Resource Packet

Provided by:

Illinois Department of Public Health

Division of Patient Safety and Quality

Healthcare-Associated Infection Prevention Program

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www.xdro.org

IDPH
ILLINOIS DEPARTMENT OF PUBLIC HEALTH

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November 2014

Dear Colleague,

The Illinois Department of Public Health (IDPH) launched the statewide Carbapenem-Resistant Enterobacteriaceae (CRE) Detect and Protect Campaign in March 2014 to provide education on CRE prevention and mandatory reporting to the Extensively Drug-Resistant Organism (XDRO) registry for healthcare facilities, laboratories, and local health departments. To assist Detect and Protect efforts, IDPH is providing this CRE resource packet to healthcare facilities. The information in this packet was gathered from national and state sources, with input from experts on the Illinois CRE Task Force. We hope that this will be a useful reference as you continue to protect patients through appropriate infection prevention practices, educate staff and patients on CRE, and report to the XDRO registry.

IDPH Division of Patient Safety and Quality has a central role in healthcare-associated infection prevention in Illinois. As a state agency, we are responsible for the protection of patients across healthcare systems and are uniquely situated to serve as a bridge between healthcare systems and the community. We thank you for partnering with IDPH in this important initiative and hope to continue working with you as we move toward a regional approach to improve CRE control.

Sincerely,

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Illinois CRE Detect and Protect Campaign

The Illinois Department of Public Health (IDPH) is leading a statewide education campaign to promote practices that prevent carbapenem-resistant Enterobacteriaceae (CRE).

- CRE are extensively drug-resistant organisms (XDROs) that can spread quickly and have been increasingly detected among patients in Illinois.
- IDPH is working with healthcare facilities, laboratories, and local health departments to adopt the Centers for Disease Control and Prevention strategy of detecting CRE and protecting patients through appropriate infection control and prevention measures.
- A statewide CRE Task Force is helping to guide efforts. This multidisciplinary group of over 30 infectious disease, infection prevention, and laboratory experts is developing recommendations to track and control the spread of these deadly superbugs.

During the campaign, IDPH Division of Patient Safety and Quality has provided educational materials and a webinar series on CRE prevention and mandatory reporting of CRE to the XDRO registry. Six archived webinars and presentation slides are available at http://www.idph.state.il.us/patientsafety/cre/webinars.htm:

Webinar Title	Topic(s)
Long-Term Care Infection Prevention Starts at the Top	• Building patient safety and quality improvement initiatives in long-term care
CRE & XDRO for Long-Term Care Facilities	• CRE prevention practices for long-term care • Interpreting lab reports • Using the XDRO registry
Patient Safety and Quality Starts at the Top	• Prioritization of infection prevention and patient outcomes through structure, focus, and measurement for hospitals
CRE & XDRO: What Hospital IC/Ps Need to Know	• CRE prevention practices for hospitals • Interpreting lab reports • Using the XDRO registry
CRE Detect and Protect: the Role of Local Health Departments	• Outbreak response • Surveillance and reporting
Laboratory Detection and Reporting of CRE	• Laboratory detection methods • Reporting to the XDRO registry

For more information, visit: http://www.idph.state.il.us/patientsafety/cre/index.htm

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Illinois Department of Public Health

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The Extensively Drug Resistant Organism (XDRO) Registry

The Illinois Department of Public Health (IDPH) has guided development of an infection control tool called the XDRO registry. The purpose of the XDRO registry is two-fold:

1. **Improve inter-facility communication:** The registry provides efficient information exchange across the spectrum of healthcare about patients who have tested positive for carbapenem-resistant Enterobacteriaceae (CRE).
2. **Improve CRE surveillance:** The registry stores CRE surveillance data and has features that can help facilities track their CRE submission history.

Reporting Requirements

- IDPH amended the Control of Communicable Diseases Code (77 Ill. Adm. Code 690) to require reporting of CRE to IDPH.
- As of November 1, 2013, the **first CRE-positive culture per patient stay** must be reported to the XDRO registry **within 7 calendar days** after the test result is finalized.
- All hospitals, hospital-affiliated clinical laboratories, independent or free-standing laboratories, longer-term care facilities, and long-term acute care hospitals in Illinois are required to report CRE isolates that meet surveillance criteria.

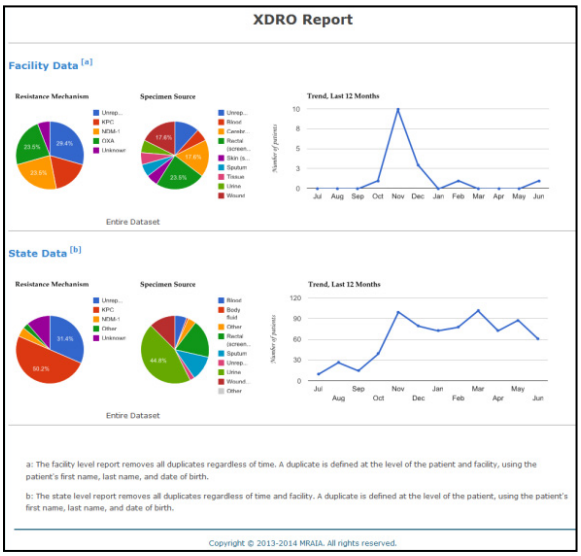
CRE surveillance criteria

Enterobacteriaceae (e.g., *E. coli, Klebsiella* spp*, Enterobacter* spp*, Proteus* spp*, Citrobacter* spp*, Serratia* spp*, Morganella* spp*, or Providentia* spp) with one of the following laboratory test results:

1. Molecular test (e.g., polymerase chain reaction [PCR]) specific for carbapenemase;
2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production;
3. Susceptibility test (**for *E. coli* and *Klebsiella* spp only**): non-susceptible (intermediate or resistant) to ONE of the following carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL of the following third generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime). *Note: ignore ertapenem for this definition.*

Highlighted Features

- The XDRO Dashboard (shown at right) graphically shows data from a user's facility and the state aggregate.
- The Search Registry function allows facilities to check whether a patient has been previously reported as CRE-positive.



For more information about and access to the XDRO registry, visit: www.xdro.org

For XDRO registry questions, contact: DPH.XDROregistry@illinois.gov

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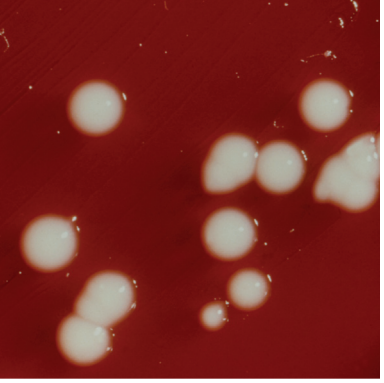
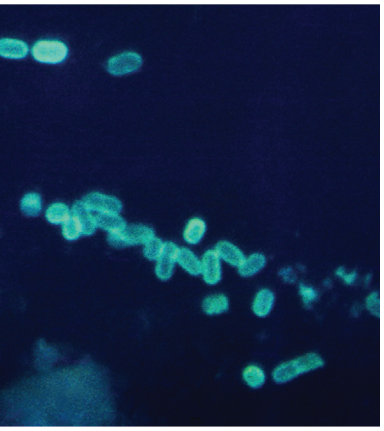
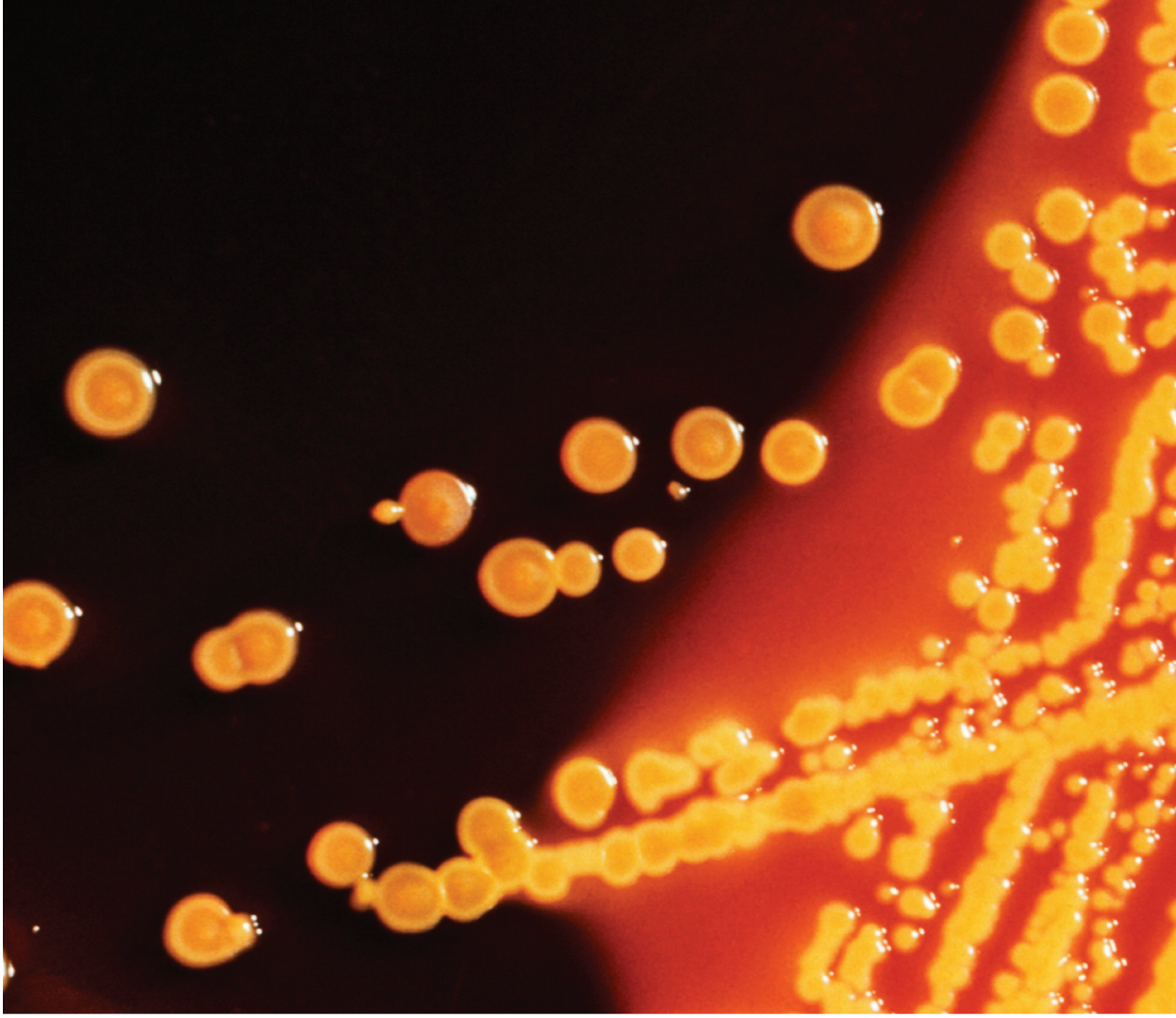






Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

2012 CRE Toolkit

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion

Guidance for Control of Carbapenem-resistant Enterobacteriaceae

This document contains two parts. Part 1 contains recommendations for healthcare facilities and is intended to expand upon the March 2009 "Guidance for Control of Carbapenem-Resistant or Carbapenemase-Producing Enterobacteriaceae in Acute-Care Facilities." Part 2 reviews the role of public health authorities in the control of carbapenem-resistant Enterobacteriaceae.

Unless otherwise specified, healthcare facilities refer to all acute care hospitals and any long-term care facility that cares for patients who remain overnight and regularly require medical or nursing care (e.g., maintenance of indwelling devices, intravenous injections, wound care, etc.). This would include all long-term acute care hospitals and skilled nursing homes (including certain rehabilitation facilities), but would generally exclude assisted living facilities and nursing homes that do not provide more than basic medical care. In addition, this toolkit is not intended for use in ambulatory care facilities.

Background

The emergence and dissemination of carbapenem resistance among Enterobacteriaceae in the United States represent a serious threat to public health. These organisms are associated with high mortality rates and have the potential to spread widely. Decreasing the impact of these organisms will require a coordinated effort involving all stakeholders including healthcare facilities and providers, public health, and industry. This document expands on the 2009 Centers for Disease Control and Prevention (CDC) and Healthcare Infection Control Practices Advisory Committee (HICPAC) recommendations and will continue to evolve as new information becomes available.

The approach to controlling transmission of these organisms in healthcare facilities includes the following:

- Recognizing these organisms as epidemiologically important
- Understanding the prevalence in their region
- Identifying colonized and infected patients when present in the facility
- Implementing regional and facility-based interventions designed to stop the transmission of these organisms

Carbapenem-resistant Enterobacteriaceae (CRE) appear to have been uncommon in the United States before 1992. However, carbapenemase-producing Enterobacteriaceae, most commonly producing *Klebsiella pneumoniae* carbapenemase (KPC), have disseminated widely throughout the United States since being first reported in 2001. Despite the spread of KPC-producing Enterobacteriaceae, the current U.S. distribution of CRE appears to be heterogeneous; these organisms are commonly isolated from patients in some parts of the United States, but they are not regularly found in patients from other regions. Even in areas where CRE are found they may be more common in some healthcare settings, such as long-term acute care, than they are in others.

In addition to KPC-producing Enterobacteriaceae, several different metallo-β-lactamase-producing strains have been identified in the United States since 2009. These include the New Delhi metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), and the imipenemase (IMP) metallo-β-lactamase. These enzymes are more common in other areas of the world and in the United States have generally been found among patients who received medical care in countries where these organisms are known to be present.

CRE are epidemiologically important for several reasons:

- CRE have been associated with high mortality rates (up to 40 to 50% in some studies).
- In addition to β-lactam/carbapenem resistance, CRE often carry genes that confer high levels of resistance to many other antimicrobials, often leaving very limited therapeutic options. "Pan-resistant" KPC-producing strains have been reported.
- CRE have spread throughout many parts of the United States and have the potential to spread more widely.

Definitions

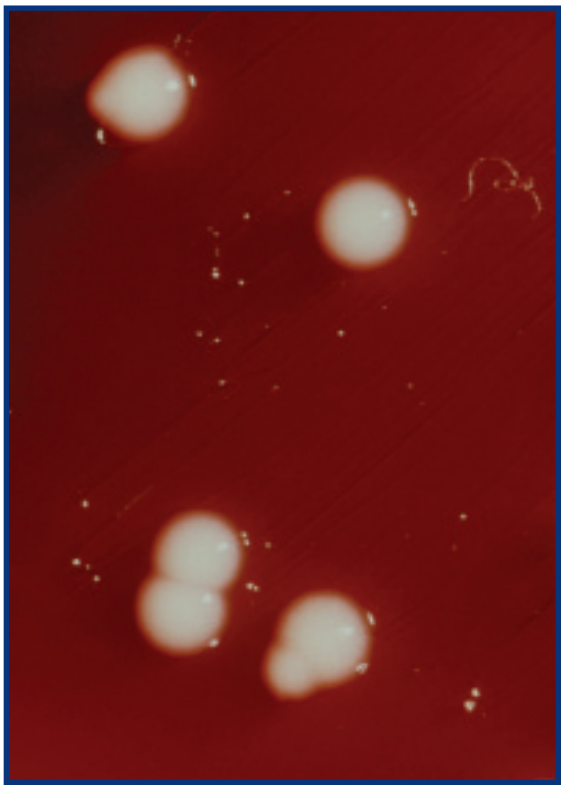
CDC has developed the following interim surveillance definition for CRE. CRE are defined as Enterobacteriaceae that are:

- Nonsusceptible to one of the following carbapenems: doripenem, meropenem, or imipenem AND
- Resistant to all of the following third-generation cephalosporins that were tested: ceftriaxone, cefotaxime, and ceftazidime. (Note: All three of these antimicrobials are recommended as part of the primary or secondary susceptibility panels for Enterobacteriaceae)
- *Klebsiella species* and *Escherichia coli* that meet the CRE definition are a priority for detection and containment in all settings; however, other Enterobacteriaceae (e.g., *Enterobacter* species) might also be important in some regions.
- For bacteria that have intrinsic imipenem nonsusceptibility (i.e., *Morganella morganii, Proteus* spp., *Providencia* spp.), requiring nonsusceptibility to carbapenems other than imipenem as part of the definition might increase specificity.
- This CRE surveillance definition is based upon the current (M100-S22 2012) Clinical and Laboratory Standards Institute (CLSI) interpretative criteria (breakpoints) for carbapenem susceptibility among Enterobacteriaceae (Appendix A); if the older CLSI breakpoints (pre-dating M100-S20 U) are being used to determine carbapenem susceptibility, consideration should be given to including ertapenem in the CRE definition to increase sensitivity.

Changes in the breakpoints are shown in Appendix A. Although the use of the current CLSI breakpoints offers laboratories a simpler and more straightforward approach to identifying CRE, adoption may be delayed by the fact that the U.S. Food and Drug Administration has not yet approved all of these breakpoints and some automated susceptibility panels currently do not include dilutions low enough to allow for application of the lower breakpoints.

Since most carbapenem resistance mediated by carbapenemases in the United States is found among *Klebsiella* spp. and *E. coli*, individual facilities or public health authorities might choose to apply the CRE surveillance definition only to these specific Enterobacteriaceae.

