antimicrobial susceptibility testing generally is not routinely available in clinical practice, and early diagnosis and effective antimicrobial treatment of patients and their partners has been the mainstay of gonorrhea control and prevention; thus, gonococcal antimicrobial resistance poses a grave challenge.

Before the 1930s, gonorrhea often was treated with patent medicines or intraurethral irrigations with compounds such as merbromin (Mercurochrome) or other antiseptics. The introduction of sulfonamide antimicrobials in the 1930s ushered in an era of effective antimicrobial therapy for gonorrhea. However, widespread gonococcal resistance to sulfonamides occurred rapidly and was common by the 1940s. Penicillin was then found to be effective for gonorrhea treatment and became the therapy of choice for several decades. During this time, however, the gonococcus acquired genetic mutations that conferred increasing penicillin resistance, necessitating increasingly higher doses of penicillin to ensure treatment success. By 1976, through further mutations, the gonococcus became able to produce beta-lactamase, an enzyme that destroys penicillin; strains that produce this enzyme are highly resistant to penicillin. During the 1980s, penicillin- and tetracycline-resistant strains became widespread in the United States, complicating gonorrhea therapy.

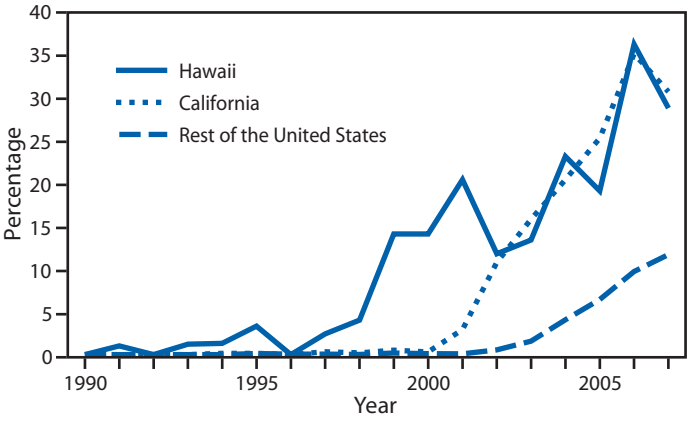
Recognizing the need for ongoing surveillance of gonococcal antimicrobial resistance, CDC developed the Gonococcal Isolate Surveillance System (GISP) in 1986. GISP is a CDC-supported sentinel surveillance system that monitors gonococcal antimicrobial susceptibility among urethral *N. gonorrhoeae* isolates collected from men attending participating sexually transmitted disease (STD) clinics.* The objectives are to provide a scientific basis for gonorrhea treatment recommendations and to allow changes in treatment recommendations before widespread treatment failures become a major public health problem.

GISP monitored emerging fluoroquinolone-resistant *N. gonorrhoeae* (QRNG) in the United States during the 1990s and 2000s. During this period, fluoroquinolones were widely used for treatment of gonorrhea because they were safe, effective, inexpensive, and available in oral forms. Gonococcal fluoroquinolone resistance, caused by the acquisition of *parC* and *gyrA* mutations that alter binding sites on enzymes DNA gyrase and topoisomerase IV, had emerged in East Asia during the 1990s and was observed sporadically in the United States by GISP. In the early 2000s, QRNG emerged in the United States, spreading initially in Hawaii and California (Figure 1). Men who have sex with men (MSM) were and remain disproportionately affected by QRNG (Figure 2). By 2007, the prevalence of QRNG was >5% among GISP isolates collected throughout the United States, prompting CDC to no longer recommend the use of fluoroquinolones for gonorrhea treatment (*3*) Spectinomycin, an alternative treatment, had not been available in the United States since 2006, so cephalosporins (such as cefixime and ceftriaxone) were the only remaining antimicrobials recommended for treatment of gonococcal infections.

