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Enterovirus D68–Associated Acute Respiratory Illness — New Vaccine Surveillance Network, United States, July–October, 2017 and 2018

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In the fall of 2014, an outbreak of enterovirus D68 (EV-D68)–associated acute respiratory illness (ARI) occurred in the United States (*1*,*2*); before 2014, EV-D68 was rarely reported to CDC (*2*,*3*). In the United States, reported EV-D68 detections typically peak during late summer and early fall (*3*). EV-D68 epidemiology is not fully understood because testing in clinical settings seldom has been available and detections are not notifiable to CDC. To better understand EV-D68 epidemiology, CDC recently established active, prospective EV-D68 surveillance among pediatric patients at seven U.S. medical centers through the New Vaccine Surveillance Network (NVSN) (*4*). This report details a preliminary characterization of EV-D68 testing and detections among emergency department (ED) and hospitalized patients with ARI at all NVSN sites during July 1–October 31, 2017, and the same period in 2018. Among patients with ARI who were tested, EV-D68 was detected in two patients (0.8%) in 2017 and 358 (13.9%) in 2018. Continued active, prospective surveillance of EV-D68–associated ARI is needed to better understand EV-D68 epidemiology in the United States.

NVSN conducts active, prospective, population-based surveillance for ARI* among children and teens aged <18 years at seven U.S. medical centers at Cincinnati, Ohio; Houston, Texas; Kansas City, Missouri; Nashville, Tennessee; Pittsburgh, Pennsylvania; Rochester, New York; and Seattle, Washington (*4*). Respiratory specimens (mid-turbinate nasal, oropharyngeal swabs, or both) from patients with ARI were tested at each site for EV-D68 using a validated real-time reverse transcription–polymerase chain reaction assay. Two NVSN sites (Nashville and Pittsburgh) tested all ARI specimens for EV-D68 directly. Five sites (Cincinnati, Houston, Kansas City, Rochester, and Seattle) used a two-step algorithm, wherein all ARI specimens were first tested for enterovirus/rhinovirus (EV/RV) using molecular diagnostic assays approved by the Food and Drug Administration or CDC; all EV-positive or RV-positive specimens were subsequently tested for EV-D68. Demographic and admission status information were collected from medical charts. EV-D68 detections were analyzed by year, month, site, admission status, and patient sex and age.

* A child (aged <18 years) was eligible for inclusion in NVSN ARI surveillance if he or she visited the emergency department or were admitted to the hospital in the 48 hours preceding enrollment, with one or more of the following symptoms/events: fever; cough; earache; nasal congestion; runny nose; sore throat; vomiting after coughing; wheezing; shortness of breath/rapid or shallow breathing; apnea; apparent life-threatening event or brief resolved unexplained event; or myalgias and the duration of illness at the time of enrollment was <14 days. Children with a known nonrespiratory cause for hospitalization/ED visit were excluded from enrollment, as were children residing outside the surveillance area.

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Based on preliminary data, test results were positive for EV-D68 for two (0.08%) of 2,433 patients with ARI who were tested during 2017 and 358 (13.9%) of 2,579 tested during 2018. In 2017, one patient whose test result was positive for EV-D68 was hospitalized in Houston, and one was evaluated in the ED in Rochester. In 2018, patients with EV-D68-positive test results were identified at all seven sites, and 242 of 358 patients (67.6%) were hospitalized (range by site = 53.3%–76.8%) (Table). EV-D68 was detected in 9.2% of patients with ED visits for ARI and 18.3% of hospitalized patients with ARI. Approximately half (169; 47.2%) of the 2018 EV-D68 detections occurred in September (Figure). The peak of detections varied by site, with Cincinnati and Kansas City peaking in late August through September; Houston, Pittsburgh, and Rochester in mid-September; and Nashville and Seattle in October. The median age of patients testing positive for EV-D68 was 3 years (range = 1 month–17 years; interquartile range = 1.5–5 years), and 211 (58.9%) were male. Among 42 EV-D68–positive specimens from 2018 sequenced at CDC, all were lineage B3.

Summary

What is already known about this topic?

A nationwide outbreak of enterovirus D68 (EV-D68), which is associated with acute respiratory illness (ARI), occurred in 2014. EV-D68 epidemiology is not fully understood because testing in clinical settings is limited and reporting to CDC is voluntary.

What is added by this report?

Based on active, prospective surveillance of ARI through the New Vaccine Surveillance Network, EV-D68 was detected in two (0.8%) patients in 2017 and 358 (13.9%) in 2018. Detections in 2018 peaked in September.

What are the implications for public health practice?

Continued active, prospective surveillance is needed to better understand trends in EV-D68 circulation.

Discussion

During 2018, ARI surveillance through NVSN detected EV-D68 at levels substantially higher than those during the same period in 2017. European countries also reported EV-D68 activity in 2018 (*5*,*6*). Although EV-D68 infection more commonly causes respiratory illness, previous investigations have suggested that EV-D68 might also be associated with acute flaccid myelitis (AFM), a rare neurologic condition characterized by acute flaccid limb weakness (*7*,*8*). Contemporaneous with the 2014 outbreak of EV-D68 associated with respiratory illness, CDC received increased reports of AFM, supporting a temporal association between EV-D68 and AFM (*7*). Since 2015, CDC has conducted surveillance for AFM in the United States using a standardized case definition (*9*). As of March 1, 2019, CDC has confirmed 223 AFM cases in 2018, with peak onset of limb weakness in September 2018; in 2017, CDC confirmed 35 cases (*8*,*10*). Although AFM is rare in the United States, these AFM surveillance data, along with the EV-D68 activity documented