Definitions for CRE are complicated by a number of factors including the diversity of the genera. Another important challenge to developing a standardized definition of CRE is a recent (mid-2010) change in the Clinical and Laboratory Standards Institute (CLSI) interpretative criteria (breakpoints) for determining susceptibility to carbapenems among Enterobacteriaceae. These new recommendations lowered the breakpoints and removed the requirement for testing for carbapenemase (e.g., modified Hodge Test) to determine susceptibility. These breakpoints were further modified in January 2012 (M100-S22).



Klebsiella pneumonia

Part 1: Facility-level CRE Prevention

Surveillance

Inpatient facilities should have an awareness of whether or not CRE (at least *E. coli* and *Klebsiella* spp.) have ever been cultured from patients admitted to their facility and, if so, whether these positive cultures were collected within 48 hours of admission.

If CRE have been present, facilities should also determine:

- If there is evidence of intra-facility transmission
- Which wards/units are most affected

Facilities that do not have this information should consider performing an evaluation to quantify the clinical incidence of these organisms, such as a review of archived lab results to determine the number and/or proportion of Enterobacteriaceae that meet the CRE definition over a pre-specified time period (e.g., 6 to 12 months).
In addition, facilities should consider collecting information on the basic epidemiology of patients colonized or infected with these organisms in order to understand common characteristics of these individuals. This might include patient demographics, dates of admission, outcomes, medications, and common exposures (e.g., wards, surgery, procedures, etc).

Facility-level Prevention Strategies

The following briefly summarizes an approach to preventing CRE transmission in healthcare settings. For a more in-depth review, please refer to the CDC HICPAC guidelines "Management of Multidrug-Resistant Organisms in Healthcare Settings, 2006" (http://www.cdc.gov/hicpac/mdro/mdro_toc.html).

Core Measures for All Acute and Long-term Care Facilities

There are 8 core measures facilities should follow.

1. Hand Hygiene

Hand hygiene is a primary part of preventing multidrug-resistant organism (MDRO) transmission. Facilities should ensure that healthcare personnel are familiar with proper hand hygiene technique as well as its rationale. Efforts should be made to promote staff ownership of hand hygiene using techniques like developing local (e.g., unit) hand hygiene champions. It is not enough to have policies that require hand hygiene; hand hygiene adherence should be monitored and adherence rates should be fed directly back to front line staff. Immediate feedback should be provided to staff who miss opportunities for hand hygiene. In addition, facilities should ensure access to adequate hand hygiene stations (i.e., clean sinks and/or alcohol-

based hand rubs) and ensure they are well stocked with supplies (e.g. towels, soap, etc.) and clear of clutter. Further information on hand hygiene is available at www.cdc.gov/handhygiene/. This intervention is applicable to both acute and long-term care settings.

2. Contact Precautions

Patients in acute care settings who are colonized or infected with CRE should be placed on Contact Precautions. Systems should be in place to identify patients with a history of CRE colonization or infection at admission so that they can be placed on Contact Precautions if not known to be free of colonization. In addition, clinical laboratories should have an established protocol for notifying clinical and/or infection prevention personnel when CRE are identified from clinical or surveillance cultures.

There is not enough information for a firm recommendation about when to discontinue Contact Precautions among infected patients; however, CRE colonization in some patients identified during CDC investigations has been prolonged (> 6 months). If surveillance cultures are used to decide if a patient remains colonized, more than one culture should be collected in an attempt to improve sensitivity. One recent study found that among rectal CRE carriers, predictors of rectal CRE carriage at a future healthcare encounter included exposure to antimicrobials (especially fluoroquinolones), admission from another healthcare facility, and less than 3 months' elapsed time since their first positive CRE test.

The probability of being CRE positive at the next encounter increased to 50% if one predictor was present. Presence of ongoing risk factors for carriage such as these should be considered before discontinuing use of Contact Precautions in these patients. The presence of CRE infection or colonization alone should not preclude transfer of a patient from one facility to another (e.g., acute care to long-term care). Facilities should ensure that Contact Precautions are used correctly by staff caring for all patients with epidemiologically important MDROs including CRE.

Proper use of Contact Precautions includes:

- Performing hand hygiene before donning a gown and gloves
- Donning gown and gloves before entering the affected patient's room
- Removing the gown and gloves and performing hand hygiene prior to exiting the affected patient's room

Ensuring healthcare personnel (HCP) are educated about the proper use and rationale for Contact Precautions is an important part of this process. In addition, facilities should ensure that there is a process to monitor and improve HCP adherence to Contact Precautions. This might include conducting periodic surveillance on the use of Contact Precautions and providing feedback to frontline staff about these results.

Preemptive Contact Precautions, often in conjunction with surveillance cultures, might be used on patients transferred from high-risk settings (see supplemental interventions) pending results of screening cultures. Examples include transferred patients from hospitals in countries or areas in the United States where CRE are common or patients transferred from facilities known to have outbreaks or clusters of CRE colonized or infected patients.

In long-term care settings, Contact Precautions are still indicated for residents infected or colonized with CRE; however, these might be modified to fit the inherent differences between acute and long-term care facilities. Contact Precautions should be used for residents with CRE who are at higher risk for transmission, including patients who are totally dependent upon HCP for their activities of daily living, are ventilator-dependent, are incontinent of stool, or have wounds with drainage that is difficult to control. For other residents who are able to perform hand hygiene, are continent of stool, are less dependent on staff for their activities of daily living, and are without draining wounds, the requirement for Contact Precautions might be relaxed. However, in these situations Standard Precautions should still be observed, including the use of gloves and/or gowns when contact with colonized/infected sites or body fluids is possible.

3. Healthcare Personnel Education

HCP in all settings who care for patients with MDROs, including CRE, should be educated about preventing transmission of these organisms. At a minimum this should include information on the proper use of Contact Precautions and hand hygiene. This intervention is applicable to both acute and long-term care settings.

4. Use of Devices

Use of devices (e.g., central venous catheters, endotracheal tubes, urinary catheters) puts patients at risk for device-associated infections and minimizing device use is an important part of the effort to decrease the incidence of these infections. Additionally, device use has been associated with carbapenem resistance among Enterobacteriaceae. Therefore, minimizing device use in all healthcare settings should be part of the effort to decrease the prevalence of all MDROs including CRE. In acute and long-term care settings, device use should be reviewed regularly to ensure they are still required and devices should be discontinued promptly when no longer needed. For more information on preventing device-associated infection including appropriate use of devices please see www.cdc.gov/hicpac/BSI/BSI-guidelines-2011.html and www.cdc.gov/hicpac/cauti/002_cauti_toc.html.

5. Patient and Staff Cohorting

When available, patients colonized or infected with CRE should be housed in single patient rooms and if not available these patients should be cohorted together. In addition, consideration should be given to cohorting patients with CRE in specific areas (e.g., units or wards), even if in single patient rooms, and to using dedicated staff to care for them. This recommendation applies to both acute and long-term care settings. Preference for single rooms should be given to patients at highest risk for transmission such as patients with incontinence, medical devices, or wounds with uncontrolled drainage.

6. Laboratory Notification

Laboratories should have protocols in place that facilitate the rapid notification of appropriate clinical and infection prevention staff whenever CRE are identified from clinical specimens to ensure timely implementation of control measures. This is true for both facilities with on-site laboratories and those sending cultures off-site and is applicable to acute and long-term care settings.

7. Antimicrobial Stewardship

Antimicrobial stewardship is another primary part of MDRO control. Although the role of this activity specifically for CRE has not been well studied, multiple antimicrobial classes have been shown to be a risk for CRE colonization and/or infection. Further, restricting use of carbapenems has been associated with a lower incidence of carbapenem-resistant *Pseudomonas aeruginosa* in one ecological analysis. As part of an antimicrobial stewardship program designed to minimize transmission of MDROs, facilities should work to ensure that 1) antimicrobials are used for appropriate indications and duration and 2) that the narrowest spectrum antimicrobial that is appropriate for the specific clinical scenario is used. For more information on antimicrobial stewardship in healthcare settings please see http://www.cdc.gov/getsmart/healthcare. This intervention is applicable to both acute and long-term care settings.

8. CRE Screening

Screening is used to identify unrecognized CRE colonization among epidemiologically-linked contacts of known CRE colonized or infected patients as clinical cultures will usually identify only a fraction of all patients with CRE. Generally, this screening has involved stool, rectal, or peri-rectal cultures and sometimes cultures of wounds or urine (if a urinary catheter is present). A laboratory protocol for evaluating rectal or peri-rectal swabs for CRE is available at http://www.cdc.gov/hai/pdfs/labsettings/Klebsiella_or_E_coli.pdf; however, it is important to note that this procedure has only been validated for *E. coli* and *Klebsiella* spp. CRE screening of epidemiologically linked patients is a primary prevention strategy for all healthcare facilities; however, it is particularly important for healthcare facilities with CRE outbreaks or facilities that do not or only rarely admit patients with CRE infection or colonization. This intervention is applicable to both acute and long-term care settings.

CRE screening might include:

- Point prevalence surveys:
  Point prevalence surveys might be an effective way for facilities to rapidly evaluate the prevalence of CRE in particular wards/units. This could be useful in a situation where a review of clinical cultures using laboratory records identifies unreported CRE patients in certain wards/units. A point prevalence survey is generally conducted by screening all patients in that ward/unit. Point prevalence surveys might be done only once if few or no additional CRE colonized patients are identified or might be done serially if colonization is more widespread or to follow the effect of an intervention.

- Screening of epidemiologically linked patients:
  If previously unrecognized CRE carriers are identified, screening of patient contacts could be conducted to identify transmission instead of a wider point prevalence survey. Those patients considered contacts may vary from setting to setting; however, they usually include roommates of the unrecognized CRE patients as well as patients who might have shared HCP.

Supplemental Measures for Healthcare Facilities with CRE Transmission

These additional measures should be considered when baseline core prevention practices are not effective in reducing CRE incidence.

Active Surveillance Testing

This process involves culturing patients who might not be epidemiologically linked to known CRE patients but who meet certain pre-specified criteria. This could include everyone admitted to the facility, pre-specified high-risk patients (e.g., those admitted from long-term care facilities), and/or patients admitted to high-risk settings (e.g., intensive care units [ICUs]). Active surveillance testing has been used in control efforts for several MDROs including CRE; however, the exact contribution of this practice to decreases in CRE is not known.

As described above, active surveillance testing is based on the finding that clinical cultures will identify only a minority of those patients colonized with CRE; unrecognized colonized patients might not be on Contact Precautions and are a potential source for CRE transmission. If done, surveillance testing could be focused on patients admitted to certain high-risk settings (e.g., ICUs, long-term acute care) or could target specific patients (i.e., patients with risk factors, patients admitted from high-risk settings like long-term acute care or transferred from areas with high CRE

prevalence). This testing is generally done at admission but can also be done periodically during admission (e.g., weekly). Patients identified as positive by this surveillance testing should be treated as colonized (i.e., placed on Contact Precautions, etc.). In some situations (e.g., patients admitted from high-risk settings) patients might be placed in preemptive Contact Precautions until surveillance testing is found to be negative.

As with screening of epidemiologically linked CRE contacts, the use of active surveillance testing to control CRE is applicable to both acute and long-term care settings.

Chlorhexidine Bathing

Chlorhexidine bathing has been used successfully to prevent certain types of healthcare-associated infections (e.g., bloodstream infections) and to decrease colonization with specific MDROs, primarily in ICUs. For CRE, it has been used as part of a multifaceted intervention to reduce the prevalence of CRE during an outbreak in a long-term acute care facility. During chlorhexidine bathing, diluted liquid chlorhexidine (2%) or 2% chlorhexidine-impregnated wipes are used to bathe patients (usually daily) while in high-risk settings (e.g., ICUs). The chlorhexidine is usually not used above the jaw line or on open wounds. When chlorhexidine bathing is used for a particular patient population or in a particular setting, it is usually applied to all patients regardless of CRE colonization status.

In long-term care settings this type of an intervention might be used on targeted high-risk residents (e.g., residents that are totally dependent upon healthcare personnel for activities of daily living, are ventilator-dependent, are incontinent of stool, or have wounds whose drainage is difficult to control) or high-risk settings (e.g., ventilator unit). In addition, chlorhexidine bathing might be less frequent in long-term care depending on the facility's usual bathing protocol.

Recommendations for Facilities with No or Rare CRE

Experience with other MDROs suggests that it might be most effective to intervene on emerging MDROs when they first are recognized in a facility before they become common. For this reason facilities that rarely (e.g., < 1 per month) or never have patients admitted who are colonized or infected with CRE should be aggressive about controlling these organisms when they are identified. An example of one approach to CRE control in these settings is shown in Appendix B.

In addition, if a facility without previous CRE performs a review of archived clinical laboratory results for CRE and identifies previously unrecognized CRE-colonized or -infected patients, the facility should consider point prevalence surveys of high-risk units to further clarify the CRE prevalence. If additional CRE colonized patients are identified, facilities should also follow the approach in Appendix B. Facilities without CRE that receive patients that are transferred from facilities known to have CRE colonized or infected patients could also consider screening those patients for CRE at admission and placing them in preemptive Contact Precautions pending the result of surveillance cultures.

Summary Of Prevention Strategies For Acute And Long-Term Care Facilities

Core Measures for All Acute and Long-term Care Facilities

1. Hand hygiene

- Promote hand hygiene
- Monitor hand hygiene adherence and provide feedback
- Ensure access to hand hygiene stations

2. Contact Precautions

Acute care

- Place CRE colonized or infected patients on Contact Precautions (CP)
    - Preemptive CP might be used for patients transferred from high-risk settings
- Educate healthcare personnel about CP
- Monitor CP adherence and provide feedback
- No recommendation can be made for discontinuation of CP
- Develop lab protocols for notifying clinicians and IP about potential CRE

Long-term care

- Place CRE colonized or infected residents that are high-risk for transmission on CP (as described in text); for patients at lower risk for transmission use Standard Precautions for most situations

3. Patient and staff cohorting

- When available cohort CRE colonized or infected patients and the staff that care for them even if patients are housed in single rooms
- If the number of single patient rooms is limited, reserve these rooms for patients with highest risk for transmission (e.g., incontinence)

4. Minimize use of invasive devices

5. Promote antimicrobial stewardship

6. Screening

- Screen patient with epidemiologic links to unrecognized CRE colonized or infected patients and/or conduct point prevalence surveys of units containing unrecognized CRE patients

Supplemental Measures for Healthcare Facilities with CRE Transmission

1. Conduct active surveillance testing

- Screen high-risk patients at admission or at admission and periodically during their facility stay for CRE. Preemptive CP can be used while results of admission surveillance testing are pending
- Consider screening patients transferred from facilities known to have CRE at admission

2. Chlorhexidine bathing

- Bathe patients with 2% chlorhexidine

Public Health Engagement

Inter-facility Transmission of CRE

Patients colonized or infected with CRE may seek medical care in more than one hospital and serve as a reservoir that can facilitate the spread of CRE from one facility to another. With the pressure to reduce length of stay in acute care hospitals, patients who require complex medical treatment are often transferred to long-term care facilities (e.g., long-term acute care hospitals and skilled nursing homes) to complete their treatment. These patients frequently require readmission either to the same or different hospitals. This extensive inter-facility sharing of patients across the continuum of care has the potential to facilitate widespread regional transmission of CRE.

Regional Approach to CRE Control

To prevent the emergence and further spread of CRE, a coordinated regional control effort among healthcare facilities is recommended. The implementation of such an approach was successful in controlling vancomycin-resistant enterococci in the Siouxland region of the United States and for reducing CRE incidence at the national level in Israel. Given the ability of state and local health departments to interface with different types of facilities, public health is in a unique position to coordinate the local and regional response to MDROs, like CRE, by providing situational awareness within their jurisdiction and facilitating the implementation of appropriate control measures.

The optimal public health response will vary depending on the prevalence of CRE within a given jurisdiction. Based on an initial evaluation of the prevalence or incidence of CRE, prevention strategies can be tailored for geographical regions according to the following classifications: regions without CRE, regions with few CRE colonized- or infected-patients, and regions where CRE are common. (Although there is no standard definition for the latter two categories, some criteria that can be considered to determine a region's classification are provided below.) In regions where there are no or few CRE colonized- or infected-patients, there may be a critical opportunity to prevent further emergence of CRE by taking an aggressive approach early in the process. For regions where CRE have already become common, certain general prevention measures may need to be applied more broadly as outlined in the respective section. However, because of the challenges associated with high CRE prevalence, it is recommended that further tailoring of supplemental measures be determined in consultation with CDC and in accordance with the 2006 CDC HICPAC "Guidelines for Management of Multidrug-Resistant Organisms in Healthcare Settings" (http://www.cdc.gov/hicpac/pdf/guidelines/MDROGuideline2006.pdf).

For this document, a region could represent part of a state, a whole state, or even multiple states. In some regions, patients may be shared between facilities located in different jurisdictions and/or states. Ideally for MDRO control, state health departments would take the lead and coordinate with local health departments. However, depending on the region targeted, prevention strategies may also require coordination between states.

Regional Surveillance for CRE

Health departments should understand the prevalence or incidence of CRE in their jurisdiction by performing some form of regional surveillance for these organisms. As described above, the interim CDC surveillance definition for CRE is Enterobacteriaceae that are nonsusceptible to one of the carbapenems and resistant to all of the third-generation cephalosporins that were tested. At a minimum, initial surveillance efforts should focus on key organisms (i.e., *K. pneumoniae, E. coli*, and *Enterobacter* spp. that meet the CRE definition).