This is another in a series of occasional MMWR *reports titled CDC Grand Rounds. These reports are based on grand rounds presentations at CDC on high-profile issues in public health science, practice, and policy. Information about CDC Grand Rounds is available at http://www.cdc.gov/about/grand-rounds.*

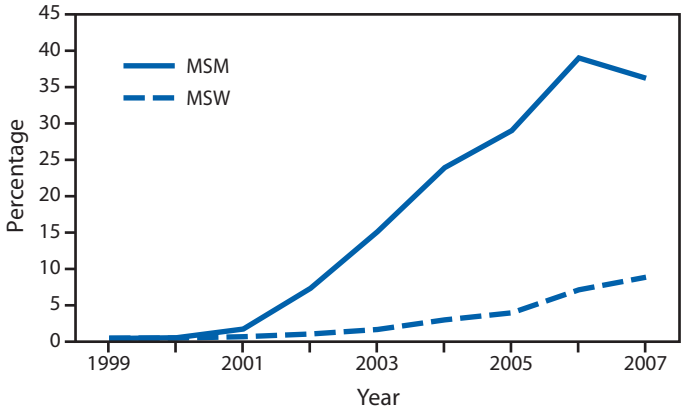
* In GISP, *N. gonorrhoeae* isolates are collected from the first 25 men with urethral gonorrhea attending STD clinics each month in approximately 28 cities in the United States. At regional laboratories, the susceptibilities of these isolates to penicillin, tetracycline, spectinomycin, ciprofloxacin, ceftriaxone, cefixime, and azithromycin are determined by agar dilution. Minimum inhibitory concentrations are measured, and values are interpreted according to criteria recommended by the Clinical and Laboratory Standards Institute. The GISP protocol, which describes the methodology, is available at http://www.cdc.gov/std/gisp/gisp-protocol07-15-2010.pdf. Additional information is available at http://www.cdc.gov/std/gisp/default.htm.

FIGURE 1. Prevalence of ciprofloxacin resistance* in urethral *Neisseria gonorrhoeae* isolates collected from men in the United States, by location — Gonococcal Isolate Surveillance Project, 1990–2007



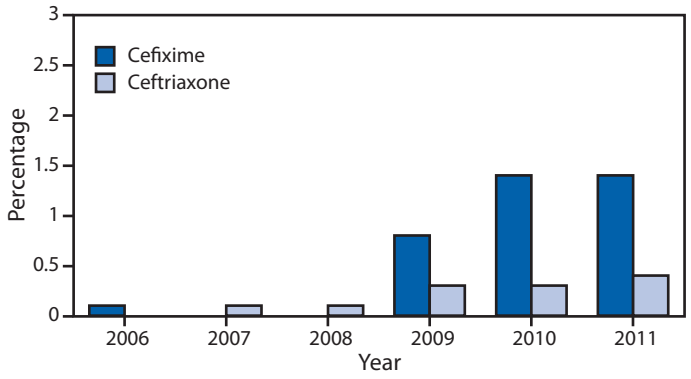
* Defined as minimum inhibitory concentrations ≥1 μg/mL.

FIGURE 2. Prevalence of ciprofloxacin resistance* in urethral *Neisseria gonorrhoeae* isolates collected from men in the United States, by gender of sex partner — Gonococcal Isolate Surveillance Project, 1999–2007



Abbreviations: MSM = men who have sex with men; MSW = men who have sex exclusively with women.
* Defined as minimum inhibitory concentrations ≥1 μg/mL.

FIGURE 3. Percentage of urethral *Neisseria gonorrhoeae* isolates with elevated cefixime minimum inhibitory concentrations (MICs) and elevated ceftriaxone MICs* — Gonococcal Isolate Surveillance Project, 2006–2011†



* Elevated cefixime MICs defined as ≥0.25 μg/mL; elevated ceftriaxone MICs defined as ≥0.125 μg/mL.
† Isolates not tested for cefixime susceptibility in 2007 and 2008.

Cephalosporins remained the foundation of gonorrhea treatment in the 2010 CDC STD treatment guidelines (*4*). These updated guidelines increased the recommended dosage of ceftriaxone to 250 mg and included broadened recommendations for combination therapy: a cephalosporin, preferably ceftriaxone 250 mg as a single intramuscular dose, should be administered with a second antimicrobial. Combination therapy treats frequently co-occurring pathogens (e.g., *Chlamydia trachomatis*) and might hinder the spread of cephalosporin antimicrobial resistance.

Unsuccessful treatment of gonorrhea with oral cephalosporins, such as cefixime, was identified in East Asia, beginning in the early 2000s, and in Europe within the past few years. Ceftriaxone-resistant isolates have been identified in Japan (2009), France (2010), and Spain (2011) (*5*–*7*). GISP now provides growing evidence that cephalosporin resistance might be emerging in the United States. Cefixime minimum inhibitory concentrations (MICs) recently increased, suggesting that the effectiveness of cefixime might be threatened. The percentage of isolates with elevated cefixime MICs (≥0.25 μg/mL) increased from 0.1% in 2006 to 1.4% in 2011 (Figure 3). The increases were most pronounced in isolates collected from men in the western United States and from MSM, the region and population in which QRNG first emerged (*8*). The acquisition of a mosaic *penA* gene encoding a remodeled penicillin binding protein (PBP2) and overproduction of an efflux pump in *N. gonorrhoeae* appears responsible, at least in part, for reduced susceptibility to cephalosporins.