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TABLE. Number of patients with acute respiratory illness (ARI) who were tested and received results positive for EV-D68, by admission status and network surveillance site — New Vaccine Surveillance Network (NVSN), United States, July 1–October 31, 2018

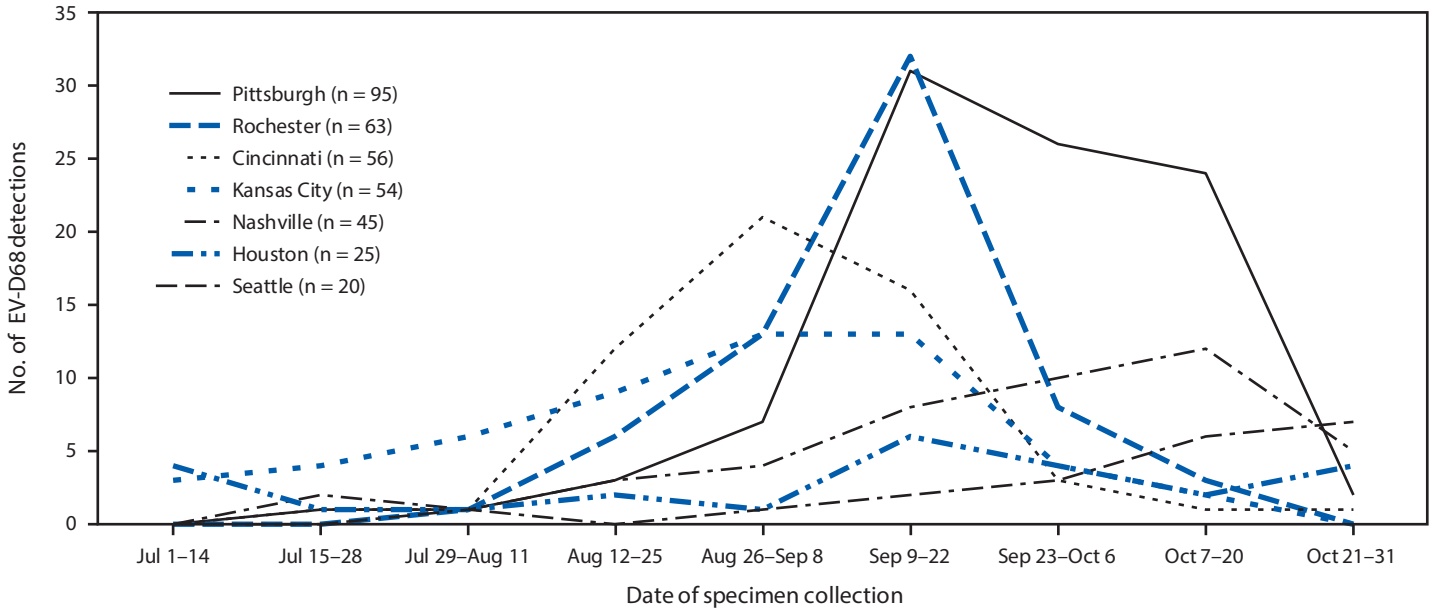
Admission status/NVSN site	No. of ARI patients tested	No. (%) of EV/RV-positive patients	EV-D68-positive patients		
			No. of patients	% Among EV/RV- positive patients	% Among ARI patients tested
Emergency department visit					
Cincinnati	148	40 (27.0)	13	32.5	8.8
Houston	157	58 (36.9)	9	15.5	5.7
Kansas City	306	163 (53.3)	21	12.9	6.9
Nashville	282	N/A	21	N/A	7.4
Pittsburgh	198	N/A	25	N/A	12.6
Rochester	61	34 (55.7)	18	52.9	29.5
Seattle	104	73 (70.2)	9	12.3	8.7
All sites	1,256	368 (47.4)*	116	19.0†	9.2
Inpatient					
Cincinnati	235	102 (43.4)	43	42.2	18.3
Houston	220	62 (28.2)	16	25.8	7.3
Kansas City	139	92 (66.2)	33	35.9	23.7
Nashville	202	N/A	24	N/A	11.9
Pittsburgh	269	N/A	70	N/A	26.0
Rochester	161	108 (67.1)	45	41.7	28.0
Seattle	97	58 (59.8)	11	19.0	11.3
All sites	1,323	422 (49.5)*	242	35.1†	18.3
Total	**2,579**	**790 (48.5)***	**358**	**27.6†**	**13.9**

Abbreviations: EV = enterovirus; N/A = not applicable; RV = rhinovirus.

* These percentages only include ARI patients at sites that first tested for EV/RV (Cincinnati, Houston, Kansas City, Seattle, and Rochester). For comparison, in 2017, a total of 715 of 1,714 (41.7%) ARI patients first tested positive for EV/RV.

† These percentages only include EV-D68-positive patients at sites that first tested for EV/RV (Cincinnati, Houston, Kansas City, Seattle, and Rochester. For comparison, in 2017, two of 715 (0.3%) EV/RV-positive patients tested positive for EV-D68.

FIGURE. Enterovirus-D68 (EV-D68) detections, by date of specimen collection and surveillance network site (N = 358) — New Vaccine Surveillance Network, United States, July 1–October 31, 2018



through NVSN, provide additional supporting evidence for a temporal association between EV-D68 respiratory illness and AFM. CDC, in collaboration with clinical and public health partners, continues to investigate the relationship between AFM and enteroviruses, including EV-D68.

The findings in this report are subject to at least two limitations. First, this report describes EV-D68 testing within NVSN during July–October of each year, but additional cases likely occurred outside this period in 2018. Therefore, the results might not be representative of the entire EV-D68 season.