Options for performing surveillance include making CRE a laboratory-reportable event or surveying Infection Preventionists and/or laboratory directors of healthcare facilities by telephone or email (e.g., using online survey). An example of a survey for Infection Preventionists in acute care and long-term acute care hospitals can be found in Appendix C; this survey could also be modified for use in other long-term care facilities.

It is recommended that CRE surveys conducted by health departments collect, at a minimum, the following facility-level data:

- Facility demographics including location and facility name if possible
- Overall frequency of CRE detection (e.g., daily, weekly, monthly, etc.)
- Frequency of CRE cases by timing of detection (e.g., within 48 hours or greater than 48 hours of admission)
- If surveying Infection Preventionists, determine whether recommended surveillance and infection prevention measures are being implemented, as outlined in Part 1

Email reminders or phone calls to non-responders are encouraged to facilitate survey completion in a timely fashion (e.g., 1-2 weeks) and increase response rates. Based on survey/surveillance results, prevention strategies can be tailored accordingly as outlined below and in the algorithms provided in appendix D.

Regional Prevention Strategies

Regions with No CRE Identified

Regional Surveillance and Feedback of Results

In regions that have no identified CRE colonized- or infected-patients, it is recommended that health departments take an aggressive approach to future CRE detection, such as making CRE a reportable event (e.g., laboratory reportable) to ensure that CRE are recognized when they occur. If CRE reporting is not feasible, health departments should periodically survey healthcare facilities for the presence of CRE and provide feedback to increase awareness. The frequency of surveillance may depend on the prevalence of CRE in neighboring areas or jurisdictions. For example, in an area where nearby locations have known CRE colonized- or infected-patients, quarterly or even monthly surveillance may be reasonable. To maintain an understanding of CRE prevalence in surrounding regions, neighboring health departments should consider establishing a mechanism for communicating updates with one another about the level of CRE activity within their respective jurisdictions.

Education of Healthcare Facilities

Health departments should also increase awareness among healthcare facilities about the public health importance of CRE, recommended prevention measures, and the importance of timely recognition of any CRE colonized- or infected-patients. This could include targeted education of Infection Preventionists and other healthcare personnel and could take place at conferences, training sessions, or through webinars or newsletters.

Regions with Few CRE Identified

The prevention strategies described in this section apply to regions where the majority of healthcare facilities do not regularly have patients with CRE admitted. This would include regions where several facilities may have identified CRE colonized- or infected-patients on an infrequent basis (e.g., monthly basis or greater), as well as regions where some facilities may have several CRE colonized- or infected-patients but are surrounded by facilities with only a few or none. In these situations, health departments should still take an aggressive approach to contain CRE. This may require working more closely with specific healthcare facilities and targeting prevention efforts to certain parts of the region. Regions with few CRE are also most in need of increased situational awareness across all facilities regarding which facilities are being most impacted by CRE.

Regional Surveillance and Feedback of Results: Targeted Prevention

Health departments should consider making CRE a reportable event (e.g., laboratory reportable) to track CRE rates within their jurisdiction for the purposes of identifying new cases and assessing the efficacy of infection prevention measures. If this is not feasible, health departments should still continue to periodically survey acute and long-term care facilities for the presence of CRE.

CRE surveillance results should be shared with facilities (e.g., via newsletters, emails, or presentations at regional conferences), including facility administrators, in order to provide awareness of the current regional situation with respect to CRE; knowing which facilities have CRE colonized- or infected-patients may be one of the most important benefits of a coordinated regional approach to CRE control, allowing nearby facilities to take appropriate action. For example, patients admitted from facilities that have CRE could be placed preemptively on Contact Precautions pending surveillance culture results. Even if facility identifiers cannot be revealed, health departments can provide feedback of results stratified by facility type or by geographical distribution. Knowing which parts of the region have CRE can allow nearby facilities to intensify CRE prevention efforts (e.g., using supplemental measures) in consultation with the health department.

Implementation of Prevention Measures

In all facilities, health departments should ensure that core prevention measures (e.g., hand hygiene, Contact Precautions, patient and staff cohorting) are being implemented accordingly. Particularly in facilities that have CRE, it is recommended that health departments work closely with the infection prevention personnel to review and improve facility adherence to recommended practices. This may involve ongoing communication with infection prevention personnel, conducting site visits where feasible, providing in-service training, and engaging the facility directors and/or administrators in discussions about the importance of CRE prevention.

In facilities without CRE, health departments should take steps to ensure that a plan is in place in the event that a CRE colonized- or infected-patient is identified. Additionally, health departments should work closely with individual facilities that have not identified CRE to determine appropriate supplemental interventions. These measures may include targeting active surveillance testing and preemptive Contact Precautions to patients admitted from facilities with ongoing transmission of CRE (e.g., CRE detection on at least a weekly basis or in a CRE outbreak situation). If facility identifiers cannot be disclosed, targeted use of active surveillance testing and preemptive Contact Precautions can be guided by the local epidemiology of CRE. Specifically, in facilities without CRE but located in areas where CRE are present, active surveillance testing and preemptive Contact Precautions could be applied to the following patients: (a) those admitted from long-term care facilities (e.g., long-term acute care hospitals), where there may be a large reservoir of CRE colonized- or infected-patients as a result of inter-facility patient sharing and longer length of stay and/or (b) those with potential risk factors for CRE (e.g., patients with open wounds, presence of indwelling devices, and/or high antimicrobial usage).

In facilities with known CRE, health departments should promote implementation of surveillance measures to identify additional cases in order to prevent further intra-facility CRE transmission. These interventions may include screening patients with epidemiologic links to previously unrecognized cases and conducting periodic point prevalence surveys in high-risk settings (e.g., ICUs). Health departments should also promote inter-facility communication as described in the following section. As needed, health departments should consult with CDC and/or regional experts for additional guidance.

Inter-facility Communication

To reduce inter-facility transmission of all MDROs, all facilities should be encouraged to routinely complete inter-facility transfer forms whenever a patient is transferred to another facility; this becomes especially important when a patient with known CRE colonization or infection is to be transferred to another facility. The form should indicate whether the patient has ever been colonized and/or infected with CRE and other MDROs (if available, the dates and results of any relevant clinical and/or surveillance cultures should be provided) and whether the patient has any open wounds and/or indwelling devices. In addition, if the patient is currently being given antimicrobials, information should be included describing why the patient is receiving them and how much longer treatment is required. An example of an inter-facility transfer form developed by CDC is available for facilities to use (http://www.cdc.gov/HAI/toolkits/InterfacilityTransferCommunicationForm11-2010.pdf)

Education of Healthcare Facilities

Education for healthcare facility staff about CRE and recommended surveillance and prevention measures should continue to be provided as described above. This might be especially important for facilities that have not detected CRE in order to increase their vigilance.

Regions Where CRE are Common

In general, CRE are considered common in regions where the majority of healthcare facilities have identified cases, and these facilities regularly have CRE colonized- or infected-patients admitted (e.g., CRE detected at least weekly).

Whereas a targeted approach to prevention may be successful in regions with few CRE cases, limited experiences indicate that a broad, public health approach is required when CRE are common. The national implementation of a centrally-coordinated intervention in Israel succeeded in containing CRE. Their success was attributed in part to the creation of a task force dedicated to ensuring that all hospitals complied with national CRE guidelines. Based on Israel's experience and the 2006 CDC HICPAC "Guidelines for Management of Multidrug-Resistant Organisms in Healthcare Settings" (http://www.cdc.gov/hicpac/pdf/guidelines/MDROGuideline2006.pdf), the following prevention measures are recommended for regions where CRE are common:

Dedicated Personnel

To effectively coordinate infection prevention across the region, health departments should have dedicated personnel assigned to this task. Ideally, these personnel should have an adequate understanding of CRE/MDRO prevention practices. As needed, a health department-led advisory panel consisting of experienced professionals in infection prevention and clinical microbiology can be established to provide additional technical support to facilities.

Engagement of Healthcare Facilities

As an initial step to engaging all facilities in the region, health departments should first communicate to appropriate personnel the CRE prevalence within the region and the importance of a regional approach to prevention. This may involve discussions with the facility directors and/or administrators in addition to the infection prevention personnel. The purpose of these discussions is to convey the urgency of the situation and to obtain facility leadership support to prioritize CRE prevention.

Reinforcement of Core Prevention Measures

Health departments should review current infection control policies and practices related to CRE at all acute and long-term care facilities within the region. At a minimum, all facilities should be implementing the core measures for CRE prevention (e.g., hand hygiene, Contact Precautions, patient and staff cohorting). To reinforce best practices, targeted education and in-service training may need to be provided to individual facilities.

Implementation of Supplemental Measures

Additional measures to be implemented by facilities should be determined in close consultation with the health department and in accordance with the interventions summarized in Part 1 of this document and the Tier 2 recommendations of the 2006 CDC HICPAC Guidelines for Management of Multidrug-resistant Organisms in Healthcare Settings (http://www.cdc.gov/hicpac/pdf/guidelines/MDROGuideline2006.pdf). These interventions may include performing active surveillance testing and/or chlorhexidine bathing.

Assessing Facility Compliance to Prevention Measures

Health departments should periodically assess for facility compliance to recommended practices (e.g., on a monthly basis). This may be based on reporting by facility Infection Preventionists or assessed through site visits to individual facilities if feasible. Depending on compliance rates, additional educational outreach, such as in-service trainings and webinars, may need to be provided to individual facilities. To increase staff adherence, performance feedback should be shared with facility directors and/or administrators. Health departments can also consider providing feedback of aggregate compliance data stratified by facility type and/or by geographical distribution, so that individual facilities can compare their performance with others.

Inter-facility Communication

As described previously, an inter-facility transfer form should be completed whenever a patient is being transferred to another facility. This should indicate the CRE status of the patient and the presence of open wounds and indwelling devices and antimicrobial usage.

Regional Surveillance and Feedback of Results

Health departments should continue to perform periodic regional surveillance to assess efficacy of infection prevention measures and to feedback results to facilities. Although it may not be practical to make every CRE case reportable in a region where CRE are common, certain events to consider making reportable could be an increase in CRE rate above baseline or CRE cases with unique features (e.g., all fatalities or healthy patients with fatal outcome).

Appendix A: Previous and Current Clinical and Laboratory Standards Institute Interpretive Criteria for Carbapenems and Enterobacteriaceae

Agent	Previous Breakpoints (M100-S19) MIC (µg/mL)			Current Breakpoints (M100-S22) MIC (µg/mL)		
	Susceptible	Intermediate	Resistant	Susceptible	Intermediate	Resistant
Doripenem	-	-	-	≤1	2	≥4
Ertapenem	≤2	4	≥8	≤0.5	1	≥2
Imipenem	≤4	8	≥16	≤1	2	≥4
Meropenem	≤4	8	≥16	≤1	2	≥4

Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty Second Informational Supplement (January 2012). CLSI document M100-S22. Wayne, Pennsylvania, 2012.

Appendix B: General Approach to Carbapenem-resistant Enterobacteriaceae (CRE) Control in Facilities that Rarely or Have Not Identified CRE

New CRE-colonized or CRE-infected patient identified

↓

- Notify appropriate personnel (i.e., clinical staff, infection prevention staff)
- Notify public health if indicated

↓

- Place patient on Contact Precautions in single room (if available)
- Reinforce hand hygiene and use of Contact Precautions on affected ward/unit
- Educate healthcare personnel about preventing CRE transmission

↓

- Screen epidemiologically-linked patient contacts (e.g., roommates) for CRE with at least stool, rectal, or peri-rectal cultures and/or consider point prevalence survey of affected unit
- Consider preemptive Contact Precautions of these patients pending results of screening cultures

↓

- If screening cultures or further clinical cultures identify additional CRE-colonized or -infected patients, consider additional surveillance cultures of contacts or point prevalence surveys of affected units (if not already done)
- Consider cohorting patients and staff

↓

- Ensure if patient transferred within the facility that precautions are continued
- Ensure if patient transferred to another facility CRE information is shared with accepting facility

Appendix C: Example of a Survey for Infection Preventionists

Instructions for Administering Survey for Carbapenem-resistant Enterobacteriaceae (CRE)

Given the increasing incidence of CRE in parts of the United States and the potential for widespread dissemination, health departments are encouraged to assess the incidence of CRE within their jurisdictions to guide response efforts. To facilitate this activity, the attached survey has been designed to be used by health departments to determine: 1) the frequency of CRE colonized- or infected patients identified, 2) the type of surveillance conducted, and 3) the infection control measures implemented to prevent transmission.

It is recommended that health departments administer this survey by telephone to infection prevention personnel of all acute care hospitals and long-term acute care hospitals within their jurisdictions; this survey could also be modified for use in other long-term care facilities. The survey consists of 7 questions and will take approximately 5 minutes to complete.

Survey of Healthcare Facilities for Carbapenem-resistant Enterobacteriaceae (CRE)

1. Does the microbiology laboratory that performs cultures for your facility have an established system for alerting infection prevention staff in a timely manner (i.e., within 24 hrs) whenever a carbapenem-resistant Enterobacteriaceae isolate is identified?

☐ Yes ☐ No

2. In the past 12 months, have any CRE infected- or colonized-patients been present in your facility?

☐ Yes ☐ No

If YES,

a. In general, how often do you identify CRE infected- or colonized-patients from clinical cultures?

☐ Daily ☐ Weekly ☐ Monthly ☐ Biannually ☐ Yearly

b. Specifically, how often are CRE infected- or -colonized patients identified from clinical cultures collected in the following categories:

i. From cultures collected before or within 48 hours of admission (i.e., transfers or community-onset)?

☐ Daily ☐ Weekly ☐ Monthly ☐ Biannually ☐ Yearly ☐ Not Identified

ii. From cultures collected after 48 hours of admission (i.e., hospital-onset)?

☐ Daily ☐ Weekly ☐ Monthly ☐ Biannually ☐ Yearly ☐ Not Identified

3. If CRE cases have not been identified or have only rarely been identified (i.e., 0-3 cases per quarter), has your facility ever reviewed 6 to 12 months of microbiology records to detect any previously unrecognized CRE cases?

☐ Yes ☐ No

If YES, did your review identify any previously unrecognized CRE cases?

☐ Yes ☐ No

4. Has your facility ever conducted a point prevalence survey (single round of active surveillance cultures) for CRE in high-risk units (e.g., units where previously unrecognized cases were identified, ICU, and units with high antimicrobial utility)?

☐ Yes ☐ No

If YES, did your facility identify any unrecognized CRE?

☐ Yes ☐ No

5. If a CRE case is identified, does your facility conduct active surveillance testing of patients with epidemiologic links to the CRE case (e.g., patients in same unit or who were provided care by same healthcare personnel)?

☐ Yes ☐ No

6. If a patient infected or colonized with CRE is identified, which of the following measures are implemented (check all that apply):

a. Place on Contact Pecautions ☐ Yes ☐ No

b. Place in single-patient rooms when possible ☐ Yes ☐ No

c. Other:_____

_____

7. In your opinion, does your facility consider CRE to be an epidemiologically important multidrug-resistant organism for which specific infection control practices are indicated to eliminate transmission?

☐ Strongly Agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly Disagree

Regions With No CRE Identified

In regions without known CRE, the emphasis should be on regional surveillance for CRE and education of healthcare personnel (e.g., infection prevention staff) to increase awareness.

Recommended Health Department Action

I. Regional Surveillance and Feedback

A.

Make CRE laboratory-reportable

OR

Survey all IPs or lab directors by phone or email (refer to Appendix C for an example of an IP survey)

B.

- If no CRE cases are identified:
  - Feedback results to IPs and/or lab directors
  - Promote facility-level CRE guidance[1]
- If CRE cases are identified:
  - For regions with few CRE identified, refer to appropriate algorithm
  - For regions where CRE are common, refer to the appropriate algorithm

C.

Repeat survey/surveillance at least quarterly if CRE are present in neighboring jurisdictions; otherwise, repeat at least every 6 months

II. Education of All Healthcare Facilities[2]

- Explain importance of CRE and provide updates on national and/or neighboring regional prevalence and epidemiology
- Review recommended surveillance and prevention measures[1]
- Increase vigilance for CRE detection

1. Refer to Part 1: Facility-Level Recommendations
2. Refers to all acute care hospitals and long-term care facilities that provide medical or nursing care (e.g., long-term acute care hospitals and skilled nursing facilities). Refer to the text for more details.

Regions with Few CRE Identified

In regions where CRE have been identified but cases remain uncommon, an aggressive approach to prevention is needed to prevent further transmission and widespread emergence of CRE. This will require increased prevention efforts targeting select facilities in the region where CRE are found.

Recommended Health Department Action

I. Regional Surveillance and Feedback

A.

Make CRE laboratory-reportable

OR

Survey all IPs or lab directors by phone or email (refer to Appendix C for an example of an IP survey)

B.

Feedback results to IPs and/or lab directors and to facility administrators (e.g., director) by email or letter

- Strongly consider providing facility identifiers; if not feasible, stratify results by geographic area and/or by facility type (acute vs. long-term care)
- Engage Hospital Association, Quality Improvement Organizations, and other relevant partners as needed to facilitate communication with facility leadership
- Provide facility-level CRE guidance[1]

C.

