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CDC Health Advisory

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Alert to U.S. Healthcare Facilities: First mcr-1 Gene in E. coli Bacteria found in a Human in the United States

Summary

The Centers for Disease Control and Prevention (CDC) is collaborating in a coordinated public health response to the Department of Defense (DoD) announcement on May 26 of the first mcr-1 gene found in bacteria from a human in the United States (http://aac.asm.org/content/early/2016/05/25/AAC.01103-16.full.pdf+html). Escherichia coli (E. coli) bacteria carrying the mcr-1 gene were found in a urine sample from a person in Pennsylvania with no recent travel outside of the United States who presented to a clinic with a urinary tract infection. The mcr-1 gene makes bacteria resistant to the antibiotic colistin, which is used as a last-resort drug to treat patients with infections caused by multidrug-resistant bacteria, including carbapenem-resistant Enterobacteriaceae (CRE). The mcr-1 gene exists on a plasmid, a small piece of DNA that is capable of moving from one bacterium to another, potentially spreading antibiotic resistance to other bacterial species. CDC is issuing this HAN notice as a reminder to U.S. healthcare facilities about recommendations to prevent antibiotic resistant infections and alert them to additional recommendations for detecting and reporting bacteria with the mcr-1 gene.

Background

In November 2015, a report from China first described plasmid-mediated colistin-resistance caused by the mcr-1 gene. Following that report, retrospective investigations of historical isolates from outside the United States have identified the rare occurrence of mcr-1 in Enterobacteriaceae from the 1980s. Bacteria with this resistance mechanism have now been identified from humans, food, environmental samples, and food animals in at least 20 countries around the world. Most reports to date have identified the mcr-1 gene in E. coli, but it has also been reported from Salmonella species, Shigella sonnei, and Klebsiella pneumoniae.

Three mcr-1 producing E. coli have been identified in the United States as of June 7, 2016: one in a clinical specimen from a person in Pennsylvania and two from intestinal samples from pigs. The E. coli isolate from the patient was also resistant to antibiotics in at least five additional antibiotic classes, including cephalosporins, fluoroquinolones, sulfonamides, aminoglycosides, and tetracyclines. The sample from one pig also was resistant to other antibiotics, including ampicillin, streptomycin, sulfisoxazole, and tetracycline. No additional resistance was found in the isolate from the second pig. The presence of the mcr-1 gene on a plasmid means that

colistin resistance can be shared with other more resistant bacteria such as CRE, raising the possibility that untreatable bacteria could develop. A rapid public health response is underway to identify and contain any potential spread from the patient. CDC laboratories have developed protocols for testing microorganisms for the mcr-1 gene and are performing screening tests to see if people in contact with the patient with mcr-1 might be colonized with this organism. CDC is increasing its surveillance of human samples from U.S. healthcare settings. CDC's National Antimicrobial Resistance Monitoring System, in collaboration with the Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA), will continue to look for mcr-1 mediated colistin resistance in enteric bacteria from humans, retail meat, and food animals.

Recommendations

Given the discovery of mcr-1 in a person in Pennsylvania, CDC reiterates the importance of measures to prevent transmission of antibiotic resistant bacteria, including those resistant to colistin or carrying the mcr-1 gene. CDC recommends the following:

- **Infection Prevention:** Healthcare providers should follow Standard and Contact Precautions (http://www.cdc.gov/hicpac/2007IP/2007ip_part3.html) for any patients colonized or infected with antibiotic resistant bacteria, including patients who are found to have mcr-1 mediated resistant organisms. Healthcare facilities should follow manufacturers' instructions for device cleaning and reprocessing.
- **Laboratory Testing:** If laboratories are testing to determine whether colistin can be used clinically, Enterobacteriaceae isolates with a minimum inhibitory concentration (MIC) to colistin of 4 µg/ml or higher should be tested for confirmation and the presence of mcr-1. Thus far, all microorganisms that have contained the mcr-1 gene can safely be tested in a biosafety level-2 (BSL-2) laboratory. Isolates should be sent to CDC for confirmatory testing via the state or local public health department, per the CDC test directory (http://www.cdc.gov/laboratory/specimen-submission/list.html), if local testing is not available. The results and test method that were used for initial colistin testing should be included with any isolates submitted for confirmatory testing. CDC laboratories are in the process of validating a rapid polymerase chain reaction (PCR) test to detect mcr-1 in bacteria with elevated colistin MICs. It is not necessary to test Enterobacteriaceae with intrinsic colisitin resistance (e.g., Proteus, Providencia, Morganella, and Serratia species). Additionally, since Enterobacter species often have MICs of >=2 mcg/ml to colisitin, they should be sent for mcr-1 testing only if other risk factors exist, such as a recent history of travel outside the United States to a country where mcr-1 has been found to be more common (http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21403).
- **Validation of Laboratory Testing:** CDC is making test-bacteria with elevated colistin MICs, available to laboratories, researchers, and others through the FDA-CDC Antimicrobial Resistance Bacteria Isolate Bank (http://www.cdc.gov/drugresistance/resistance-bank/) for use in validation of colistin-resistance testing in U.S. clinical laboratories.