Second, NVSN sentinel surveillance sites are geographically varied, but might not be representative of all regions of the United States.

Through recently established active, prospective, ARI surveillance in NVSN, EV-D68 was detected in 0.8% of patients tested in 2017 and 13.9% in 2018. Continued surveillance for EV-D68–associated ARI is needed to better understand the epidemiology of EV-D68 in the United States.

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Imported Toxin-Producing Cutaneous Diphtheria — Minnesota, Washington, and New Mexico, 2015–2018

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From September 2015 to March 2018, CDC confirmed four cases of cutaneous diphtheria caused by toxin-producing *Corynebacterium diphtheriae* in patients from Minnesota (two), Washington (one), and New Mexico (one). All patients had recently returned to the United States after travel to countries where diphtheria is endemic. *C. diphtheriae* infection was not clinically suspected in any of the patients; treating institutions detected the organism through matrix-assisted laser desorption/ionization–time-of-flight mass spectrometry (MALDI-TOF) testing of wound-derived coryneform isolates. MALDI-TOF is a rapid screening platform that uses mass spectrometry to identify bacterial pathogens. State public health laboratories confirmed *C. diphtheriae* through culture and sent isolates to CDC's Pertussis and Diphtheria Laboratory for biotyping, polymerase chain reaction (PCR) testing, and toxin production testing. All isolates were identified as toxin-producing *C. diphtheriae*. The recommended public health response for cutaneous diphtheria is similar to that for respiratory diphtheria and includes treating the index patient with antibiotics, identifying close contacts and observing them for development of diphtheria, providing chemoprophylaxis to close contacts, testing patients and close contacts for *C. diphtheriae* carriage in the nose and throat, and providing diphtheria toxoid–containing vaccine to incompletely immunized patients and close contacts. This report summarizes the patient clinical information and response efforts conducted by the Minnesota, Washington, and New Mexico state health departments and CDC and emphasizes that health care providers should consider cutaneous diphtheria as a diagnosis in travelers with wound infections who have returned from countries with endemic diphtheria.

Patient 1

In September 2015, a Minnesota woman aged 35 years returned from Somalia and sought medical care for a painful abdominal wound. *Staphylococcus aureus* and a coryneform isolate (identified as *C. diphtheriae* via MALDI-TOF and confirmed as toxin-producing) grew from the wound culture (Table). The patient was not tested for *C. diphtheriae* carriage. Throat and nasal swabs from four asymptomatic household contacts were obtained both before and at least 24 hours after a prophylactic course of penicillin; all cultures were negative for *C. diphtheriae*. The patient and household contacts were unimmunized but refused diphtheria toxoid–containing vaccines.

Patient 2

In September 2017, a Minnesota man aged 48 years returned from Ethiopia with an infected leg wound. The wound culture grew group A *Streptococcus, Pseudomonas*, and a coryneform isolate (identified as *C. diphtheriae* via MALDI-TOF and confirmed as toxin-producing). The patient was not tested for *C. diphtheriae* carriage, and a contact investigation was not undertaken because the patient lived alone and reported no close contacts. The patient reported that he had received a diphtheria toxoid–containing vaccine upon emigration to the United States 8 years earlier; therefore, no vaccine was administered. Because the wound had healed by the time the infecting organism was identified, no antibiotic treatment was administered.

Patient 3

In September 2017, a Washington girl aged 12 years was evaluated for possible meningitis (which was unrelated to the cutaneous diphtheria later diagnosed) after travel to the Philippines. While she was receiving medical care, infected insect bites on her lower extremities were noted; wound cultures grew a coryneform isolate (identified as *C. diphtheriae* via MALDI-TOF and confirmed as toxin-producing). The patient was not tested for *C. diphtheriae* carriage. Sixteen household and other close contacts of the patient were identified. Nasal and throat swabs from 11 asymptomatic contacts were obtained before administration of a prophylactic course of erythromycin; all cultures were negative. Swabs were not collected from five contacts who had already started antibiotic prophylaxis. The patient and 12 contacts were up-to-date for diphtheria toxoid–containing vaccine and did not require additional doses. Four unvaccinated close contacts received diphtheria toxoid–containing vaccines.

Patient 4

In February 2018, a New Mexico man aged 42 years returned from the Philippines with an exudative lower leg wound (Figure). Specimens were collected from the leg wound, and the culture grew group A *Streptococcus* and a coryneform isolate (identified as *C. diphtheriae* via MALDI-TOF and confirmed as toxin-producing). The patient was tested for *C. diphtheriae* carriage by nasal and throat swabs after antibiotics were administered,

TABLE. Epidemiologic and clinical characteristics of four cases of toxin-producing cutaneous diphtheria — Minnesota, Washington, and New Mexico, 2015–2018

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4
State of residence	Minnesota	Minnesota	Washington	New Mexico
Age (yrs)	35	48	12	42
Sex	F	M	F	M
Country of travel	Somalia	Ethiopia	Philippines	Philippines
DT-containing vaccination status	unvaccinated	unknown	UTD	unknown
Interval from onset of skin lesion to initial treatment	18 days	32 days	unknown	17 days
Wound culture findings	*Staphylococcus aureus*, corynebacteria	Group A *Streptococcus*, *Pseudomonas*, corynebacteria	Corynebacteria	Group A *Streptococcus*, corynebacteria
Corynebacterium diphtheriae method of identification	MALDI-TOF	MALDI-TOF	MALDI-TOF	MALDI-TOF
C. diphtheriae biovar*	Mitis	Mitis	Mitis	Mitis
Treatment after *C. diphtheriae* identification	penicillin V	none; wound healed by time of identification	erythromycin	penicillin
No. of close contacts identified	4	0	16	3
DT-containing vaccination status of close contacts	4/4 unvaccinated	N/A	4/16 unvaccinated; 12/16 UTD	3/3 unvaccinated