Repeat CRE surveillance and feedback at least quarterly

II. Infection Prevention

For facilities without CRE but located in areas of the region where CRE are present:

- Engage facility administrators to prioritize CRE prevention
- Ensure a CRE control plan is in place
- Reinforce core prevention measures
- Guide implementation of active surveillance testing and preemptive Contact Precautions for
  - Patients admitted from facilities with ongoing CRE transmission
  - Patients admitted from long-term care facilities (e.g., long-term acute care hospitals) or with CRE risk factors (e.g., open wounds, indwelling devices, high antimicrobial use)

Algorithm Continued for Regions with Few CRE Identified:

For facilities with CRE:

- Engage facility administrators to prioritize CRE prevention
- Review infection prevention practices to ensure core prevention measures are in place
- Provide in-service training (as needed)
- Ensure CRE screening is in place and guide implementation of supplemental measures[1]
- If CRE rates do not decrease, consult CDC and/or regional experts for additional guidance

III. Inter-facility Communication

Ensure facilities with known CRE complete an inter-facility transfer form when transferring patients (indicate CRE status of patient, presence of open wounds/devices, antimicrobial use and ength of therapy)[2]

IV. Education of All Healthcare Facilities[3]

- Explain importance of CRE and provide updates on regional prevalence and epidemiology
- Review recommended surveillance and prevention measures[1]
- Increase vigilance for CRE detection

1. Refer to Part 1: Facility-Level Recommendations
2. http://www.cdc.gov/HAI/toolkits/InterfacilityTransferCommunicationForm11-2010.pdf
3. Includes all acute care facilities and long-term care facilities that provide medical or nursing care (e.g, long-term acute care hospitals and skilled nursing facilities). Refer to the text for more details.

Regions Where CRE are Common

CRE containment in high-prevalent regions will require the implementation of core and supplemental prevention measures across all acute care and long-term care facilities that provide medical or nursing care (e.g., long-term acute care hospitals and skilled nursing facilities).

Recommended Health Department Action

I. Dedicated Personnel to Engage Healthcare Facilities

- Assign specific personnel to this task
- Form advisory panel if additional technical support is needed
- Engage all facility administrators (e.g., director) and IP personnel early in process
  - Engage Hospital Association, QIOs, and other relevant partners as needed to facilitate communication with facility leadership

II. Regional Surveillance and Feedback

A.

Perform steps for CRE surveillance and feedback of results to IPs and/or lab directors and facility administrators as outlined for regions with few CRE identified

- Ensure that urgency of situation is appropriately conveyed to facility leadership

B.

Determine if certain CRE events should be made reportable (e.g., fatalities)

C.

Repeat CRE surveillance and feedback at least quarterly

III. Infection Prevention

A.

Reinforce core prevention measures in all facilities

- Work closely with IPs to review practices
- Provide in-service training

B.

Consider supplemental measures in all facilities[1,2]

- Active surveillance testing and preemptive Contact Precautions for
  - Patients admitted from facilities with ongoing CRE transmission or high CRE prevalence
  - Patients admitted from long-term care facilities (e.g., long-term acute care hospitals) or with CRE risk factors (e.g., open wounds, indwelling devices, high antimicrobial use)
  - Patients being admitted to high-risk units (e.g., ICUs)
- Chlorhexidine bathing on high-risk patients

C.

Assess Compliance to Prevention Measures

- At least monthly assessment (e.g., report from IPs)
- Share performance measures with facility administrators
- As needed, provide additional in-service training

IV. Inter-facility Communication

Ensure facilities with CRE cases complete an inter-facility transfer form (indicate CRE status, presence of open wounds/devices, antimicrobial use and length of therapy)[3]

V. Assess Efficacy of Infection Prevention Measures

If CRE rates do not decrease,

- Intensify efforts in select facilities as needed
- Implement additional interventions in consultation with CDC and/or regional experts and in accordance with CDC HICPAC MDRO guidelines[2]

1. Refer to Part 1: Facility-Level Recommendations
2. http://www.cdc.gov/ncidod/dhqp/pdf/ar/MDROGuideline2006.pdf
3. http://www.cdc.gov/HAI/toolkits/InterfacilityTransferCommunicationForm11-2010.pdf

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CDC Vitalsigns™
March 2013

Making Health Care Safer

Stop Infections from Lethal CRE Germs Now

4% & 18%

About 4% of US hospitals had at least one patient with a CRE (carbapenem-resistant Enterobacteriaceae) infection during the first half of 2012. About 18% of long-term acute care hospitals* had one.

42

One type of CRE infection has been reported in medical facilities in 42 states during the last 10 years.

1 in 2

CRE germs kill up to half of patients who get bloodstream infections from them.

Untreatable and hard-to-treat infections from CRE germs are on the rise among patients in medical facilities. CRE germs have become resistant to all or nearly all the antibiotics we have today. Types of CRE include KPC and NDM. By following CDC guidelines, we can halt CRE infections before they become widespread in hospitals and other medical facilities and potentially spread to otherwise healthy people outside of medical facilities.

Health Care Providers can

◇ Know if patients in your facility have CRE.

- Request immediate alerts when the lab identifies CRE.
- Alert the receiving facility when a patient with CRE transfers, and find out when a patient with CRE transfers into your facility.

◇ Protect your patients from CRE.

- Follow contact precautions and hand hygiene recommendations when treating patients with CRE.
- Dedicate rooms, staff, and equipment to patients with CRE.
- Prescribe antibiotics wisely.
- Remove temporary medical devices such as catheters and ventilators from patients as soon as possible.

*Long-term acute care hospitals provide complex medical care, such as ventilation or wound care, for long periods of time.

→ See page 4

Want to learn more? Visit

www http://www.cdc.gov/vitalsigns

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion

Action is needed now to stop these deadly infections.

Problem

CRE germs have found ways to beat antibiotics.

- CRE infections are caused by a family of germs that are a normal part of a person's healthy digestive system. These germs can cause infections when they get into the bladder, blood, or other areas where germs don't belong.
- Some of these germs have become resistant to all or almost all antibiotics, including last-resort drugs called carbapenems. These resistant germs are called CRE.
- Almost all CRE infections happen to patients receiving serious medical care. CRE infections are hard to treat, and in some cases, untreatable. CRE kill up to half of patients who get bloodstream infections from them.
- In addition to spreading among people, CRE easily spread their antibiotic resistance to other kinds of germs, making those potentially untreatable as well.

CRE infections are spreading, and urgent action is needed to stop them.

- Although CRE germs are not very common, they have increased from 1% to 4% in the past decade. One type of CRE has increased from 2% to 10%.
- CRE are more common in some US regions, such as the Northeast, but 42 states report having had at least one patient test positive for one type of CRE.
- About 18% of long-term acute care hospitals and about 4% of short-stay hospitals in the US had at least one CRE infection during the first half of 2012.
- CRE's ability to spread themselves and their resistance raises the concern that potentially untreatable infections could appear in otherwise healthy people.

CRE infections can be prevented.

- Medical facilities in several states have reduced CRE infection rates by following CDC's prevention guidelines (see box).
- Israel decreased CRE infection rates in all 27 of its hospitals by more than 70% in one year with a coordinated prevention program.
- The US is at a critical time in which CRE infections could be controlled if addressed in a rapid, coordinated, and consistent effort by doctors, nurses, lab staff, medical facility leadership, health departments/states, policy makers, and the federal government.

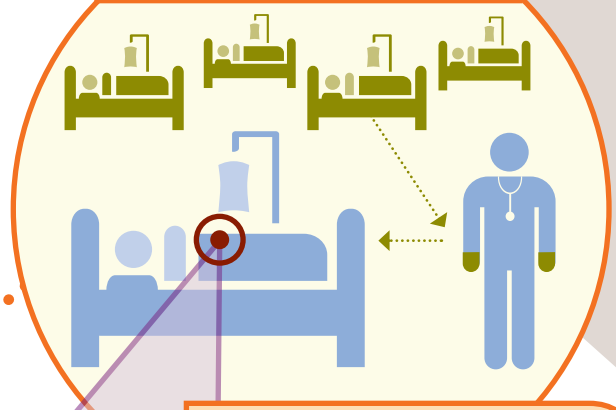
CDC's 2012 CRE Toolkit provides CRE prevention guidelines for doctors and nurses, hospitals, long-term acute care hospitals, nursing homes, and health departments. It gives step-by-step instructions for facilities treating patients with CRE infections and for those not yet affected by them. (http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html)

Risk of CRE Infections

1. Local Short-Stay Hospital

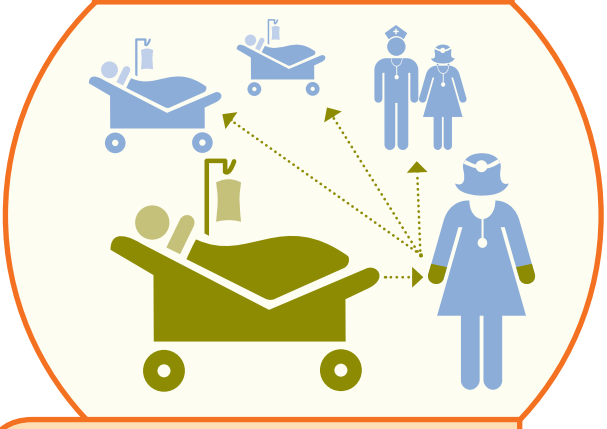
Jan has a stroke and is in the hospital. She is stable but needs long-term critical care at another facility.

2. Long-Term Acute Care Hospital



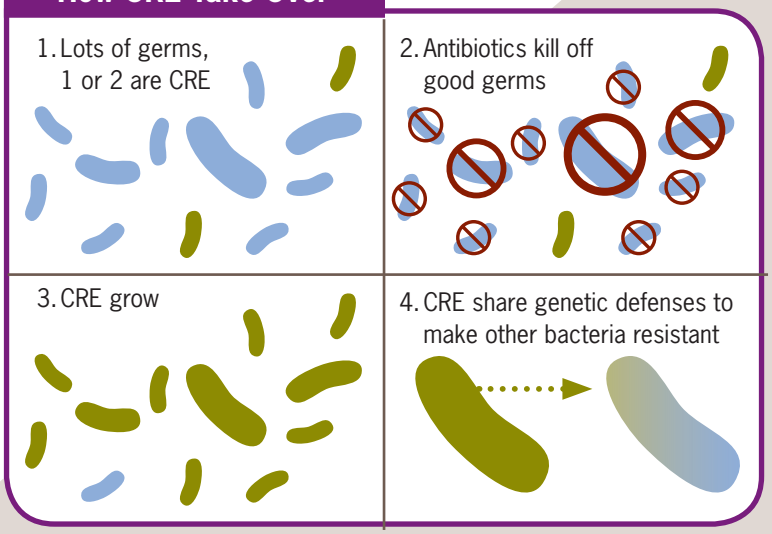
Other patients in this facility have CRE. A nurse doesn't wash his hands, and CRE are spread to Jan. She develops a fever and is put on antibiotics without proper testing.

3. Local Short-Stay Hospital



Jan becomes unstable and goes back to the hospital, but her new doctors don't know she has CRE. A doctor doesn't wash her hands after treating Jan. CRE are spread to other patients.

How CRE Take Over



SOURCE: CDC Vital Signs, 2013

CO

Colorado Department of Public Health and Environment

- Colorado requires laboratories to report CRE and actively tracks the germs' presence.
- CDC, Colorado, and several facilities implemented CDC recommendations to control an outbreak of CRE.

Result: The outbreak was stopped.

Florida Department of Health

FL

- CDC worked with Florida to stop a year-long CRE outbreak in a long-term acute care hospital.
- Improved use of CDC recommendations such as educating staff; dedicating staff, rooms, and equipment to patients with CRE; and improving use of gloves and gowns.
- **Result:** The percentage of patients who got CRE at the facility dropped from 44% to 0.

What Can Be Done

Federal Government is

- Monitoring the presence of and risk factors for CRE infections through the National Healthcare Safety Network (NHSN) and Emerging Infections Program (EIP).
- Providing CRE outbreak support such as staff expertise, prevention guidelines, tools, and lab testing to states and facilities.
- Developing detection methods and prevention programs to control CRE. CDC's "Detect and Protect" effort supports regional CRE programs.
- Helping medical facilities improve antibiotic prescribing practices.

States and Communities can

- Know CRE trends in your region.
- Coordinate regional CRE tracking and control efforts in areas with CRE. Areas not yet or rarely affected by CRE infections can be proactive in CRE prevention efforts.
- Require facilities to alert each other when transferring patients with any infection.
- Consider including CRE infections on your state's Notifiable Diseases list.

Health Care CEOs/Medical Officers can

- Require and strictly enforce CDC guidance for CRE detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify CRE and alert clinical and infection prevention staff when these germs are present.
- Know CRE trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about infections, including CRE.
- Join or start regional CRE prevention efforts, and promote wise antibiotic use.

Health Care Providers can

- Know if patients with CRE are hospitalized at your facility, and stay aware of CRE infection rates. Ask if your patients have received medical care somewhere else, including another country.
- Follow infection control recommendations with every patient, using contact precautions for patients with CRE. Whenever possible, dedicate rooms, equipment, and staff to CRE patients.
- Prescribe antibiotics wisely (http://www.cdc.gov/getsmart/healthcare). Use culture results to modify prescriptions if needed.
- Remove temporary medical devices as soon as possible.

Patients can

- Tell your doctor if you have been hospitalized in another facility or country.
- Take antibiotics only as prescribed.
- Insist that everyone wash their hands before touching you.

www http://www.cdc.gov/vitalsigns

For more information, please contact
Telephone: 1-800-CDC-INFO (232-4636)
***TTY*: 1-888-232-6348**
E-mail: cdcinfo@cdc.gov
Web: www.cdc.gov
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Vital Signs: Carbapenem-Resistant Enterobacteriaceae

Abstract

Background: Enterobacteriaceae are a family of bacteria that commonly cause infections in health-care settings as well as in the community. Among Enterobacteriaceae, resistance to broad-spectrum carbapenem antimicrobials has been uncommon. Over the past decade, however, carbapenem-resistant Enterobacteriaceae (CRE) have been recognized in health-care settings as a cause of difficult-to-treat infections associated with high mortality.

Methods: The percentage of acute-care hospitals reporting at least one CRE from health-care–associated infections (HAIs) in 2012 was estimated using data submitted to the National Healthcare Safety Network (NHSN) in 2012. The proportion of Enterobacteriaceae infections that were CRE was calculated using two surveillance systems: 1) the National Nosocomial Infection Surveillance system (NNIS) and NHSN (for 2001 and 2011, respectively) and 2) the Surveillance Network–USA (TSN) (for 2001 and 2010). Characteristics of CRE culture-positive episodes were determined using data collected as part of a population-based CRE surveillance project conducted by the Emerging Infections Program (EIP) in three states.

Results: In 2012, 4.6% of acute-care hospitals reported at least one CRE HAI (short-stay hospitals, 3.9%; long-term acute-care hospitals, 17.8%). The proportion of Enterobacteriaceae that were CRE increased from 1.2% in 2001 to 4.2% in 2011 in NNIS/NHSN and from 0% in 2001 to 1.4% in 2010 in TSN; most of the increase was observed in *Klebsiella* species (from 1.6% to 10.4% in NNIS/NHSN). In the EIP surveillance, 92% of CRE episodes occurred in patients with substantial health-care exposures.

Conclusions: Carbapenem resistance among common Enterobacteriaceae has increased over the past decade; most CRE are associated with health-care exposures.

Implications for Public Health: Interventions exist that could slow the dissemination of CRE. Health departments are well positioned to play a leading role in prevention efforts by assisting with surveillance, situational awareness, and coordinating prevention efforts.

Introduction

The Enterobacteriaceae are a large family of gram-negative bacilli that are normal inhabitants of the gastrointestinal tract of humans and other animals (*1*). These organisms are a common cause of community-acquired and health-care–acquired infections. Although this family includes more than 70 genera, the health-care–associated Enterobacteriaceae most commonly reported to CDC's National Healthcare Safety Network (NHSN) surveillance system are *Escherichia coli*, *Klebsiella* species, and *Enterobacter* species (*2*). The past several decades have seen the spread of Enterobacteriaceae with resistance to broad-spectrum antimicrobials; however, clinicians in the United States have relied on the carbapenem antimicrobial class (imipenem, meropenem, doripenem, and ertapenem) to treat infections caused by these resistant organisms. Carbapenem-resistant Enterobacteriaceae (CRE) were relatively uncommon in the United States before 2000 (*3*). Unlike resistance in methicillin-resistant *Staphylococcus aureus* (MRSA), which is one bacterial species and is mediated by a single mechanism, carbapenem resistance is complex; it

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can occur in different Enterobacteriaceae and be mediated by several mechanisms, including production of enzymes that inactivate carbapenems (carbapenemases). *Klebsiella pneumoniae* carbapenemase (KPC), an enzyme encoded by a highly transmissible gene, was first identified from a *Klebsiella* isolate in 2001 (*4*) and has now spread widely throughout the United States and around the world. In addition to KPC, a number of additional carbapenemases that have emerged among Enterobacteriaceae outside the United States (e.g., New Delhi metallo-beta-lactamase [NDM]) have been identified in this country. CRE can spread in health-care settings and cause infections with mortality rates of 40% to 50% (*5*–*7*). In this report, recent changes in the epidemiology and incidence of CRE in the United States are described.