The development and spread of cephalosporin resistance in *N. gonorrhoeae,* particularly ceftriaxone resistance, would greatly complicate treatment of gonorrhea. Previously recommended antimicrobials likely cannot again be routinely prescribed for empiric gonorrhea treatment. *N. gonorrhoeae* maintains previously acquired antimicrobial resistance phenotypes, even if the antimicrobial is no longer used for treatment. In 2011, 11.8% of isolates in GISP were penicillin-resistant, 22.7% were tetracycline-resistant, and 13.3% were fluoroquinolone-resistant (*1*). Unlike resistance mutations in many other bacteria, resistance mutations in *N. gonorrhoeae* might actually improve the survival of resistant strains, even in the absence of antimicrobials (*9*).

New antimicrobial treatment options are needed. However, the number of new systemic antimicrobials approved each year by the Food and Drug Administration has fallen steadily during the past 30 years (*10*). At this time, only one new

antimicrobial is undergoing clinical study (NCT01591447) as a potential treatment for gonorrhea. The National Institute for Allergy and Infectious Diseases, in collaboration with CDC, is conducting a clinical trial (NCT00926796) to study the efficacy of two combinations of existing antimicrobials. The National Institutes of Health currently supports 137 basic science research grants on gonorrhea, including translational research to identify targets for antimicrobial development. Many candidate molecules must be evaluated to find a few that are safe and effective. Antimicrobial drug development is needed now, particularly because the development process for new drugs can take more than a decade.

Challenges in detecting and responding to the emergence of multidrug-resistant gonorrhea also exist. Rapid detection of resistant infections is facilitated by local antimicrobial susceptibility testing, which at this time requires live organisms isolated by culture. However, as the use of nucleic acid amplification tests (NAATs) has expanded, the number of *N. gonorrhoeae* cultures performed by public health laboratories has decreased rapidly (*11,12*), and the capacity of U.S. laboratories to perform culture for *N. gonorrhoeae* has declined. In addition, many local and state STD programs have experienced reductions in funding and infrastructure in recent years (*13*), which might hamper the ability of these programs to detect resistant infections and ensure that patients and partners are treated effectively.

What Public Health Agencies and Partners Can Do

Several steps taken now might delay the emergence of cephalosporin-resistant strains, mitigate the public health consequences of expanded resistance, and prevent a return to the era of untreatable gonorrhea. Local and state STD control programs are encouraged to use local surveillance data to prioritize high-prevalence areas and populations for enhanced primary prevention, screening, or partner services. Clinicians can help prevent sequelae and spread of gonorrhea by eliciting sexual histories from their patients, screening sexually active MSM and high-risk sexually active women for gonorrhea at least annually at exposed anatomic sites, and treating appropriately (*4*). Clinicians also can counsel sexually active adults, particularly those living in high prevalence areas, to engage in mutually monogamous partnerships with uninfected partners and to consistently and correctly use latex condoms, which can reduce transmission.

Ensuring effective treatment is critical. Based on surveillance trends, CDC recently updated its treatment recommendations: gonorrhea at any anatomic site should be treated with a single 250 mg intramuscular dose of ceftriaxone plus either 1 g of azithromycin as a single oral dose or 100 mg of doxycycline orally twice daily for 7 days (*8*). If this recommended regimen cannot be used, two alternative treatment options exist for urogenital or rectal gonorrhea: 1) if ceftriaxone is not available, clinicians can consider cefixime 400 mg as a single oral dose and either azithromycin 1 g as a single oral dose or doxycycline 100 mg orally twice daily for 7 days, or 2) if the patient is cephalosporin-allergic, clinicians can consider azithromycin 2 g as a single oral dose. If either of these two alternative regimens is prescribed, the patient should return in 1 week for a test of cure. CDC will continue to update treatment recommendations based on surveillance data and clinical research.