Abbreviations: DT = diphtheria toxoid; F = female; MALDI-TOF = matrix-assisted laser desorption/ionization–time-of-flight mass spectrometry; M = male; N/A = not applicable; UTD = up-to-date.
* A biovar is a strain variant distinguishable by biochemical or physiologic characteristics.

and both cultures were negative for *C. diphtheriae*. Nasal and throat swabs were collected from three asymptomatic household contacts before a prophylactic course of penicillin. All cultures were negative for *C. diphtheriae.* The patient's vaccination status was unknown, and no contacts were up to date with their vaccinations; all received diphtheria toxoid–containing vaccines.

Discussion

Diphtheria is a rare, vaccine-preventable, bacterial disease caused by toxin-producing strains of *C. diphtheriae*. Infections are primarily respiratory or cutaneous and are transmitted from person to person by respiratory droplets or direct contact with discharge from skin lesions. Respiratory disease can be life-threatening and is characterized by the development of an adherent pseudomembrane in the upper respiratory tract. Cutaneous disease is typically characterized by well-demarcated ulcers that might have a membrane; the lesions are slow-healing and might act as a reservoir from which bacteria can be transmitted to susceptible contacts, potentially resulting in cutaneous or respiratory disease (*1*,*2*). Disease severity is mediated by successful bacterial expression of diphtheria toxin, encoded by a toxin gene introduced by corynebacteriophages. Nontoxin-producing strains of *C. diphtheriae* can also cause disease; it is generally less severe, although invasive disease associated with nontoxin-producing strains has been reported (*3*). Vaccination with diphtheria toxoid–containing vaccine might not prevent cutaneous colonization or infection with *C. diphtheriae* (*4*).

Respiratory diphtheria is nationally notifiable in the United States, but cutaneous diphtheria was not notifiable during 1980–2018; thus, the incidence of cutaneous diphtheria is not well defined (*4*). For reporting purposes, before 2019, a confirmed case of diphtheria was defined by clinically compatible respiratory disease and isolation of *C. diphtheriae*; confirmation of toxin production was not required.* However, to better identify disease with public health implications, a modification to the case definition was accepted by the Council of State and Territorial Epidemiologists and was implemented in January 2019.† The modification restricts reporting to cases with toxin-producing disease, regardless of site.

Several common characteristics were observed among the patients with cutaneous diphtheria in this series, which might be useful for future case recognition. All had recently traveled to countries with endemic diphtheria; several European countries have also reported travel-related toxin-producing cutaneous diphtheria (*5*,*6*). *C. diphtheriae* was not clinically suspected in any of the patients and was only detected through laboratory testing. In three of four cases, *C. diphtheriae* was detected along with other more typical cutaneous pathogens, and similar coinfections have been described previously (*7*–*9*). To prevent delayed diagnosis and further disease transmission, it is important that health care providers be aware that diphtheria can manifest as a cutaneous infection, particularly in persons with wound infections and recent travel to countries with endemic diphtheria, even when *C. diphtheriae* is isolated with other potential pathogens.

When *C. diphtheriae* is identified through testing such as culture, PCR, or MALDI-TOF, it is critical that state and local public health laboratories submit specimens or isolates to CDC for confirmatory testing. CDC's Pertussis and Diphtheria

* https://www.cste.org/resource/resmgr/PS/09-ID-05.pdf.
† https://www.cste.org/resource/resmgr/2018_position_statements/18-ID-03.pdf.

FIGURE. *Corynebacterium diphtheriae*–infected lower leg wound — New Mexico, 2018

Photo/New Mexico Department of Health (provided by patient 4 and used with permission)

Laboratory routinely performs culture and biotyping to confirm *C. diphtheriae* and is currently the only laboratory in the United States that tests for toxin production. Based on available data from 1998 to 2017, 248 human *C. diphtheriae* isolates were tested at CDC's Pertussis and Diphtheria Laboratory, including 130 (52%) cutaneous isolates. Among 243 isolates with known toxin production status, five (2%) were toxin-producing: three were cutaneous isolates (described in this report), and two were respiratory isolates from patients who did not have clinically compatible disease. The fourth cutaneous isolate described in this report was identified in 2018 and was outside the time frame of available data. Since 1998, both the number of isolates confirmed as *C. diphtheriae* by CDC's Pertussis and Diphtheria Laboratory and the proportion of *C. diphtheriae* isolates originating from cutaneous sites have increased. During 1998–2011, an average of three isolates were confirmed as *C. diphtheriae* annually; this increased tenfold to 33 per year during 2012–2017 (CDC, unpublished data). Among the 130 cutaneous isolates, 95% were received during 2012–2017, possibly because of increased use of MALDI-TOF as a diagnostic tool. Current surveillance data might still underestimate the incidence of cutaneous diphtheria, because health care providers might not clinically suspect or test for diphtheria in patients, and because nonrespiratory diphtheria cases were not nationally notifiable during 1980–2018.

Summary

What is already known about this topic?

Cutaneous diphtheria has not been notifiable in the United States since 1980, and U.S. disease incidence data are limited.

What is added by this report?