Methods

The objectives of this evaluation were to 1) describe the extent of CRE spread among acute-care hospitals, 2) estimate the proportion of clinical isolates of Enterobacteriaceae that are resistant to carbapenems in the United States, and 3) determine characteristics of CRE culture-positive episodes. Because no single surveillance system includes all the data required for these analyses, data from three systems are included in this report. CRE definitions used for objectives 1 and 2 were slightly different than that used for objective 3 because of the use of these different systems.

The first objective was accomplished using NHSN data for the first 6 months of 2012. All facilities performing surveillance for central-line–associated bloodstream infections (CLABSIs) or catheter-associated urinary tract infections (CAUTIs) were reviewed for reports of CRE isolates, defined as *E. coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Enterobacter cloacae*, or *Enterobacter aerogenes* that were nonsusceptible to imipenem, meropenem, or doripenem.

For the second objective, data from NHSN and its predecessor, the National Nosocomial Infection Surveillance system (NNIS), were used. Intensive-care unit (ICU) CLABSIs, ICU CAUTIs, and surgical site infections after colon surgery or coronary artery bypass grafting reported to NNIS in 2001 or NHSN in 2011 for which an isolate of one of the Enterobacteriaceae listed above was reported were included. To evaluate infections across another set of isolates collected hospital-wide, a similar analysis was performed by the Center for Disease Dynamics, Economics, and Policy, using data from the Surveillance Network-USA (TSN) (managed by Eurofins Medinet; Chantilly, Virginia). TSN is an electronic repository of susceptibility test results collected from approximately 300 laboratories that are selected to be demographically representative of the United States at the level of the nine U.S. Census regions (*8*). Similar definitions were used for the TSN analysis; however, *K. oxytoca* was not included, and surveillance periods included 2001 and the first 6 months of 2010.

The third objective was accomplished using data collected during the internally funded pilot of a population-based CRE surveillance project conducted through CDC's Emerging Infections Program (EIP) at three sites (Atlanta, Georgia; Minneapolis-St. Paul, Minnesota; and Portland, Oregon metropolitan areas). Laboratories were asked for reports of CRE, defined in this report as Enterobacteriaceae from sterile-site and urine cultures that were nonsusceptible to imipenem, meropenem, or doripenem and resistant to all third-generation cephalosporins tested (e.g., ceftriaxone, cefotaxime, and ceftazidime). Resistance to third-generation cephalosporins was included in this surveillance system to increase the specificity for carbapenemase-producing Enterobacteriaceae. Medical records for CRE patients were reviewed. CRE-positive clinical cultures were classified as hospital-onset if the culture was taken from a hospital inpatient after the third day of admission. A health-care exposure was defined as a recent (i.e., within the past year) hospitalization, long-term–care admission, surgery, dialysis, or the presence of an indwelling device in the 2 days before the positive culture.

Results

During the first 6 months of 2012, among the 3,918 U.S. acute-care hospitals performing surveillance for either CAUTI or CLABSI in any part of their hospital, 181 (4.6%) reported one or more infections with CRE (145 [3.9%] in short-stay hospitals; 36 [17.8%] in long-term acute-care hospitals [LTACHs]). The percentage of facilities with CRE was stratified by selected characteristics; of note, the percentage of hospitals reporting CRE was highest in the Northeast and among larger and teaching hospitals (Table 1).

The percentage of Enterobacteriaceae that were CRE reported to NNIS in 2001 was 1.2%; in NHSN in 2011, it was 4.2%. The proportion CRE varied by organism and increased most for *Klebsiella* species, from 1.6% to 10.4% (Table 2). Data from TSN demonstrated an increase from 0% to 1.4%, with the largest increase among *K. pneumoniae* (0% to 5.3%).

During the 5-month EIP project pilot, 72 CRE were identified from 64 patients (56 patients had one positive culture; eight had two). Most came from the Atlanta metropolitan area (59) followed by Minneapolis-St. Paul (10), and Portland (three). Most CRE were *Klebsiella* species (49) followed by *Enterobacter* species (14) and *E. coli* (nine). The most common source was urine (89%), followed by blood (10%). CRE culture-positive episodes were stratified by selected characteristics (Table 3). Most isolates were from cultures collected outside of acute-care hospitals (47 of 71); however, most of these community-onset isolates were from patients with health-care exposures (41 of 47), particularly recent hospitalization (72%).

TABLE 1. Number and percentage of facilities reporting carbapenem-resistant* Enterobacteriaceae† from a catheter-associated urinary tract infection (CAUTI) or a central-line–associated bloodstream infection (CLABSI), by selected characteristics — United States, National Healthcare Safety Network, January–June 2012

Characteristic	No. of facilities with carbapenem-resistant Enterobacteriaceae from CAUTI or CLABSI	Total no. of facilities performing CAUTI or CLABSI surveillance (N = 3,918)	(%)§¶
Facility type			
All acute-care hospitals	181	3,918	(4.6)
Short-stay acute-care hospital	145	3,716	(3.9)
Long-term acute-care hospital	36	202	(17.8)
Hospital size (no. of beds)			
<100	48	1,609	(3.0)
100–299	46	1,480	(3.1)
300–499	41	541	(7.6)
≥500	45	258	(17.4)
Medical school affiliation			
Yes	102	1,079	(9.5)
No	53	2,839	(1.9)
U.S. Census region**			
Northeast	63	658	(9.6)
Midwest	30	927	(3.2)
South	50	1,503	(3.3)
West	29	804	(3.6)
Other††	9	26	(34.6)

* Intermediate or resistant to imipenem, meropenem, or doripenem.
† *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Escherichia coli*, *Enterobacter aerogenes*, or *Enterobacter cloacae*.
§ Total percentage of facilities performing any surveillance for any CAUTI and CLABSI during the first 6 months of 2012.
¶ For each category, p<0.01 by chi-square test.
** *Northeast*: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont; *Midwest*: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin; *South*: Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia; *West*: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.
†† Armed Forces, Puerto Rico, and U.S. Virgin Islands.

Conclusions and Comment

Although CRE remain relatively uncommon in most acute-care hospitals in the United States, they have become an increasingly recognized cause of infection during the past decade, especially among *Klebsiella*, likely because of the emergence of carbapenemase-producing strains. In 2012, the number of facilities reporting CRE as a cause of infection was small, and spread of these organisms appears to be uneven both regionally and among facilities within regions. Fewer than 5% of short-stay acute-care hospitals reported CRE from health-care–associated infections in the first half of 2012; CRE more often were reported from LTACHs. Data from population-based surveillance suggest most CRE clinical isolates came from cultures collected outside of hospitals from patients with substantial health-care exposures. These findings suggest that although CRE are increasing in prevalence, their distribution is limited.

CRE are important for several reasons. First, invasive infections (e.g., bloodstream infections) with CRE are associated with mortality rates exceeding 40% (*5*); this is significantly higher than mortality rates observed for carbapenem-susceptible Enterobacteriaceae. Of note, because the majority of positive cultures were from urine, overall in-hospital mortality rates associated with positive cultures were lower in the EIP CRE surveillance (4%). Second, carbapenem-resistant strains frequently possess additional resistance mechanisms that render them resistant to most available antimicrobials; pan-resistant CRE have been reported (*9*). Further, novel antimicrobials for multidrug-resistant gram-negative bacilli are in early stages of development and not likely to be available soon (*10*). Third, CRE can spread rapidly in health-care settings (*11,12*). Fourth, Enterobacteriaceae are a common cause of community infections, and CRE have the potential to move from their current niche among health-care–exposed patients into the community (*13*). Multidrug-resistance is a problem in other gram-negative bacilli such as *Pseudomonas* and *Acinetobacter* species. However, these organisms are a less common cause of health-care infections and have less potential to spread resistance to other bacteria and into the community (*2*).

Current CRE prevention strategies are based on the identification of patients colonized or infected with CRE followed by implementation of contact precautions. Colonization commonly is detected through rectal surveillance cultures of patients at risk for CRE (e.g., patients exposed to known cases of CRE). Active case detection and immediate implementation of interventions, often including cohorting staff and CRE patients (i.e., segregating CRE-colonized or CRE-infected patients and the health-care personnel who care for them from those without CRE and the health-care personnel who care for them), has been used successfully to control CRE in acute-care and long-term–care settings (*6,7,14*). Efforts to ensure appropriate antibiotic use in hospitals and nursing homes also are critical to slowing CRE emergence.* Patients who are colonized or infected with CRE often are cared for in multiple types of health-care institutions during their illnesses. Therefore, having a broader, multi-institutional or regional approach to prevention is necessary for control, particularly in regions where CRE are just beginning to be recognized. Regional efforts to control multidrug-resistant

* Detailed prevention recommendations for acute-care and long-term–care facilities are available at http://www.cdc.gov/hai/organisms/cre/cre-toolkit.

TABLE 2. Number of Enterobacteriaceae isolates, percentage reported to be tested against carbapenems, and percentage reported as carbapenem-resistant,* by data source, year, and type of organism — United States, National Nosocomial Infections Surveillance system (NNIS), National Healthcare Safety Network (NHSN), and the Surveillance Network–USA (TSN)†

	NNIS (2001)			NHSN (2011)		
Type of organism	No. of isolates	Reported as tested against ≥1 carbapenem No. (%)	Reported as carbapenem-resistant* No. (%)	No. of isolates	Reported as tested against ≥1 carbapenem No. (%)	Reported as carbapenem-resistant* No. (%)
Klebsiella pneumoniae and *oxytoca*	654	253 (38.7)	4 (1.6)	1,902	1,312 (69.0)	136 (10.4)
Escherichia coli	1,424	421 (29.6)	4 (1.0)	3,626	2,348 (64.8)	24 (1.0)
Enterobacter aerogenes and *cloacae*	553	288 (52.1)	4 (1.4)	1,045	728 (69.7)	26 (3.6)
Total	**2,631**	**962(36.6)**	**12 (1.2)**	**6,573**	**4,388 (66.8)**	**186 (4.2)**

	TSN (2001)			TSN (2010)§		
Type of organism	No. of isolates	Reported as tested against ≥1 carbapenem No. (%)	Reported as carbapenem-resistant* No. (%)	No. of isolates	Reported as tested against ≥1 carbapenem No. (%)	Reported as carbapenem-resistant* No. (%)
Klebsiella pneumoniae	19,522	19,522 (100.0)	0 —	11,155	11,155 (100.0)	593 (5.3)
Esherichia coli	47,603	47,603 (100.0)	0 —	31,890	31,890 (100.0)	32 (0.1)
Enterobacter aerogenes and *cloacae*	14,764	14,764 (100.0)	3 (0)	5,768	5,768 (100.0)	69 (1.2)
Total	**81,889**	**81,889 (100.0)**	**3 (0)**	**48,813**	**48,813 (100.0)**	**694(1.4)**

* Intermediate or resistant to imipenem, meropenem, or doripenem.

† NNIS and NHSN include Enterobacteriaceae reported from hospital infections (i.e., intensive-care unit central-line–associated bloodstream infections, intensive-care unit catheter-associated urinary tract infections, and surgical site infections after colon surgery or coronary artery bypass grafting). TSN includes Enterobaceriaceae isolates from clinical cultures from acute-care hospitals submitted to participating laboratories.

§ Includes isolates reported during January–June 2010.

organisms (MDROs) have been employed successfully, including a coordinated effort to control vancomycin-resistant *Enterococcus* in the Siouxland region of Iowa, Nebraska, and South Dakota (*15*) and a national response to MRSA in the Netherlands (*16*). For CRE, Israel has effectively employed a nationwide coordinated control effort since KPC-producing strains emerged there in 2006 (*6*).

State and local health departments are well positioned to lead CRE control efforts because of their expertise in surveillance and prevention and their ability to interact among all the health-care facilities in their jurisdiction. To date, many health departments have conducted surveillance efforts in an attempt to identify the CRE incidence in their region (*17*).† In addition, six states have made CRE reportable, and three additional states are actively pursuing this option. Requiring CRE reporting can allow for a better understanding of the changing CRE burden and can help facilitate intervention. Beyond surveillance, several states have developed and implemented plans to assist health-care facilities with control efforts when CRE are identified. As new MDROs emerge over time, this regional approach to MDRO prevention has implications beyond CRE as well.

† An example of a survey that has been adapted by health departments to evaluate CRE incidence and CRE prevention activities in a region is available at http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html.

The findings in this report are subject to at least three limitations. First, antimicrobial susceptibility data reported to NNIS and NHSN were generated at individual institutions rather than a central laboratory, and testing methodologies vary between facilities. Second, susceptibility interpretation is based on the recommended breakpoints used when tested. Although carbapenem breakpoints for Enterobacteriaceae were lowered in 2010 (*18*) and might have influenced the increase in the percentage of isolates that were carbapenem-resistant, most laboratories would not have incorporated those changes by 2011. Finally, in some instances, complete susceptibility test results, particularly for carbapenems, were not reported to NNIS or NHSN, leading to a subset of isolates that were not included in these analyses. Not reporting results for carbapenems would be more likely when organisms were susceptible to less broad-spectrum antimicrobials; therefore, many of the organisms for which carbapenem susceptibility information was not available might have been susceptible. As a result, the percentage resistant reported from NNIS and NHSN likely represents an overestimate of the actual percentage resistant; however, the proportion of NHSN facilities reporting at least one CRE should not be affected.

The high proportion of LTACHs with CRE in 2012 highlights the need to expand prevention outside of short-stay acute-care hospitals into settings that, historically, have had less developed infection prevention programs. Additional research is needed to

TABLE 3. Number and percentage of episodes of positive cultures for carbapenem-resistant* *Enterobacteriaceae*† (N = 72) from three communities,§ by selected characteristics — United States, Emerging Infections Program, August–December 2011

Characteristic	No.	(%)
Patient characteristics		
Female sex	36	(50)
White race	32	(45)
Median age (range) (yrs)	60	(8–91)
<18	2	(3)
≥65	30	(42)
Type of health-care exposure¶		
Hospitalization	34	(72)
Presence of urinary catheter within the past 2 days	22	(47)
Long-term care facility	17	(36)
Surgery	12	(26)
Presence of other indwelling device within the past 2 days	11	(23)
Presence of central line within the past 2 days	9	(19)
None	6	(4)
Dialysis	3	(13)
Outcome		
Hospitalized	59	(82)
Intensive-care unit within 7 days of positive culture	16	(22)
Died	3	(4)

* Nonsusceptible to imipenem, meropenem, or doripenem and resistant to all third-generation cephalosporins tested (e.g., ceftriaxone, cefotaxime, ceftazidime).

† *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Escherichia coli*, *Enterobacter aerogenes*, or *Enterobacter cloacae*.

§ Atlanta, Georgia; Minneapolis-St. Paul, Minnesota; and Portland, Oregon.

¶ Within the past year, unless noted otherwise, among community-onset cultures (n=47).

clarify unanswered questions, including assessing which CRE prevention strategies are most effective and investigating new prevention approaches such as decolonization. Fortunately, many regions are in a position to prevent the further emergence of these organisms if they act aggressively. To do so will require expanded and coordinated action from clinicians, facility administrators, and public health officials.

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Key Points

- Enterobacteriaceae are gram-negative bacteria (e.g., *Klebsiella, Proteus, Serratia, Enterobacter, and Escherichia coli*) that can cause invasive disease but generally have been susceptible to a variety of antibiotics. Carbapenem-resistant Enterobacteriaceae (CRE) are Enterobacteriaceae that have become highly resistant to most or all antibiotics through several mechanisms. Carbapenem resistance, while relatively uncommon among Enterobacteriaceae (observed in about 4% of Enterobacteriaceae in this study), has increased from about 1% during the past decade. CRE bloodstream infections are associated with mortality rates approaching 50%.
- CRE has now spread throughout the United States but in most areas they remain relatively uncommon; about 4% of acute-care hospitals and 18% of long-term acute-care hospitals reported at least one CRE to the National Healthcare Safety Network in the first 6 months of 2012. Nearly all patients with CRE were currently or recently treated in a health-care setting. However, CRE could spread into the community among otherwise healthy persons.
- Preventing spread is important before CRE gains a foothold in more hospitals or in the community. This requires active case detection and contact precautions for colonized or infected patients as well as cohorting of patients and staff; appropriate antibiotic use in all settings; and communication about infections when patients transfer. Regional and state-based approaches have been shown to be effective in reducing incidence.
- Additional information is available at http://www.cdc.gov/vitalsigns.

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EXPERT REVIEWS

Epidemiology and prevention of carbapenem-resistant Enterobacteriaceae in the United States

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Carbapenem-resistant Enterobacteriaceae (CRE) are multidrug-resistant organisms with few treatment options that cause infections associated with substantial morbidity and mortality. CRE outbreaks have been increasingly reported worldwide and are mainly due to the emergence and spread of strains that produce carbapenemases. In the United States, transmission of CRE is primarily driven by the spread of organisms carrying the *Klebsiella pneumoniae* carbapenemase enzyme, but other carbapenemase enzymes, such as the New-Delhi metallo-β-lactamase, have also emerged. Currently recommended control strategies for healthcare facilities include the detection of patients infected or colonized with CRE and implementation of measures to prevent further spread. In addition to efforts in individual facilities, effective CRE control requires coordination across all healthcare facilities in a region. This review describes the current epidemiology and surveillance of CRE in the United States and the recommended approach to prevention.