In the United States, GISP is the foundation of gonococcal antimicrobial susceptibility surveillance and has successfully identified important shifts in antimicrobial susceptibility. GISP's effectiveness can be complemented through enhanced surveillance by local and state health departments. Clinicians can strengthen surveillance by maintaining vigilance for treatment failures, collecting isolates for susceptibility testing from such patients, and promptly notifying the local public health STD program. Local public health laboratories can contribute by maintaining or rebuilding capacity to perform culture for *N. gonorrhoeae* or partnering with laboratories that can. Laboratories that conduct gonococcal antimicrobial susceptibility testing are requested to promptly notify the ordering clinician and local STD control program of isolates with elevated cephalosporin MICs (cefixime MIC ≥0.25 μg/mL or ceftriaxone MIC ≥0.125 μg/mL). Local and state health departments are encouraged to promptly notify CDC of suspected treatment failures or isolates with elevated cephalosporin MICs.

Local and state STD control programs are encouraged to develop local response plans. When a suspected cephalosporin-resistant infection is detected, local public health authorities should interview the patient and ensure adequate treatment and ensure that all recent partners are evaluated and treated appropriately. Working case definitions and more detailed guidance can be found in CDC's recently released cephalosporin-resistant *N. gonorrhoeae* public health response plan (*14*).

Within several years, molecular assays for detecting genetic mutations associated with resistance might be available and could enhance surveillance and clinical management. However, molecular assays will not supplant culture-based antimicrobial susceptibility testing for surveillance, which still will be needed to detect novel resistance phenotypes and genotypes. Although a gonococcal vaccine remains an elusive goal, efforts to develop a vaccine are continuing.

Based on past and current data, *N. gonorrhoeae* will continue to acquire antimicrobial resistance. However, experience and current data suggest that public health actions outlined in this report provide the best chance of averting the unfavorable outcome of multidrug-resistant gonorrhea, greater disease burden, heightened risk for sequelae, and greater health-care costs.

Reported by

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Notes from the Field

Salmonella Bredeney Infections Linked to a Brand of Peanut Butter — United States, 2012

In 2012, CDC collaborated with state health and agricultural agencies and the Food and Drug Administration (FDA) to investigate an outbreak of *Salmonella* Bredeney infections associated with exposure to peanut products manufactured by Sunland, Inc. of Portales, New Mexico (*1*).

On August 23, 2012, CDC PulseNet, a molecular subtyping network for foodborne disease surveillance, reported a cluster of 14 *Salmonella* Bredeney infections with an indistinguishable pulsed-field gel electrophoresis (PFGE) pattern. This PFGE pattern is rare, with five to eight reports uploaded to PulseNet annually (*1*). *Salmonella* Bredeney is a rare serotype, with only one documented outbreak in the United States before 2012.

During June 11–November 8, 2012, a total of 41 cases of *Salmonella* Bredeney infections were identified in 20 states. The median age of patients was 6 years (range: <1–79 years); 63% of patients were aged <10 years, and 60% were male. Among 36 patients for whom information was available, 10 (28%) were reported to have been hospitalized. No deaths have been reported.

Of the 32 patients for whom information was available, 25 (78%) had eaten a Trader Joe's brand Valencia peanut butter product manufactured by Sunland, Inc. Testing conducted by the New Jersey Department of Health, Virginia Division of Consolidated Laboratory Services, and Washington State Department of Agriculture laboratories isolated the outbreak strain of *Salmonella* Bredeney from three opened jars of Trader Joe's Creamy Salted Valencia Peanut Butter collected from three different patients' homes.

During September 17–October 16, 2012, FDA conducted an inspection of Sunland, Inc. manufacturing facilities (*2*). Environmental samples and samples from unopened peanut butter jars collected by FDA from the nut butter production facility yielded the outbreak strain of *Salmonella* Bredeney.

On September 24, 2012, Sunland, Inc. announced a voluntary recall of almond butter and peanut butter products manufactured in the Sunland, Inc. nut butter production facility during May 1–September 24, 2012. On October 4, 2012, Sunland, Inc. expanded its recall to include all products made in its nut butter production facility during March 1, 2010–September 24, 2012. On October 12, 2012, Sunland, Inc. extended the voluntary recall to include raw and roasted shelled and in-shell peanuts processed in its peanut processing plant (*2*). Approximately 300 products have been recalled (*3*).

CDC recommends that consumers not eat recalled Sunland, Inc. products or foods containing recalled products and discard or return any remaining recalled products.