Toxin-producing *Corynebacterium diphtheriae* was identified in cutaneous wounds from four U.S. residents after return from international travel. Public health response for toxin-producing diphtheria includes treating patients, providing chemoprophylaxis to close contacts, testing patients and close contacts for *C. diphtheriae* carriage, and providing diphtheria toxoid–containing vaccine to incompletely immunized patients and close contacts.

What are the implications for public health practice?

Cutaneous toxin-producing diphtheria should be considered in travelers with wound infections who have returned from countries with endemic disease to permit prompt public health response and prevent disease transmission.

When suspected cases of *C. diphtheriae* are identified, state health departments should be notified to ensure that appropriate diagnostic testing (including culture and testing for toxin production) is completed and to facilitate prompt public health action. If an isolate is confirmed as toxin-producing diphtheria, public health interventions should be initiated. Treating patients with a 14-day course of erythromycin or penicillin to eradicate *C. diphtheriae* will reduce symptoms of infection and prevent transmission; treatment with diphtheria antitoxin is generally not recommended, unless signs of systemic toxicity are present. Close contacts of patients should be monitored for development of respiratory or cutaneous illness for 7–10 days after their last exposure. Close contacts include all household members, persons with a history of habitual, close contact with the patient, or persons directly exposed to patient secretions. For chemoprophylaxis, close contacts should receive a 7–10 day course of erythromycin or penicillin. Before antibiotic administration, diphtheria patients and their close contacts should have nasal and throat swabs collected for culture to test for *C. diphtheriae* carriage. Clearance of the organism should be

confirmed after completion of the antibiotic course by repeat swabbing and testing. If repeat testing is still positive, another course of antibiotics should be administered. Finally, patients and close contacts who are not up-to-date with diphtheria vaccination should receive the recommended doses of diphtheria toxoid–containing vaccine (*4*).

The cases described in this report highlight the importance of recognizing cutaneous diphtheria in recent travelers to diphtheria-endemic countries with wound infections and the need for recommended diagnostic testing, including testing for toxin production, to implement a prompt public health response and prevent disease transmission.

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Candida Bloodstream Infections Among Persons Who Inject Drugs — Denver Metropolitan Area, Colorado, 2017–2018

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Candidemia, a bloodstream infection caused by *Candida* species, is typically considered a health care–associated infection, with known risk factors including the presence of a central venous catheter, receipt of total parenteral nutrition or broad-spectrum antibiotics, recent abdominal surgery, admission to an intensive care unit, and prolonged hospitalization (*1*,*2*). Injection drug use (IDU) is not a common risk factor for candidemia; however, in the context of the ongoing opioid epidemic and corresponding IDU increases, IDU has been reported as an increasingly common condition associated with candidemia (*3*) and methicillin-resistant *Staphylococcus aureus* bacteremia (*4*). Little is known about the epidemiology of candidemia among persons who inject drugs. The Colorado Department of Public Health and Environment (CDPHE) conducts population-based surveillance for candidemia in the five-county Denver metropolitan area, encompassing 2.7 million persons, through CDC's Emerging Infections Program (EIP). As part of candidemia surveillance, CDPHE collected demographic, clinical, and IDU behavior information for persons with *Candida*-positive blood cultures during May 2017–August 2018. Among 203 candidemia cases reported, 23 (11%) occurred in 22 patients with a history of IDU in the year preceding their candidemia episode. Ten (43%) of the 23 cases were considered community-onset infections, and four (17%) cases were considered community-onset infections with recent health care exposures. Seven (32%) of the 22 patients had disseminated candidiasis with end-organ dysfunctions; four (18%) died during their hospitalization. In-hospital IDU was reported among six (27%) patients, revealing that IDU can be a risk factor in the hospital setting as well as in the community. In addition to community interventions, opportunities to intervene during health care encounters to decrease IDU and unsafe injection practices might prevent infections, including candidemia, among persons who inject drugs.

Candidemia surveillance in the five-county Denver metropolitan area began in May 2017. Because candidemia is a reportable condition in the Denver metropolitan area, all surveillance area laboratories report *Candida*-positive blood cultures to CDPHE. As part of EIP surveillance, a case is defined as a blood culture positive for *Candida* spp. in a surveillance area resident; a recurrent case is defined as a new *Candida*-positive blood culture >30 days after the initial positive blood culture in the same patient. Cases were classified by patient epidemiologic exposures. Community-onset infections were defined as *Candida*-positive blood culture collected <3 days after hospital admission with no previous health care exposures (i.e., overnight hospitalizations, surgeries, long-term care, or long term acute care admissions in the previous 90 days and no central lines in place in the 2 days prior to culture collection). Health care–associated, community-onset infections were defined as a *Candida*-positive blood culture collected <3 days after hospital admission with previous health care exposures in the 90 days before the culture collection date. Hospital-onset infections were defined as blood cultures collected ≥3 days into the patient's hospitalization. Medical record reviews were performed to gather demographic and clinical information, including history of IDU, for all patients using a standardized case report form.

During the first 6 months of the surveillance program, CDPHE observed that approximately one in 10 cases of candidemia occurred in patients who had a documented history of IDU, and the majority of their *Candida*-positive blood cultures were collected on the day of hospital admission or shortly thereafter. This finding was unexpected given that candidemia typically occurs in severely ill, hospitalized patients (*1*,*2*). CDPHE and CDC conducted an epidemiologic investigation to describe candidemia among persons who inject drugs and identify potential interventions for prevention. For each case occurring in a person with documented IDU, medical records were reviewed to collect information on health care exposures, evidence of disseminated infections, coinfections, and drug use and associated practices before the *Candida*-positive cultures.