Keywords: carbapenem-resistant Enterobacteriaceae • infection prevention • *Klebsiella pneumoniae* carbapenemase • multidrug-resistant organism • New Delhi metallo-β-lactamase

In recent years, carbapenem-resistant Enterobacteriaceae (CRE) have been increasingly recognized as a cause of healthcare-associated infections in many parts of the world. Outbreaks of disease have been reported from several countries including the USA [1–6]. Although non-susceptibility to carbapenems among Enterobacteriaceae can be acquired through different mechanisms, including the combination of porin mutations that decrease carbapenem penetration with production of certain types of β-lactamases (i.e., AmpC β-lactamases or extended-spectrum β-lactamases [ESBL] [7–9]), much of the increase in CRE is due to the emergence and spread of organisms producing β-lactamases effective against the carbapenem class of antibiotics (i.e., carbapenemases). These β-lactamases are frequently encoded by transmissible genetic elements that can facilitate their spread among bacterial species. In the USA, the early expansion of CRE was largely driven by transmission of a single strain of *Klebsiella pneumoniae* (multilocus sequence type 258) producing the *K. pneumoniae* carbapenemase (KPC) that has subsequently been identified in other parts of the world [6,10–12]. To date, numerous KPC alleles have been identified; hereafter, we will refer to this class of carbapenemase as 'KPC'.

Experience investigating CRE clusters has resulted in a better understanding of effective infection prevention strategies and the development of tools and resources for healthcare facilities as well as state and local health departments. In this review, we will summarize the epidemiology of CRE in the USA, focusing primarily on carbapenemase producers, describe the surveillance and detection of CRE and discuss strategies to prevent CRE transmission at both the facility and regional level.

Epidemiology of CRE in the USA

Overview of carbapenemase-producing CRE

Data on the incidence and epidemiology of CRE in the USA are available from several surveillance systems. The Surveillance Network Database USA, which is a nationally

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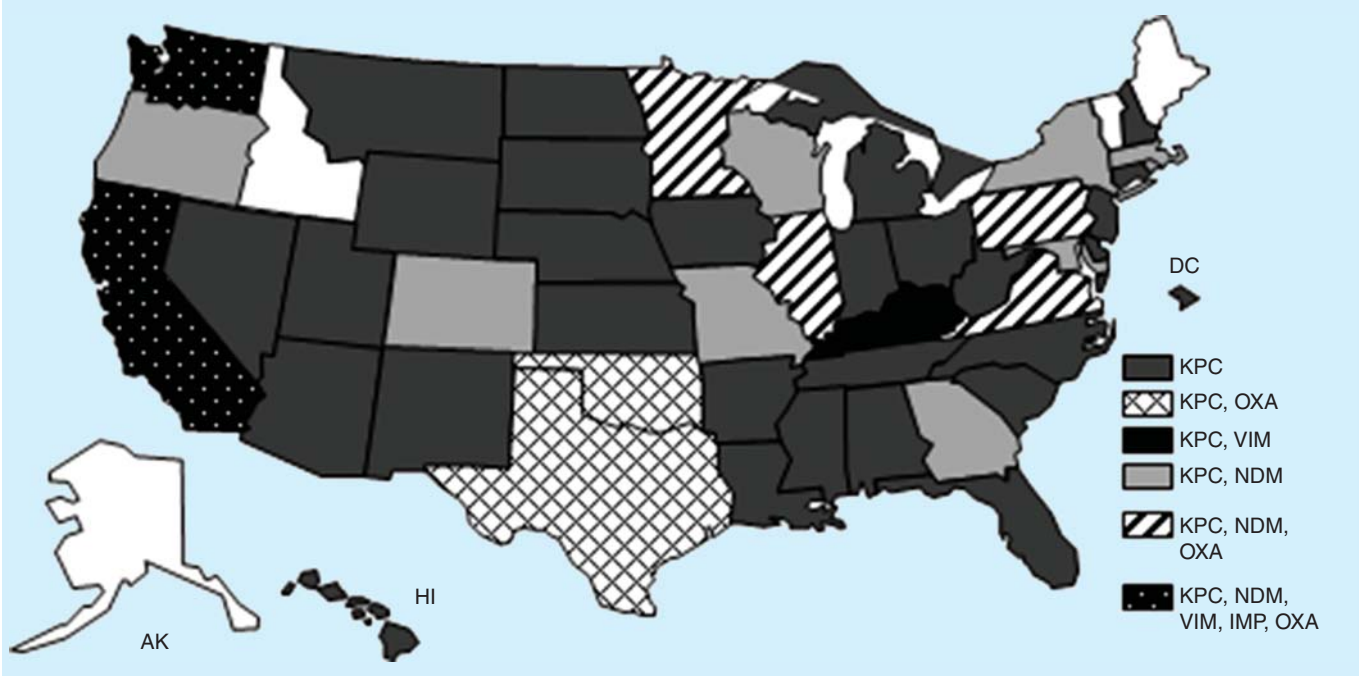

Figure 1. Geographical distribution of carbepenemase-producing Enterobacteriaceae in the USA, November 2013.
IMP: Active on imipenem; KPC: *Klebsiella pneumoniae* carbapenemase; MBL: Metallo-β-lactamases; NDM: New Delhi metallo-β-lactamase; OXA: Oxacillinases; VIM: Verona integron-encoded.

representative repository of antimicrobial susceptibility results from approximately 300 laboratories in the USA, first identified resistance to imipenem among *K. pneumoniae* in 2004 and demonstrated a gradual increase; 4.3% of all *K. pneumoniae* were imipenem resistant by 2010 [13]. Larger increases in the percent of Enterobacteriaceae non-susceptible to a carbapenem (i.e., imipenem meropenem or doripenem) have been reported from the CDC surveillance system, which includes the National Healthcare Safety Network (NHSN) and its precursor, the National Nosocomial Infection Surveillance System [14]. Collectively, approximately 1.2% of the most common Enterobacteriaceae reported to Nosocomial Infection Surveillance System in 2001 were non-susceptible to at least one of the three carbapenems listed above. However, by 2011, the percentage of Enterobacteriaceae reported to the NHSN that were non-susceptible to at least one of the three carbapenems had risen to 4.2%, with the greatest increase observed among *K. pneumoniae* (from 1.6 to 10.4%). In addition, although the sensitivity and specificity of discharge coding data for CRE is unknown, a recent report using such data suggests that, beginning in 2006, CRE emerged as an important cause of urinary tract infections associated with hospitalizations, reaching an annual rate of 0.51 cases per 1000 hospitalizations in 2009 [15].

As alluded to above, much of the increasing incidence of CRE in the USA is due to the emergence and spread of KPC-producing Enterobacteriaceae. KPC was first identified in a *K. pneumoniae* isolated from a patient in North Carolina in 1996 as part of a project evaluating antimicrobial resistance in intensive care units (ICU), but was reported in 2001 [16]. The initial spread of KPC-producing strains was concentrated in the eastern USA, particularly in parts of New York and New Jersey [17–19], but over the last 5 years, KPC-producing Enterobacteriaceae have been reported from across the country and throughout the world [6,20]. As of November 2013, at least one KPC-producing CRE isolate has been reported from 46 states (Figure 1). Among CRE isolates reported to CDC for reference testing, KPC has been primarily found in *K. pneumoniae*, *Escherichia coli* and *Enterobacter* spp. As previously noted, the majority of the US KPC-producing *K. pneumoniae* isolates belong to a common strain type, ST258 [11]. Despite the expansion of KPC-producing strains across the USA, they still remain heterogeneously distributed within most states.

While KPC remains the predominant carbapenemase among Enterobacteriaceae in the USA, other carbapenemases that are more common in other parts of the world have also been identified (Figure 1). Although still rare in the USA, the most frequently reported among these is the New Delhi metallo-β-lactamase (NDM). Of note, several NDM alleles have been identified to date; hereafter, we will refer to this class of carbapenemase as 'NDM'. The first NDM-producing isolate was recovered in 2008 from a patient in Sweden who had previously received medical care in India [21]. NDM was subsequently identified in multiple species of Enterobacteriaceae from patients in the UK, many of whom had previous hospitalizations in India and Pakistan, and from patients from various areas within the Indian subcontinent [22]. By 2010, NDM-producing CRE were being described worldwide [23–28], including the first report of a US isolate in 2009 [29]. Consistent with initial reports in the UK and other parts of the

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world [22,30], many of the early cases in the USA were in patients who had received prior medical care in countries where these organisms are more common, including the Indian subcontinent [29,31]. The majority of these early cases were either not associated with further transmission or associated with transmission only to a single patient. However, beginning in 2012, there has been a sharp rise in the number of NDM-producing CRE reported to CDC. Among the 91 US NDM-producing isolates identified as of 1 December 2013, 80 (88%) were identified since the beginning of 2012. Furthermore, the epidemiology of these organisms also appears to be changing with increasing numbers of NDM-producing CRE isolated from patients who had not traveled outside the country, suggesting local acquisition.

Three US outbreaks of NDM-producing CRE have been published to date. The first outbreak involved transmission between a hospitalized patient in Rhode Island who had recently received medical care in Vietnam and a second patient on the same hospital ward, who was identified through surveillance cultures of epidemiologically linked contacts of the initial patient [32]. No additional NDM-producing CRE were identified among other patients housed on the same ward. The second outbreak occurred in Colorado and involved eight patients with NDM-producing *K. pneumoniae* isolates that were highly related by pulsed-field gel electrophoresis (PFGE) [33]. Three of these patients had clinical infection, and five were found to be asymptomatically colonized. One of the patients had previously been hospitalized in the Philippines; none of the other patients had traveled outside of the USA. An investigation identified several hospital units that were likely transmission sites, but an index patient was never identified. The third NDM outbreak occurred in northeastern Illinois and was associated with a contaminated duodenoscope used for endoscopic retrograde cholangiopancreatography (ERCP) that resulted in transmission of NDM-producing *E. coli* to at least 29 patients [34]. Both an NDM-producing *E. coli* and KPC-producing *K. pneumoniae* were cultured from the distal part of the duodenoscope (around the elevator riser) after it had been reprocessed. All *E. coli* isolates recovered from the patients and duodenoscope were highly related by PFGE. No breaches in the recommended procedures for reprocessing of ERCP endoscopes were identified during the investigation.

In addition to NDM, Enterobacteriaceae producing other metallo-β-lactamases (MBL) have been identified in the USA. Between November 2009 and July 2013, nine patients with Enterobacteriaceae isolates producing active on imipenem (IMP) or Verona integron-encoded MBL (VIM) enzymes were confirmed at the CDC. Only three of the eight patients, for whom detailed epidemiology was available (two VIM, one IMP), had received recent medical care outside the USA.

Another group of carbapenemases found in CRE are the oxacillinases (OXA), which comprise a heterogeneous group of class D β-lactamases and have increasingly been reported among Enterobacteriaceae [5]. Of particular concern is the OXA-48 family (hereafter 'OXA-48'), which has recently emerged as one of the predominant carbapenemases in the Middle East, North Africa and Europe [35]. The first published description of OXA-48-producing CRE in the USA was of two isolates that were collected in 2009 as part of a worldwide laboratory-based surveillance of carbapenemase-producing *K. pneumoniae* isolates from intra-abdominal infections [36]. Since then, additional OXA-48-producing CRE have been identified, including a recent report of two patients with OXA-48-producing *K. pneumoniae* recovered from perirectal swabs who were hospitalized within a 4-month period at the same facility [37]. Both of these patients had previous healthcare exposures outside the USA. Including these two patients, from January 2011 to July 2013, 14 patients with OXA-48-producing CRE have been confirmed by CDC. Of note, two of the OXA-48-producing *K. pneumoniae* isolates also produced NDM.

Risk factors & outcomes associated with CRE

To evaluate factors associated with CRE-positive cultures, CDC piloted a laboratory-initiated, population-based surveillance program, known as the Multi-site Gram-negative Surveillance Initiative (MuGSI), in three US metropolitan areas beginning in August 2011 [38]. During the 5-month pilot in 2011, 72 CRE (includes both carbapenemase-producing and non-carbapenemase-producing isolates) were identified from 64 patients, with the vast majority isolated from urine specimens (89%). The majority of CRE-positive cultures (65%) were collected outside of short-stay acute care hospitals; however, they were mostly from patients with previous hospitalization or other healthcare exposures, such as admission to long-term care facilities, current maintenance dialysis or presence of indwelling medical devices. Six of these (13%) community-onset isolates were recovered from patients who did not have any healthcare exposure identified in the preceding year after thorough review of their medical records.

Several studies have evaluated the exposures that put patients at risk for colonization or infection with CRE (primarily KPC producers). Identified risk factors include prolonged hospitalization, presence of invasive devices, severity of underlying disease, low functional status, increasing colonization pressure and exposures to antimicrobials including, but not limited to, carbapenems [18,39–42]. In one study, the odds of acquiring CRE during a single hospitalization increased by 4% per day of antimicrobial therapy and by 15% for every 1% increase in the colonization pressure (defined as the percentage of patients on the unit who were CRE-positive) to which a patient was exposed [39]. Recent admission to post-acute care settings (long-term care settings), including long-term acute care hospitals, has also been strongly associated with CRE acquisition [43,44].

Another potential risk factor for CRE is endoscopy procedures [45–47]. Transmission of multidrug-resistant (MDR) bacteria following endoscopy procedures has been previously reported [48]. In addition to the NDM outbreak described above, at least three CRE outbreaks (two KPC, one OXA-48) associated with endoscopy have been reported; each of these

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three outbreaks resulted from inadequately reprocessed endoscopes used for gastrointestinal procedures [49–52]. The first outbreak occurred in the USA and involved a contaminated ERCP endoscope that resulted in transmission of KPC-producing *K. pneumoniae* to at least 10 patients [49]. Bacterial cultures from the implicated duodenoscope grew carbapenemase-producing Enterobacteriaceae. The second outbreak was reported in France and resulted from exposure to a contaminated duodenosope that had previously been used on a patient colonized with KPC-producing *K. pneumoniae* who was transferred from a hospital in Greece [50,51]. KPC-producing *K. pneumoniae* was recovered from 7 of 17 potentially exposed patients as well as from the duodenoscope; all recovered isolates were indistinguishable by PFGE. In the third CRE outbreak associated with duodenoscopy, which occurred in Germany, 10 patients became infected with OXA-48-producing *K. pneumoniae*, and 5 were found to be colonized with the organism following their exposure [52]. The implicated duodenoscope most probably had a defect that impacted its ability to be properly disinfected. In addition, NDM transmission has been linked to the endoscopic camera head used for urologic procedures, where camera sheathing was not routinely used, although the camera head was regularly cleaned with detergent wipes [53]. A second endoscopy-associated outbreak of OXA-48-producing *K. pneumoniae* was reported in Germany, which involved a contaminated bronchoscope from which bacteria were recovered [52]. The true extent of transmission of MDR organisms from contaminated endoscopes is unknown.

The percentage of patients colonized with CRE who subsequently develop a positive clinical culture has ranged from 8.8 to 47% [44,54,55], with most (86%) representing a true infection [54]. Predictors for infection among CRE carriers include admission to the ICU, having a central venous catheter, exposure to antibiotics, previous invasive surgery and diabetes mellitus [44,54]. Mortality rates associated with invasive infections caused by CRE, such as bloodstream infections, often exceed 40% and are higher than those associated with carbapenem-susceptible Enterobacteriaceae [56–58]. However, as evident in the MuGSI surveillance, the overall in-hospital mortality rate may be substantially lower (4%) when including isolates from clinical cultures of non-sterile sites, such as the genitourinary tract [38].

Spread of CRE in post-acute care settings

Certain post-acute care settings, particularly long-term acute care hospitals (LTACHs), are increasingly being recognized as a reservoir for patients colonized with carbapenemase-producing CRE, in which transmission can often go undetected [59–64]. In the USA, prevalence of CRE-colonized patients in post-acute care settings during outbreak investigations has ranged from 9 to 48% [60,62,63]. In one study that screened patients admitted to four Chicago-area hospitals, the prevalence of KPC carriage among patients admitted from post-acute care settings was 8.3%, compared with a prevalence of 0% among patients from the community [65]. Prevalence of CRE also varied by the type of post-acute care setting, with sevenfold greater odds of colonization among patients admitted from LTACHs and skilled nursing facilities (SNFs) with ventilator units, compared with patients from an SNF without ventilator care [65]. During 2010–2011, point prevalence surveys for KPC-producing CRE in the Chicago region revealed a prevalence of 30.4% among LTACH patients, compared with 3.3% among ICU patients in short-stay hospitals [66].

CRE incidence in short-stay acute care hospitals compared with LTACHs has also been evaluated using NHSN. During the first half of 2012, 3.9% of all short-stay acute care hospitals participating in NHSN surveillance for central-line-associated bloodstream infections or catheter-associated urinary tract infections reported one or more infections with CRE [14]; however, the percentage of LTACHs reporting at least one CRE infection was substantially higher (17.8%).