- **Environmental Cleaning:** Healthcare facilities should ensure rooms where patients with antibiotic-resistant infections have been placed receive thorough daily and terminal cleaning.
- **Reporting to Public Health:** Healthcare facilities and laboratories should adhere to local reporting requirements for all antibiotic resistant infections. If Enterobacteriaceae with mcr-1 are identified from patients, healthcare facilities and laboratories should notify local or state public health authorities as quickly as possible, and inform clinicians caring for the patient and responsible infection prevention staff.
- **Preparing food safely:** Cook all meat, poultry, and fish to its proper internal temperature to kill bacteria (http://www.foodsafety.gov/keep/charts/mintemp.html), viruses, and other foodborne pathogens, regardless of antibiotic resistance.

Resources for Additional Information

1. CDC Facility Guidance for Control of CRE: November 2015 Update: http://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf
2. Responding to new Forms of Antibiotic Resistance: http://www.cdc.gov/hai/pdfs/toolkits/Responding-to-New-Forms-of-Antibiotic-Resistance.pdf
3. Biosafety in Microbiological and Biomedical Laboratories, 5th Edition: http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf
4. CDC Vital Signs Report: Making Health Care Safer, Protect Patients from Antibiotic Resistance: http://www.cdc.gov/vitalsigns/protect-patients/index.html

DHEC contact information for reportable diseases and reporting requirements

Reporting of ***mcr-1* Gene in *E. coli*** is consistent with South Carolina Law requiring the reporting of diseases and conditions to your state or local public health department. (State Law # 44-29-10 and Regulation # 61-20) as per the DHEC 2016 List of Reportable Conditions available at: http://www.scdhec.gov/Library/CR-009025.pdf

Federal HIPAA legislation allows disclosure of protected health information, without consent of the individual, to public health authorities to collect and receive such information for the purpose of preventing or controlling disease. (HIPAA 45 CFR §164.512).

Regional Public Health Offices – 2016

Mail or call reports to the Epidemiology Office in each Public Health Region

MAIL TO:

Lowcountry	**Midlands**	**Pee Dee**	**Upstate**
4050 Bridge View Drive, Suite 600 N. Charleston, SC 29405 Fax: (843) 953-0051	2000 Hampton Street Columbia, SC 29204 Fax: (803) 576-2993	145 E. Cheves Street Florence, SC 29506 Fax: (843) 661-4859	200 University Ridge Greenville, SC 29602 Fax: (864) 282-4373

CALL TO:

Lowcountry	**Midlands**	**Pee Dee**	**Upstate**
Berkeley, Charleston, Dorchester Phone: (843) 953-0043 Nights/Weekends: (843) 441-1091	**Kershaw, Lexington, Newberry, Richland** Phone: (803) 576-2749 Nights/Weekends: (888) 801-1046	**Chesterfield, Darlington, Dillon, Florence, Marlboro, Marion** Phone: (843) 661-4830 Nights/Weekends: (843) 915-8845	**Anderson, Oconee** Phone: (864) 260-5801 Nights/Weekends: (866) 298-4442
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For information on reportable conditions, see http://www.scdhec.gov/Health/FHPF/ReportDiseasesAdverse Events/ReportableConditionsInSC/

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Categories of Health Alert messages:

Health Alert	Conveys the highest level of importance; warrants immediate action or attention.
Health Advisory	Provides important information for a specific incident or situation; may not require immediate action.
Health Update	Provides updated information regarding an incident or situation; unlikely to require immediate action.
Info Service	Provides general information that is not necessarily considered to be of an emergent nature.