Among 203 candidemia cases reported during May 2017–August 2018, 23 (11%) were identified in 22 patients with IDU in the past year; one patient had recurrent candidemia. Among these 22 patients, the average age was 37 years (range = 21–59 years), and 14 (64%) were women (Table). Eighteen (82%) of the patients were white, and four (18%) were Hispanic or Latino. Eleven (50%) patients had experienced homelessness or lived in transitional housing before the candidemia episode. Among the 22 candidemia patients with IDU, 10 (45%) had hepatitis C infection, including one who also had chronic hepatitis B infection and one who also had human immunodeficiency virus (HIV) infection. Other comorbidities included chronic lung disease; neurologic conditions such as seizures, epilepsy, or neuropathy; diabetes; alcohol abuse; and smoking tobacco during the preceding year.

TABLE. Characteristics of 22 patients with candidemia and a history of injection drug use — Denver metropolitan area, Colorado, May 2017–August 2018

Characteristic	No. (%)
Mean age, yrs (range)	37 (21–59)
Sex	
Women	14 (64)
Men	8 (36)
Race	
White	18 (82)
Asian	1 (5)
American Indian/Alaska Native	1 (5)
Unknown	2 (9)
Ethnicity	
Not Hispanic or Latino	18 (82)
Hispanic or Latino	4 (18)
Comorbidities	
Hepatitis C, chronic	9 (41)
Hepatitis C, acute	1 (5)
Hepatitis B, chronic	1 (5)
Human immunodeficiency virus infection	1 (5)
Chronic lung disease*	4 (18)
Neurologic condition†	8 (36)
Diabetes	5 (23)
Alcohol abuse	4 (18)
Smoking tobacco	18 (82)
Experiencing homelessness/Transitional housing	11 (50)
Outcome	
Died	4 (18)
Left against medical advice	3 (14)
Survived	15 (68)
***Candida* species in incident blood culture§**	
Candida glabrata	8 (35)
Candida albicans	6 (26)
Candida parapsilosis	3 (13)
Candida dubliniensis	2 (9)
Candida lusitaniae	1 (4)
Candida lypolitica	1 (4)
Candida rugosa	1 (4)
C. albicans and Candida famata	1 (4)
Epidemiologic class§	
Community-onset¶	10 (43)
Health care–associated, community-onset**	4 (17)
Hospital-onset††	9 (39)
Hospitalization for candidemia, (median days, range)§	23 (10, 1–139)
Risk factors before *Candida*-positive blood culture§	
Admission to an intensive care unit§§	6 (26)
Recent abdominal surgery	0
Presence of a central venous catheter¶¶	11 (48)
Receipt of broad-spectrum antibiotics§§	20 (87)
Receipt of total parenteral nutrition	0

* Includes chronic pulmonary diseases such as chronic obstructive pulmonary disease, emphysema, chronic bronchitis, bronchiectasis, interstitial lung disease, and asthma.
† Includes epilepsy/seizure/seizure disorder and neuropathy.
§ Among 23 candidemia cases, which included one recurrent case.
¶ Positive blood culture <3 days after hospital admission without prior health care exposures in the previous 90 days.
** Positive blood culture collected <3 days after hospital admission with prior health care exposure in the previous 90 days.
†† Positive blood culture ≥3 days into hospital admission.
§§ 14 days before the *Candida*-positive blood culture.
¶¶ On the day of, or in the 2 calendar days before the *Candida*-positive blood culture.

Three patients left the hospital against medical advice, possibly without completing treatment for candidemia. Three additional patients had left against medical advice from at least one other medical encounter in the 6 months before their candidemia episode. Four (18%) patients died in the hospital 1–17 days after the *Candida*-positive blood culture, although whether candidemia was the direct cause of death was unknown.

Among the 23 infections in these 22 patients, the most common *Candida* species identified were *Candida glabrata*, *Candida albicans*, and *Candida parapsilosis* (Table). Ten (43%) of the 23 cases were identified as community-onset infections. Four (17%) cases were identified within 1 day of the patient's hospital admission or during a previous emergency department (ED) visit or hospitalization, after which the patient returned for treatment; these patients also had other health care exposures and were classified as health care–associated, community-onset infections. Nine (39%) cases were classified as hospital-onset infections. Among the nine patients with hospital-onset candidemia, the median interval from hospital admission to collection of the *Candida*-positive blood culture was 17 days (range = 4–107 days). Among all 23 candidemia cases, the median length of the candidemia-associated hospitalization was 10 days (range = 1–139 days).

In the 6 months before developing candidemia, the 22 patients had a mean of three previous inpatient or ED visits (range = 0–10). Including the admission for candidemia, the most common reasons for admission or ED visit were conditions related to drug use (i.e., dependence or withdrawal); nonspecific pain; mental or behavioral disorders; and infections and associated complications, including bacteremia, osteomyelitis, and sepsis.

Fifteen (68%) of the 22 patients had a blood culture yielding another organism (most commonly *Staphylococcus aureus*) either during the candidemia hospitalization or in the 6 months preceding the candidemia episode. In 10 (45%) patients, at least one other organism was identified in the same blood culture set as the one that yielded *Candida* spp. These included *Staphylococcus aureus,* coagulase negative *Staphylococcus, Stenotrophomonas maltophilia, Pseudomonas fluorescens, Serratia marcescens, Enterobacter asburiae, Comamonas acidovorans, Pantoea* spp., viridans *Streptococcus,* and *Mucorales* spp. Seven (32%) patients had disseminated candidiasis with end-organ dysfunctions, including endophthalmitis (one), septic emboli (one), osteomyelitis (three), and abscesses of the pelvis, psoas muscle, and upper mediastinum (three).