LTACHs can also play an important role in the regional emergence of CRE [64]. By serving as a point of convergence for patients at high risk for CRE colonization, LTACHs may facilitate the amplification and dissemination of CRE as colonized patients are transferred to surrounding facilities providing higher and lower levels of care [63,64]. This process was described in a report of a multistate outbreak of KPC affecting 26 healthcare facilities; 60% of 40 cases were linked to one LTACH [64]. In this and other regional outbreaks, lack of knowledge about CRE among facility staff early in the outbreak period and lack of communication between facilities during patient transfers contributed to the spread of CRE [60,63,64].

Clinical & epidemiologic importance of CRE

Slowing the spread of CRE, particularly carbapenemase-producing strains, has become an important public health goal in the USA for several reasons. First, invasive infections caused by CRE are associated with high mortality rates [56–58]. Second, CRE often carry other resistance genes, thereby reducing the number of effective antimicrobials and substantially limiting treatment options. Pan-resistant CRE strains have been reported [67], and it may be years before new antimicrobial agents are available that have activity against these organisms. Third, as with any MDR organism, CRE have spread from patient to patient through healthcare systems as colonized or infected patients move across the continuum of care. In addition, because of the mobile nature of the plasmids that harbor these resistance genes, resistance can be transmitted between different species of Enterobacteriaceae. Finally, in the USA, CRE are primarily identified from patients with exposure to healthcare, but Enterobacteriaceae are also a common cause of infections in the community. It follows that potential exists for CRE to become a more common cause of community infections. Spread outside of healthcare has already been described for NDM-producing CRE in other countries, both as a source of community-acquired infection [22,68] and from the community environment in both India (drinking and seepage water) [69] and Vietnam (seepage water) [70].

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CRE surveillance & laboratory detection

The first step to CRE control is to understand how commonly these organisms are encountered at the facility and regional level. For healthcare facilities, this may include a retrospective review of microbiology records to determine the frequency with which CRE are identified from clinical cultures over the past 6–12 months. At a regional level, surveillance efforts might consist of surveys of local laboratories or Infection Preventionists from all facilities within the region.

In general, Enterobacteriaceae that are non-susceptible to a carbapenem represent multidrug-resistant organisms (MDROs) and should be managed accordingly [71]. Of particular concern are CRE strains that produce carbapenemases; these organisms appear to have been responsible for much of the spread of CRE in the USA since 2001. However, surveillance for carbapenemase-producing CRE is complicated by the fact that current guidance for detection of CRE in clinical specimens does not recommend routine testing for the mechanism of resistance; resistance mechanism testing is suggested only for special epidemiologic studies [72]. Furthermore, only one mechanism-specific test, the modified Hodge test (MHT), is widely used in the US clinical laboratories. The MHT was developed and evaluated during a time when carbapenemases other than KPC were exceedingly rare in the USA, and although it demonstrated good sensitivity for carbapenemase detection, even then it was known to have poor specificity among Enterobacteriaceae producing AmpC or ESBL enzymes combined with porin loss [73–76]. Since that time, as additional carbapenemase enzymes have been detected in the USA, sensitivity of the MHT has been called into question, especially for detection of NDM. In addition to the MHT, several other methods have been developed to detect carbapenemases (e.g., Carba NP test, matrix-associated laser desorption ionization-time-of-flight mass spectrometry) [77–80]. Although these methods are currently used in other parts of the world, they are not yet in widespread use in the USA.

Developing a phenotypic definition that predicts carbapenemase production has been difficult because non-carbapenemase-producing CRE can exhibit an antimicrobial susceptibility pattern that can be very similar to CRE that produce carbapenemase. In an attempt to increase specificity for CRE that produce carbapenemases (i.e., KPC, NDM), CDC has utilized the following CRE surveillance definition: non-susceptibility to imipenem, meropenem or doripenem (using current Clinical and Laboratory Standards Institute interpretive criteria) [81], and resistant to all the third-generation cephalosporins that were tested (because many plasmid-mediated carbapenemases also inactivate β-lactam antimicrobial agents) [82]. However, based on CDC reference testing for CRE, even when these more stringent criteria are applied, specificity for carbapenemase-producing strains can remain low in regions with low CRE prevalence and for certain Enterobacteriaceae. For example, among 114 CRE isolates submitted to CDC from the six US states or metropolitan areas between December 2011 and August 2013 that met this surveillance definition, 54 (47%) were carbapenemase-producing strains (specifically KPC). The majority of KPC-producing strains (>74%) submitted from five of the sites were *K. pneumoniae*, whereas 53% of the KPC-producing strains from Minnesota were *Enterobacter cloacae*. In addition, this surveillance definition has the potential to exclude some carbapenemase-producing CRE, including those that can be susceptible to the third-generation cephalosporins (e.g., OXA-48-producing CRE).

Preventing CRE transmission

Preventing CRE transmission in healthcare settings can be challenging, but is critical to delaying the further emergence of these organisms. A number of complex issues need to be considered when designing facility-specific CRE control interventions, including the extended periods that CRE-positive patients remain colonized and the inherent differences between short-stay acute care hospitals and long-term care settings which necessitate different approaches to implementation. Although much of the effort to control MDROs like CRE has been done at the facility level, the interconnectedness of the healthcare system also underscores the importance of working 'regionally' across facilities that share patients to prevent transmission. The next two sections will describe interventions for controlling CRE transmission at both facility and regional levels.

Several resources containing recommendations for the prevention of CRE transmission have been developed. In 2009, CDC released CRE-specific recommendations for the US acute care facilities [83] based on strategies outlined in the 2006 Guidelines for the Management of MDROs [71]. These recommendations were updated in 2012 with the release of the CDC CRE Toolkit [82]; this document expands upon the 2009 guidance by including facility-level interventions for both acute and long-term care settings. In addition, the CRE Toolkit provides regional prevention strategies for state and local health department implementation. Several state health departments have also developed state-specific resources and tools to guide facilities in their CRE prevention efforts [84–88].

Facility level CRE prevention

Current CDC recommendations for preventing CRE transmission in healthcare facilities are organized into core measures and supplemental interventions (Box 1). Core prevention measures are well-supported by evidence and should be utilized by all facilities regardless of the prevalence of CRE in the facility or region. These are based on Standard Precautions as well as Contact Precautions that apply to any MDRO. Supplemental interventions are either less well-supported by evidence or more difficult to implement. These can be used by facilities when the prevalence or incidence of CRE has not decreased, despite the use of core strategies or as part of a more aggressive initial approach when the first case or an outbreak has been identified within a facility or unit. For the purpose of this review, the next section will

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Box 1. Core and supplemental carbapenem-resistant Enterobacteriaceae prevention activities for acute and long-term care facilities in the USA.

Core measures

- Enhance hand hygiene
  - Promote and improve hand hygiene as part of routine uptake of Standard Precautions
  - Monitor hand hygiene adherence and provide feedback
  - Ensure access to hand hygiene stations and supplies
- Implement CP
  - Develop protocols for notifying appropriate staff when a patient with CRE is identified
  - In short-stay acute care hospitals and long-term acute care hospitals, place CRE-colonized or -infected patients on CP
  - In lower-acuity long-term care facilities (e.g., skilled nursing facilities, nursing homes), place CRE-colonized or -infected residents that are high-risk for transmission on CP; for residents at lower risk for transmission use Standard Precautions for most situations
  - Preemptive CP might be used for patients transferred from high-risk settings
  - Educate healthcare personnel about CP
  - Monitor CP adherence and provide feedback
  - No recommendation can be made for discontinuation of CP
- Promote patient and staff cohorting
  - Whenever possible, cohort CRE-colonized or -infected patients with designated staffing even if patients are housed in single rooms
  - If the number of single patient rooms is limited, reserve these rooms for patients at highest risk for transmission
- Educate healthcare personnel about CRE
- Minimize use of invasive devices and dedicate noncritical or disposable devices to individual patient use
- Promote antimicrobial stewardship
- Screen CRE among epidemiologically-linked contacts
  - Screen current and prior roommates of CRE-colonized or -infected patients
  - Screening may also include patients who have shared the same healthcare personnel or those located on the same ward or unit (i.e., point prevalence surveys) as CRE-colonized or -infected patients
- Perform inter-facility communication
  - When transferring patients, facilities should notify accepting facilities of the patient's CRE status, type and duration of any invasive devices, and duration of any ongoing antimicrobial therapy

Supplemental interventions

- Conduct active surveillance testing for CRE
  - Screen high-risk patients at admission or at admission and periodically during their facility stay; preemptive CP can be used while results of admission surveillance testing are pending
  - Consider admission screening of patients transferred from facilities known to have CRE
- Implement chlorhexidine bathing
  - Bathe all patients in targeted unit or ward daily with 2% chlorhexidine

CP: Contact precautions; CRE: Carbapenem-resistant enterobacteriaceae.
Data taken from [82].

focus on selected core and supplemental interventions, which may include aspects that are less familiar to facilities and public health professionals or that pose implementation challenges. While the focus of the following discussion is on carbapenemase-producing CRE, many of the interventions (e.g., Contact Precautions) described below also apply to non-carbapenemase-producing CRE.

Contact precautions

The intent of Contact Precautions is to prevent transmission of epidemiologically important organisms, such as CRE, by minimizing the contamination of healthcare personnel when they are interacting with colonized or infected patients [71]. In order to be effective, adherence to Contact Precautions requires the appropriate use of gown and gloves by healthcare personnel for all interactions that may involve contact with the patient or the patient's environment. In general, gowns and gloves should be discarded before leaving the patient-care environment and should not be reused between patients.

CDC recommends that patients colonized or infected with CRE who are in short-stay acute care hospitals or LTACHs should be placed on Contact Precautions. The use of Contact

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Precautions for residents in lower-acuity long-term care settings (e.g., skilled nursing facilities, nursing homes) is more complex and must include consideration of the potential impact of these interventions on their wellbeing and rehabilitation potential as well as the overall risk that they pose as a source for additional transmission based on their functional and clinical status [71,83]. For example, use of Contact Precautions should be prioritized for residents who are colonized or infected with CRE who are ventilator-dependent, incontinent of stool that is difficult to contain, have draining secretions or wounds that cannot be controlled or are completely dependent on healthcare personnel for all activities of daily living. For more functional residents who are able to perform hand hygiene and are able to contain stool and secretions, the use of strict Contact Precautions might be relaxed by allowing them to attend common gatherings in the facility (e.g., meals). However, healthcare personnel should continue using Standard Precautions when interacting with these residents, including strict adherence to hand hygiene and gown and glove use for any anticipated exposures that might contaminate their hands or clothes.

To facilitate prompt implementation of Contact Precautions, both acute and long-term care facilities should have systems in place to identify patients with a history of CRE colonization or infection when they are readmitted. In addition, facility protocols should be developed that ensure prompt notification of appropriate staff by laboratory personnel when CRE are identified from clinical or surveillance cultures.

At present, CDC does not have recommendations for identifying patients for whom Contact Precautions might be discontinued; however, several factors are important to consider when making decisions about when this might be acceptable. First, the duration of CRE colonization can be prolonged. Zimmerman *et al.* found that the rate of CRE carriage declined over time following the initial positive culture for hospitalized CRE patients; however, the mean time from the initial positive CRE culture to the first negative culture without a subsequent positive was 387 days [89]. Second, certain exposures might increase the risk of prolonged carriage. The same authors also found that having multiple repeat hospitalizations and clinical disease due to CRE were both significantly associated with persistent carriage [89]. Schechner *et al.* also assessed factors associated with persistent carriage and found that patients with rectal cultures positive for CRE were 50% more likely to be positive again at their next hospital encounter if they had prior antimicrobial use (particularly fluoroquinolones), admission from another healthcare facility or duration of 3 months or less since their first positive CRE test [90]. If none of these factors was present, the risk of being CRE positive at the next admission was 14%. In another study, Feldman *et al.* followed known CRE carriers monthly with serial rectal cultures for 3–6 months after discharge from a short-stay acute care hospital [91]. They found that the presence of an invasive device was significantly associated with persistent CRE carriage. Other risk factors for persistent carriage included low functional status and long-term care facility residence among patients with recent CRE acquisition (within preceding 4 months) and high co-morbidity index (Charlson's score) among patients with remote CRE acquisition (4 months or longer). Consistent with the other two studies, Feldman *et al.* found that the percentage of patients with positive CRE rectal cultures declined over time, from a 74% positivity rate when testing within 30 days of initial CRE detection to <30% when testing after 6 months. Importantly, only 67% of CRE carriers in this study with at least one negative rectal surveillance culture for CRE remained negative on subsequent cultures [91], suggesting that a single negative rectal culture might be inadequate to rule out ongoing CRE colonization.

Patient & staff cohorting

In addition to placing CRE-colonized or -infected patients in single-patient rooms, acute care hospitals and long-term care facilities should consider cohorting CRE patients together in the same ward or unit. If feasible, there should be designated staffing to care exclusively for patients with CRE to minimize the risk of transmission to other patients. In several outbreak investigations where multiple interventions were combined in a step-wise fashion to halt transmission, the use of patient and staff cohorting with spatial separation from other patients was found to be one of the most beneficial interventions in decreasing CRE transmission in the affected unit or facility [12,63,92–95]. For example, during a CRE outbreak involving an ICU, where a two-phase intervention was employed, cohorting of patients and staff during the second phase was shortly followed by a decrease in the number of new cases [12].

Antimicrobial stewardship

Hospitals that have established antimicrobial stewardship programs have shown reductions in rates of infections caused by certain MDROs, such as *Clostridium difficile* and MDR Enterobacteriaceae following the implementation of these programs [96,97]. However, the direct impact of antimicrobial stewardship on limiting the emergence of carbapenem resistance among epidemiologically important Gram-negative pathogens has not been widely studied [98]. Of the few studies available, most have focused on *Pseudomonas aeruginosa* and have found that the restriction of certain antimicrobials, such as carbapenems or fluoroquinolones, was associated with a lower incidence of carbapenem-resistant *P. aeruginosa* [99,100]. In one of the few studies that assessed other MDR Gram-negative pathogens, including Enterobacteriaceae, a comprehensive antimicrobial stewardship program implemented in two ICU that included protocols for therapeutic antibiotics and surgical prophylaxis and quarterly rotation of antibiotic classes demonstrated a significant decrease in the proportion of healthcare-associated infections caused by MDR Gram-negative pathogens during the study period (37.4 to 8.5%) [101]. In a study at a tertiary care oncology hospital in India, a reduction in the prevalence of CRE was observed following restriction of certain antimicrobial agents, including carbapenems, colistin and tigecycline, along with enforcement of infection control measures [102].

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Several elements that comprise successful hospital antimicrobial stewardship programs have been described, including commitment from facility leadership to support antimicrobial stewardship efforts, designation of personnel to lead stewardship programs and implementation of policies and interventions to support optimal antimicrobial use (e.g., 'antibiotic time out' after 48 h) [103–106]. Additional components might include having a system in place to monitor and regularly report information on antibiotic use and antimicrobial resistance patterns to relevant staff as well as providing education on optimal prescribing practices [103–106]. CDC has developed a checklist that hospitals can use to assess key elements and actions to ensure optimal antibiotic prescribing and limit overuse and misuse of antibiotics [107].

CRE screening

Patients colonized with CRE are frequently not detected by diagnostic cultures obtained during the course of routine clinical care. One study found that only 31% of CRE-colonized patients had a clinical culture positive for CRE [108]. Unrecognized CRE-colonized patients can serve as a potential source for transmission of CRE to other patients. Given that clinical cultures are likely to identify only a minority of patients colonized with CRE, surveillance cultures have been used to detect colonization. Samples for surveillance cultures are generally collected from stool, the rectum or the peri-rectal area, although one study found that rectal cultures were more sensitive than peri-rectal cultures [108]. Intact skin, including the inguinal and axillary sites, can also be colonized with CRE, and one small study found that adding inguinal cultures to stool/rectal cultures increased sensitivity for detecting CRE [109]. Screening cultures for CRE can be labor intensive and costly and may not be readily available in all clinical laboratories. CDC has recommended a protocol for screening for carbapenem-resistant *Klebsiella* spp. and *E. coli* from rectal swabs [110]. In brief, the protocol recommends inoculating trypticase soy broth that contains a 10 mg ertapenem or meropenem disc with a rectal culture swab. After incubation, the specimen is vortexed and plated on MacConkey agar. Lactose-fermenting colonies are then screened for carbapenemase or tested for susceptibility to carbapenems. Although complicated and time-intensive, this protocol should be implementable in most clinical laboratories. Other screening tests that require less time (e.g., use of chromogenic agars) [111] or that can directly determine the resistance mechanism (e.g., direct PCR) [112] are not yet widely adopted in the USA, and none are approved by the US FDA for detection of CRE from surveillance specimens. How well these screening methods perform relative to each other warrants further evaluation.

Screening of epidemiologically linked contacts

Identification of CRE from a culture of a patient or resident of the facility should generally prompt screening of epidemiologically linked contacts to assess for unrecognized transmission that may have occurred. The decision to screen might be influenced by several factors including whether or not the patient had been on Contact Precautions, how common CRE are in the facility or region or how long the patient has been in the facility. Typically, screening includes current and prior roommates of the index patient who are still hospitalized and might also include patients who have shared the same healthcare personnel or patients located on the same unit or ward (i.e., point prevalence survey). This approach has been used for the control of outbreaks of other MDROs [71] and has also effectively identified unrecognized CRE transmission in several investigations [33,60,63]. Point prevalence surveys may also be used on a regular basis (e.g., monthly) to assess for ongoing transmission and to evaluate the effectiveness of CRE control interventions.