Reported by

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Notes from the Field

Hospital Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* Producing New Delhi Metallo-Beta-Lactamase — Denver, Colorado, 2012

On August 16, 2012, the Colorado Department of Public Health and Environment was notified of two patients at an acute-care hospital in Denver with carbapenem-resistant Enterobacteriaceae (CRE), specifically *Klebsiella pneumoniae* (CRKP), isolated from respiratory specimens during July–August. Both isolates produced New Delhi metallo-beta-lactamase (NDM). A review of microbiology records identified a third patient with NDM-producing CRKP isolated from a respiratory specimen, admitted in May. Active surveillance cultures in September identified an additional five patients colonized with NDM-producing CRKP. An investigation was launched by the hospital and the Colorado Department of Public Health and Environment to guide infection control measures and limit transmission.

A case was defined as NDM-producing CRE isolated from clinical or active surveillance cultures collected from a patient while hospitalized during January 1–October 30, 2012. Medical records were reviewed for clinical and epidemiologic characteristics. Relatedness of isolates was evaluated by pulsed-field gel electrophoresis (PFGE).

The eight patients were aged 23–75 years and had been hospitalized at one or more of 11 different units in the hospital for a median of 18 days (range: 12–83 days) before CRKP identification. Three were treated for CRKP infection, and five were found to be asymptomatically colonized; none died. Initial isolates were resistant to all antimicrobials except tigecycline, to which all were susceptible. Colistin minimum inhibitory concentrations for six isolates were low (≤2 μg/mL), suggesting this agent might be a treatment option. All isolates were highly related by PFGE. Epidemiologic tracing to determine temporal overlap of patients on units in the hospital indicated multiple transmission events had occurred, and three units were likely transmission sites. Acquisition of NDM-producing CRE by some patients was not explained by direct overlap and suggested that undetected, asymptomatically colonized patients were involved in some transmission routes. How NDM-producing CRE was introduced to the facility is unclear.

NDM, a carbapenemase enzyme first described in 2009 in a patient who had received medical care in India (*1*), has since been detected and reported worldwide (*2*). In the United States, before this outbreak, only 16 isolates in clusters with two or fewer cases had been identified since 2009; 14 isolates were from patients who had received medical care in endemic (South Asian) regions. The cases described here represent the largest U.S. outbreak of NDM-producing CRE to date, highlighting the risk for spread of these organisms among persons receiving medical care inside the United States. Evidence that undetected, asymptomatically colonized patients likely contributed to the size of the outbreak highlights the importance of timely active surveillance cultures when CRE is identified to direct infection control measures and limit further transmission (*3*).

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References

1. Yong D, Toleman MA, Giske CG, et al. Characterization of a new metallo-beta-lactamase gene, *bla*$_{\text{NDM-1}}$, and a novel erythromycin esterase gene carried on a unique genetic structure in *Klebsiella pneumoniae* sequence type 14 from India. Antimicrob Agents Chemother 2009;53:5046–54.
2. Wilson ME, Chen LH. NDM-1 and the role of travel in its dissemination. Curr Infect Dis Rep 2012;14:213–26.
3. CDC. 2012 CRE toolkit: guidance for control of carbapenem-resistant Enterobacteriaceae (CRE). Atlanta, GA: US Department of Health and Human Services, CDC; 2012. Available at http://www.cdc.gov/hai/organisms/cre/cre-toolkit.

Announcements

American Heart Month — February 2013

February is American Heart Month. Heart disease is a major public health problem in the United States. Every year, approximately 715,000 persons in the United States have a heart attack, and approximately 600,000 die from heart disease. Heart disease is the leading cause of death for U.S. men and women, accounting for one out of every four deaths each year (*1*).

Cardiovascular disease, including heart disease and stroke, costs the United States $312.6 billion each year (*1*). This total includes the cost of health-care services, medications, and lost productivity. Cardiovascular diseases also are leading causes of disability, preventing affected persons from working and enjoying family activities.

In observance of American Heart Month, CDC will offer four heart-healthy tips per week. This social media and web-based campaign is a way to actively engage persons in heart-healthy activities. Each tip falls into one of four categories: 1) reducing sodium consumption, 2) getting active, 3) quitting smoking, and 4) controlling blood pressure. All the tips will be listed together online at http://www.cdc.gov/salt/healthy_heart_tips.htm and will be accessible all year long.

Reference

1. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. Circulation 2013;127:e6–245.