Drugs documented in the medical record or identified in urine testing in the 6 months before the candidemia episode included opioids (18 patients; 82%), methamphetamines (16; 73%), cannabinoids (seven; 32%), cocaine (six; 27%),

benzodiazepines (four; 18%), ecstasy (MDMA) (one), and barbiturates (one). Two patients (9%) experienced "cotton fever," an illness characterized by rapid fever onset immediately following the injection of drugs filtered through cotton (*5*), in the 6 months before the candidemia hospitalization; four patients (18%) were reported to have engaged in unsafe injection practices, including using old syringes, cotton, filters, and dirty needles.

Six (27%) patients were observed injecting or attempting to inject drugs, including illicit drugs and pain medications that were not prescribed to them, while hospitalized. In addition, illicit drugs and drug paraphernalia, including syringes, spoons, and lighters, were found in four of these six patients' rooms.

Discussion

Surveillance for candidemia in the Denver metropolitan area during 2017–2018 found that approximately one in 10 patients with candidemia had recent IDU. Patients with candidemia who had a history of IDU had high prevalences of IDU-associated conditions, including hepatitis C infection, homelessness, and disseminated candidiasis with end-organ dysfunction, increasing candidemia-associated morbidity; four of these patients died during their candidemia hospitalization.

Fourteen of the 22 patients in this analysis presumably became infected with *Candida* outside the hospital setting, likely related to IDU. In addition, the positive polymicrobial blood cultures in nearly half of the patients indicate that unsafe injection practices likely are prevalent, putting persons who inject drugs at risk for candidemia and other infections with bacteria, HIV, hepatitis C virus, and hepatitis B virus. Nine patients became infected in the hospital setting, likely because they either continued to inject drugs while hospitalized (six were observed injecting or attempting to inject drugs) or they had more typical health care–associated risk factors for candidemia.

The findings in this report are subject to at least two limitations. First, a relatively small number of patients with candidemia and a history of IDU were identified in the Denver metropolitan area during the study period; therefore, results of this analysis might not be generalizable to other geographic areas. Second, because IDU behaviors were identified by reviewing patient medical records, some patients with a history of IDU might have been missed if IDU practices were not documented. Similarly, information such as type of drugs used, frequency of use, and unsafe injection practices might not have been documented in the medical record.

This surveillance program identified IDU as a previously underrecognized risk factor for candidemia in Colorado. Usual candidemia prevention efforts, including antibiotic stewardship, catheter care, and antifungal prophylaxis, primarily occur in the health care setting to mitigate health care–associated risk factors. Prevention of candidemia and other infections in persons who inject drugs requires both health care and community-based interventions such as education about and resources for reducing IDU, increasing safe injection practices (e.g., cleaning the injection site, using sterile water in drug preparation, and avoiding shared injection equipment*), and initiation of medication-assisted treatment programs for persons injecting opioids.

Patients in this analysis were found to have had frequent health care encounters, including ED visits and inpatient admissions, in the 6 months preceding their candidemia episode. These health care encounters provide opportunities for targeted prevention efforts in addition to community-based interventions. Given the current opioid epidemic, it is important to monitor trends in drug use and IDU-related infections and to implement prevention interventions.

Summary

What is already known about this topic?

Candidemia is typically considered a health care–associated infection, but injection drug use (IDU) has emerged as an increasingly common condition associated with candidemia.

What is added by this report?

Among 203 candidemia cases in the Denver metropolitan area during May 2017–September 2018, 23 (11%) occurred in 22 patients who had a recent history of IDU. Many had disseminated infections with end organ dysfunction, and onset occurred both inside and outside the hospital setting. Six of the patients were observed injecting or attempting to inject drugs while hospitalized.

What are the implications for public health practice?

Opportunities to intervene during health care encounters to decrease IDU and unsafe injection practices might prevent infections, including candidemia. Preventing candidemia among persons who inject drugs requires both community-based and health care–based interventions.

* https://www.cdc.gov/hiv/risk/idu.html.

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Notes from the Field

Investigation of Colorado Tick Fever Virus Disease Cases — Oregon, 2018

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In early summer 2018, four cases of Colorado tick fever (CTF) were reported in residents of central Oregon; CTF virus infection was confirmed using CDC's reverse transcription–polymerase chain reaction (RT-PCR) assay (*1*). CTF is caused by a coltivirus that is transmitted by infected Rocky Mountain wood ticks (*Dermacentor andersoni*) (*2*). The tick is found throughout the western United States and Canada, typically at 4,000–10,000 feet (1,219–3,048 meters) above sea level in grassy areas near sage brush (*3*). CTF virus causes an acute febrile illness with nonspecific symptoms, and although fatal cases are rare, up to 30% of persons with CTF virus disease require hospitalization (*4*). Because there is no definitive treatment for CTF virus disease, clinical management is supportive. Biphasic illness pattern, leukopenia, absence of rash, and place of exposure can help distinguish CTF from other arthropod-borne infections (*2*,*5*). CTF is a reportable condition in six states, including Oregon, but is not nationally notifiable. Over the past decade, the Oregon Health Authority has reported an average of less than one case of CTF per year.

CDC and Oregon health officials conducted an investigation to describe the clinical course, exposures, and geographic distribution of patients with confirmed CTF and to identify additional cases. Information was collected through medical record review and phone interview.

Three of the four confirmed cases were in men in their 70s, and one was in a woman in her 50s. The four patients were residents of three neighboring counties, and all accessed care at the same health care system in one county. Symptom onset in all four patients was in May, and all had fever, leukopenia (white blood cell count <4.0 x $10^3/\mu$L), and thrombocytopenia (platelet count <150 x $10^3/\mu$L). Three patients reported experiencing a biphasic illness, where their initial fever and symptoms diminished and then returned again a few days later. Three patients were hospitalized (range 1–3 days), and all recovered from their illness. Although diagnostic testing for tickborne pathogens varied, all patients were tested for CTF using RT-PCR because this test is more sensitive than serology during the acute phase of infection. All patients were treated empirically with doxycycline before laboratory confirmation of CTF virus infection.

All patients reported spending ≥5 hours per day outdoors, including working in wooded or brushy areas, and all reported a tick bite in the 2 weeks preceding illness onset. Three patients reported known tick exposures in two of the counties at elevations of 3,200–4,500 feet (975–1,372 meters) above sea level; however, no geographic clustering was identified because the land area separating the three reported tick exposure locations covered approximately 540 square miles (1,399 square kilometers). All patients reported wearing long sleeves and pants during outdoor activities, but none used insect repellent.

Electronic medical records from the same health care system as that used by the patients with confirmed cases were searched using the *International Classification of Diseases, Tenth Revision* codes for fever and leukopenia to identify possible additional cases. A suspected CTF case was defined as fever and leukopenia with no alternative explanation in a patient evaluated during April 15–July 31, 2018. Patients with suspected cases or their caregivers were interviewed and offered CTF virus testing. Three suspected CTF cases were identified in two children and one adult. The adult, a male in his 60s, submitted a serum sample that was positive for CTF virus–specific neutralizing antibodies. He acquired a tick bite in the days preceding illness onset while hunting in the same county of exposure as two of the confirmed cases.

More CTF cases were identified in Oregon in 2018 than in previous years, possibly because of increased tick activity or heightened provider awareness and testing. No common locations of tick exposure were identified, indicating the pathogen was circulating in several areas of central Oregon in spring 2018. Health departments need to reinforce tick prevention measures, including use of EPA-registered insect repellents, and target messaging to persons participating in outdoor activities with high risk for tick exposure (*6*).

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Erratum

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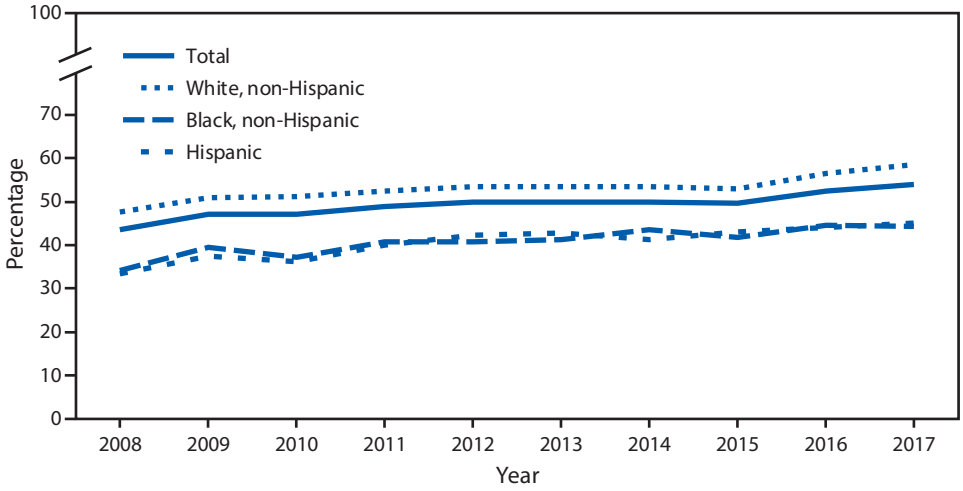
In the report "Deaths Related to Hurricane Irma — Florida, Georgia, and North Carolina, September 4–October 10, 2017," on page 829, the sixth sentence of the fifth paragraph should have read "Fourteen (10.9%) of the heat-related deaths occurred among geriatric patients with existing chronic diseases who resided in **a nursing home** in Florida that was without power for several days during a period of hot weather after the hurricane's landfall." In addition, on page 831, the second footnote of the figure should have read "[†]Fourteen of the 17 heat-related deaths occurred in residents of **a nursing home** in Florida that was without power for several days."

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Adults Who Met Federal Guidelines for Aerobic Physical Activity Through Leisure-Time Activity,* by Race/Ethnicity — National Health Interview Survey,† 2008–2017



* Based on U.S. Department of Health and Human Services 2008 Physical Activity Guidelines for Americans (https://www.health.gov/paguidelines/guidelines/default.aspx). Respondents were considered to meet aerobic activity guidelines through leisure-time activity if they reported moderate-intensity aerobic physical activity for ≥150 minutes leisure-time activity per week, vigorous-intensity aerobic physical activity for ≥75 minutes leisure-time activity per week, or an equivalent combination of moderate-intensity and vigorous-intensity leisure-time activity.

† Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population and are derived from the National Health Interview Survey Sample Adult component.

During 2008–2017, the percentage of adults aged ≥18 years who met federal guidelines for aerobic physical activity through leisure-time activity increased from 43.5% in 2008 to 54.1% in 2017. This pattern was seen in each race/ethnicity group shown, with an increase from 33.4% to 45.0% for Hispanic, 34.1% to 44.3% for non-Hispanic black, and 46.0% to 58.6% for non-Hispanic white adults. Throughout the period, non-Hispanic white adults were more likely to meet the guidelines through leisure-time activity than were non-Hispanic black and Hispanic adults.

Source: National Health Interview Survey, 2008–2017. https://www.cdc.gov/nchs/nhis/index.htm.

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