International Course in Applied Epidemiology

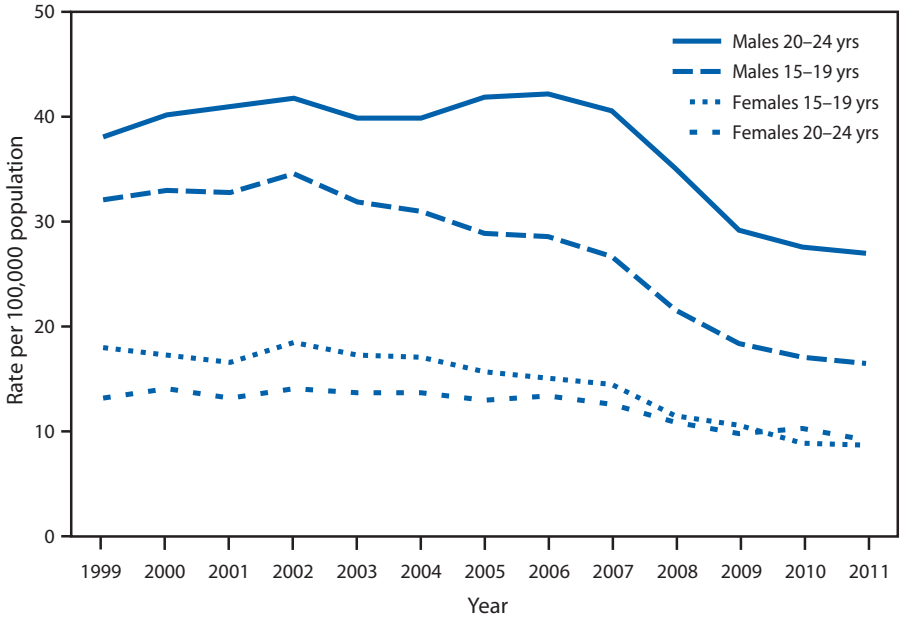
CDC and the Rollins School of Public Health at Emory University will cosponsor the course, International Course in Applied Epidemiology, from September 23 to October 18, 2013, in Atlanta, Georgia. This basic course in applied epidemiology is directed at public health professionals who work abroad and public health professionals from countries other than the United States. Its content includes presentations and discussions of epidemiologic principles, basic statistical analysis, public health surveillance, field investigations, surveys and sampling, and discussions of the epidemiologic aspects of current major public health problems in global health. Included are small group discussions of epidemiologic case exercises based on field investigations. Participants are encouraged to give a short presentation reviewing some epidemiologic data from their own country.

Computer training using Epi Info 7, a software program developed at CDC for epidemiologists, is included. Prerequisites for the course are familiarity with the vocabulary and principles of basic epidemiology, or completion of CDC's Principles of Applied Epidemiology home study course, or equivalent. Preference will be given to applicants whose work involves priority public health problems in global health. Registration deadline is June 1 or until filled. Tuition is charged. Additional information and applications are available online (http://www.sph.emory.edu/epicourses); by e-mail (pvaleri@emory.edu); by mail (Emory University, Hubert Department of Global Health, 1518 Clifton Rd. NE, CNR Bldg., Rm. 7038, Atlanta, GA 30322); by telephone (404-727-3485); or by fax (404-727-4590).

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Motor Vehicle Traffic Death Rates*† Among Persons Aged 15–24 Years, by Sex and Age Group — United States, 1999–2011§



* Motor vehicle traffic deaths as underlying cause of death are coded to V02–V04 (.1, .9), V09.2, V12–V14 (.3–.9), V19 (.4–.6), V20–V28 (.3–.9), V29–V79 (.4–.9),V80 (.3–.5), V81.1, V82.1, V83–V86 (.0–.3), V87 (.0–.8), and V89.2, according to the *International Classification of Diseases, 10th Revision*.

† Per 100,000 population. The populations used for computing death rates were enumerated as of April 1 for 2000 and 2010, postcensal estimates as of July 1 for 2011, and intercensal estimates as of July 1 for all other years.

§ Data for 2011 are preliminary.

From 1999 to 2011, motor vehicle traffic death rates declined by 49% for males aged 15–19 years, 52% for females aged 15–19 years, 29% for males aged 20–24 years, and 30% for females aged 20–24 years. During 1999–2011, the highest rates occurred among males aged 20–24 years, followed by males aged 15–19 years, females aged 15–19 years, and females aged 20–24 years. However, in 2010, the rate for females aged 20–24 years surpassed the rate for females aged 15–19 years.

Source: National Vital Statistics System. Mortality public use data files, 1999–2010. Available at http://www.cdc.gov/nchs/data_access/vitalstatsonline.htm. Unpublished mortality data, 2011.

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