Although healthcare facilities should have a low threshold for screening epidemiologically linked contacts of patients with CRE, the risk of transmission to roommates and other contacts might depend, at least in part, on the duration of exposure. In an NDM-producing *K. pneumoniae* outbreak in Canada, roommates of NDM cases who subsequently tested positive for NDM had significantly longer mean duration of exposure to the index case compared with roommates who did not test positive (26.5 vs 6.5 days) [113]. Similarly, in a study assessing transmission of ESBL-producing Enterobacteriaceae from colonized patients to roommates during the interval between collection of screening cultures at admission and available test result (mean exposure time 4.4 days), only 2 (1.5%) of 133 roommates had evidence of transmission of PFGE-matched ESBL strains; in both of these instances, the exposure time was longer than the mean (9 and 10 days) [114].

Active surveillance testing

This form of CRE screening is considered a supplemental measure in the 2012 CDC Toolkit. This intervention differs slightly from screening epidemiologically linked contacts and consists of systematic screening, usually at admission, of patients who are not necessarily known to be linked to CRE patients. Facilities that employ this approach often target patients admitted to high-risk units (e.g., ICU) or those who meet certain pre-specified criteria that may place them at higher risk of CRE colonization (e.g., those admitted from LTACHs). In one study assessing the use of active surveillance cultures on patients admitted to the ICU, 37% of all patients with carbapenem-resistant *K. pneumoniae* were first identified through active surveillance testing [115]. The authors estimated that earlier detection and implementation of Contact Precautions may have prevented approximately 1400 days of unprotected exposure to carbapenem-resistant *K. pneumoniae*. This intervention has been used effectively as part of a package of interventions during CRE outbreaks [62,63,94]. Despite these findings, the use of active surveillance testing for prevention of MDROs, including CRE, remains controversial for the following reasons. First, because active surveillance testing is often implemented together with other infection control measures, the specific contribution of this intervention in reducing MDRO transmission is difficult to determine. Second, most

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studies of active surveillance testing have been observational in nature. One of the few randomized controlled studies to assess the use of active surveillance testing found that it did not significantly reduce transmission of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci [116]. However, during the study, the turnaround time for reporting a positive surveillance result was often prolonged, and adherence to Contact Precautions and hand hygiene was suboptimal, potentially contributing to the lack of impact. The effect on transmission of other MDROs, including CRE, was not assessed in this study.

Chlorhexidine bathing

Use of chlorhexidine bathing has been demonstrated to successfully reduce bloodstream infections and colonization with methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci primarily in ICU settings [117,118], but its role in reducing CRE transmission is less clear. Limited evidence exists for its use as part of a multifaceted strategy to control CRE outbreaks [62,119]. Some CRE might have reduced susceptibility to chlorhexidine, as recently described with some clinical isolates of the epidemic ST258 strain of KPC-producing *K. pneumoniae* [120]. If used as a supplemental measure, chlorhexidine bathing should be applied to all patients in the targeted unit or ward, regardless of their CRE colonization status, and be performed daily to ensure inhibitory concentrations of chlorhexidine remain on the skin [121].

Environmental cleaning

The role of the environment in CRE outbreaks is not clear. Although environmental cleaning is not one of the interventions outlined in the 2012 CDC CRE Toolkit, several healthcare facilities have included modifications to environmental cleaning in response to CRE outbreaks [12,62,63,93]. CRE have been cultured from the environment during outbreaks [63,122,123]. However, a study performed in LTACHs with large reservoirs of CRE-colonized patients found that the environmental burden of these organisms was low [109], with CRE detected in only 2 (0.5%) of 371 environmental specimens. In instances where CRE have been detected in the healthcare environment, contamination was highest on surfaces in the immediate vicinity of the colonized patient [109,124]. Therefore, if enhanced environmental cleaning is used to supplement other CRE prevention interventions, cleaning and disinfection efforts should focus on high-touch surfaces located in areas around the patient during regular daily and terminal cleaning.

Regional approach to CRE prevention

The US healthcare system is composed of an intricate network of inpatient, outpatient and residential facilities. Patients might be cared for in several different facilities, including ambulatory, acute and long-term care facilities, during one episode of an illness. This complex movement of patients between different levels of care can facilitate the transmission of MDROs from one healthcare facility to another [125–127]. Several multifacility and regional outbreaks of MDROs [128], including CRE [60,63,64], have resulted from the flow of colonized or infected patients across facilities. In one of the largest documented outbreaks of CRE, extensive sharing of patients between facilities in the Chicago area facilitated the dissemination of CRE regionally [64].

Inter-facility communications

Given the extent of inter-facility patient sharing, an effective infection control strategy against MDROs like CRE will require engagement of healthcare facilities across the region. To minimize inter-facility spread of CRE, a healthcare facility that is discharging or transferring patients colonized or infected with CRE should notify any receiving facility of the patient's CRE status. This is critically important in assuring that appropriate precautions are implemented upon the patient's arrival. For example, lack of communications between facilities likely contributed to several multifacility outbreaks of CRE [60,63,64]. Additional information to communicate during patient transfers should include type and duration of invasive devices present as well as reasons for and recommended duration of ongoing antimicrobial use. Communication of this important information should be routinely performed as part of the patient transfer process and is an essential component of regional approaches to CRE prevention.

Regional CRE surveillance

In the USA, state and local health departments could be in a unique position to help facilitate regional MDRO control efforts by providing updates to facilities regarding the regional prevalence of CRE and promoting implementation of recommended prevention measures. One important part of regional CRE prevention is developing an understanding of how common these organisms are at the regional level. Several state health departments have surveyed facilities within their jurisdictions using either the CDC-designed survey tool (available in the CDC CRE Toolkit) or a laboratory-based survey to determine the regional frequency of CRE detection [129–131]. Alternatively, regional surveillance for CRE can be performed through mandatory reporting of CRE isolates to state health departments by facilities or clinical laboratories. As of December 2013, 15 US state health departments have established some kind of CRE reporting requirement within their state [132]. One example of a state-wide effort to improve CRE surveillance and inter-facility communications was the creation of a web-based CRE registry, known as the extensively drug-resistant organism registry (XDRO registry), by the Illinois Department of Public Health in partnership with the Chicago CDC Prevention EpiCenter [133]. Starting in November 2013, all healthcare facilities and laboratories within Illinois were required to report to the XDRO registry any CRE isolate that met the state's surveillance definition for a carbapenemase-producing organism; only the first CRE-positive culture from a patient is reportable. Healthcare

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facilities can query the registry to determine if a patient has been previously reported as CRE-positive so that appropriate precautions can be promptly implemented. The XDRO registry currently requires manual entry, but future updates may include automated uploading of patient data and electronic notification.

Coordinated regional control

'Collaborative' approaches that seek to engage all the facilities in a region to work together to develop and implement control interventions have been successful in preventing healthcare-associated infections [134,135]. By working closely to standardize and enhance uptake of infection prevention practices, healthcare facilities in two large regional prevention collaboratives reduced the rate of bloodstream infections in ICU by almost 70% [134,135]. The implementation of a regional approach has also been successful in the control of MDROs. Under public health guidance, acute and long-term care facilities in the Siouxland region of Iowa, Nebraska and South Dakota collaborated on the development and implementation of an infection-control strategy that led to a significant decrease in the regional prevalence of vancomycin-resistant enterococci [136]. The interventions included screening of patients on admission and in the ICU, use of Contact Precautions, dedicated use of non-critical medical equipment and education of healthcare personnel, patients and visitors. The collaboration among facilities in the Siouxland region also improved communication and facilitated the transfer of patients colonized with vancomycin-resistant enterococci between facilities. A nationwide outbreak of CRE in Israel was also successfully managed following the introduction of a coordinated national prevention strategy that included dissemination of guidelines to all facilities (i.e., strict adherence to contact isolation, cohorting of CRE patients with dedicated staffing) and the establishment of a national task force charged with overseeing facility adherence to recommended practices [95].

As CRE prevention has gained more attention in the USA, some state and local health departments have established dedicated programs to coordinate regional CRE prevention efforts [137,138]. Components of these regional initiatives vary, but have generally included improved CRE surveillance, dissemination of prevention recommendations, laboratory support for confirmatory susceptibility testing and mechanism detection and expert consultation about prevention when cases are identified. One example of a state-led CRE prevention initiative is Oregon's Drug-Resistant Organism Prevention and Coordinated Regional Epidemiology (DROP-CRE) Network [138]. CRE are less common in Oregon compared with other parts of the USA, with only four carbapenemase-producing CRE isolates identified statewide as of November 2013. In an aggressive effort to prevent emergence and spread of CRE in Oregon, the state health department collaborated with leading healthcare institutions within the state and CDC to form the DROP-CRE Network. Starting in December 2011, all CRE isolates that met the state's surveillance definition were reportable to the state health department. In response to reports of CRE, the health department provides real-time outbreak assistance to facilities. The Oregon State Public Health Laboratory has also expanded its capacity for carbapenem resistance mechanism testing to facilitate response efforts. In addition, a statewide database was created for tracking movement of CRE cases between facilities and capturing pertinent epidemiologic information that are reported monthly on a dedicated website. Other components of the program included a statewide education campaign on CRE and the development of a state-specific CRE Toolkit for all Oregon facilities to implement.

Expert commentary & five-year view

The emergence and spread of CRE, particularly those that produce a carbapenemase, pose a major clinical and public health challenge worldwide. Although KPC is the predominant carbapenemase found among Enterobacteriaceae in the USA, other carbapenemases, such as NDM, have increasingly been identified and have the potential to add to the overall burden of CRE. Currently recommended CRE prevention strategies are founded on basic infection control measures such as hand hygiene and standard approaches to the control of MDROs (e.g., Contact Precautions, patient and staff cohorting). Specific strategies include increased detection of patients infected or colonized with CRE. These efforts have been shown to control CRE transmission at a facility-level but they can be labor-intensive, and some interventions, such as surveillance cultures, can involve added costs. Universal adherence to recommended measures among healthcare personnel can also be challenging. In addition, efforts in individual facilities need to be complemented with coordinated regional approaches involving all the healthcare facilities in the area for maximum effect. However, more work is needed to better define the requirement of regional CRE prevention efforts and to promote their widespread implementation.

Future improvements in CRE prevention will require improved detection of carbapenemase-producing strains, including screening tests that are more sensitive and less labor intensive than the currently available culture-based techniques. Readily and rapidly available CRE resistance mechanism testing is also needed to help target prevention. Limiting transmission of CRE will also require the optimization of existing interventions. A greater understanding of how best to operationalize many of the current interventions, including Contact Precautions and CRE screening, in various types of healthcare settings is needed. Current methods of inter-facility communication about MDROs have been suboptimal and poor communication has led to CRE transmission. Future efforts in this area may include the enhancement of communications protocols, with a standardized transfer form for use among regional facilities, or creation of state-based CRE registries similar to the XDRO registry in Illinois [133]. As new antimicrobial agents to treat CRE may not be available for years, efforts to develop and expand effective antimicrobial

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stewardship programs across facilities will increasingly become a focus for CRE prevention.

In addition to the currently available interventions, novel interventions such as CRE decolonization warrant more thorough evaluation, possibly in concert with even more innovative interventions [139]. For example, one promising area involves harnessing the colonization resistance afforded by an intact microbiome to prevent, decrease or eliminate colonization and, thereby, transmission [140]. As noted, antibiotic exposure that is not limited to carbapenems is an important risk factor for CRE colonization in settings where transmission is likely. This risk is mediated by the disruption of the lower intestinal microbiome caused by a large number of different antibiotics, thereby leading to the loss of colonization resistance to CRE. Just as human fecal transplantation is being utilized to restore the intestinal microbiome and break the cycle of recurrent *C. difficile* infection (and subsequent eradication of colonization) [141], models for manipulating the microbiome to eradicate colonization caused by other MDR enteric organisms are already under development [142].

In conclusion, CRE represents an emerging MDRO of global concern. In the USA, although CRE have increased over the last decade, they remain relatively uncommon in many parts of the USA, suggesting that time is now to act aggressively to prevent their further emergence. Limiting the spread of these organisms will require a continued commitment to implement control strategies in both individual facilities and across regions.

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The findings and conclusions in the report are those of the authors and do not necessarily represent the official position of the CDC.

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Key issues

- The percent of Enterobacteriaceae that are non-susceptible to carbapenems continues to increase in the USA, likely due to the spread of carbapenem-resistant Enterobacteriaceae (CRE) strains that produce carbapenemases.
- Since *Klebsiella pneumoniae* carbapenemase first emerged, it has remained the predominant carbapenemase in the USA; however, Enterobacteriaceae producing other carbapenemases, such as the New Delhi metallo-β-lactamase, are increasingly being identified.
- Invasive infections (e.g., bloodstream infections) caused by CRE are associated with limited treatment options and high mortality rates.
- Long-term acute care hospitals may have a high prevalence of patients colonized with CRE that can play an important role in the spread of CRE across a region as patients move across the continuum of care.
- A basic element in any CRE prevention program is to understand how commonly these organisms are encountered at the facility and regional level through regular surveillance.
- Current CRE prevention strategies for individual healthcare facilities include increased detection of patients infected or colonized with CRE and implementation of interventions to prevent transmission to other patients (i.e., hand hygiene, Contact Precautions and patient and staff cohorting).
- Given the extent of inter-facility patient sharing among the US healthcare facilities, successful control of CRE will require a coordinated approach that engages all healthcare facilities that share patients in a region. State and local health departments are well-positioned to facilitate regional control efforts.
- Future research for CRE control should include the development of better laboratory methods for CRE screening and mechanism testing as well as a greater understanding of how to operationalize current prevention interventions and identification of novel CRE prevention interventions (e.g., manipulating intestinal microbiome).

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RIGHTSLINK

DETECT AND PROTECT

Stop Deadly Drug Resistant Infections

Emerging healthcare-associated infection pathogens, especially highly drug resistant pathogens, pose a significant public health threat. CDC must detect highly drug resistant "superbugs" such as carbapenem-resistant Enterobacteriaceae (CRE) and protect patients from their spread.

Threat:

Drug resistant infections are on the rise

Some of these infections are virtually untreatable with currently available drugs

In the past decade, one type of drug resistant infection, CRE has increased from

1% to 4%

42

CRE infections have been reported in medical facilities in 42 states during the last 10 years

Solution:

Implementing "detect and protect" strategies that identify pathogens and stop transmission within and between facilities in a region.

DETECT if Patients Have Drug Resistant Infections

1. Use electronic data sources like CDC's National Healthcare Safety Network to detect superbugs
2. Request alerts every time the lab identifies a patient infected with a superbug
3. When receiving or transferring patients, find out if the patient has a drug resistant infection

PROTECT Patients from Drug Resistant Infections

1. Follow contact and other precautions when treating patients with drug resistant infections
2. Dedicate rooms, equipment, and staff to patients with highly drug resistant infections
3. Take out temporary medical devices like catheters as soon as possible
4. Prescribe antibiotics carefully; monitor antibiotic use with tools such as CDC's National Healthcare Safety Network's Antimicrobial Use module

Detect and Protect Works:

Medical facilities in several states have reduced CRE infection rates by following CDC's prevention guidelines and some states are early adopters of regional prevention strategies.

Oregon created the Drug-Resistant Organism Prevention and Coordinated Regional Epidemiology (DROP-CRE) Network

- Developing a statewide multidrug-resistant organism database
- Promoting CRE education statewide
- Conducting rapid regional identification of CRE
- Providing real-time epidemiologic outbreak assistance to facilities with CRE cases
- Tracking CRE statewide across the spectrum of care

Action is needed now to stop these deadly infections

For more information please visit:http://www.cdc.gov/hai

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Patients

Carbapenem-resistant Enterobacteriaceae (CRE) Infection: Patient FAQs

What are CRE?

CRE, which stands for Carbapenem-resistant Enterobacteriaceae, are a family of germs that are difficult to treat because they have high levels of resistance to antibiotics. CRE are an important emerging threat to public health.

Common Enterobacteriaceae include *Klebsiella* species and *Escherichia coli (E. coli)*. These germs are found in normal human intestines (gut). Sometimes these bacteria can spread outside the gut and cause serious infections, such as urinary tract infections, bloodstream infections, wound infections, and pneumonia. Enterobacteriaceae can cause infections in people in both healthcare and community settings.

Carbapenems are a group of antibiotics that are usually reserved to treat serious infections, particularly when these infections are caused by germs that are highly resistant to antibiotics. Sometimes carbapenems are considered antibiotics of last resort for some infections. Some Enterobacteriaceae can no longer be treated with carbapenems because they have developed resistance to these antibiotics (i.e., CRE); resistance makes the antibiotics ineffective in killing the resistant germ. Resistance to carbapenems can be due to a few different mechanisms. One of the more common ways that Enterobacteriaceae become resistant to carbapenems is due to production of *Klebsiella pneumoniae* carbapenemase (KPC). KPC is an enzyme that is produced by some CRE that was first identified in the United States around 2001. KPC breaks down carbapenems making them ineffective. Other enzymes, in addition to KPC, can breakdown carbapenems and lead to the development of CRE, but they are uncommon in the United States.

How are CRE spread?

To get a CRE infection, a person must be exposed to CRE germs. CRE germs are usually spread person to person through contact with infected or colonized people, particularly contact with wounds or stool. CRE can cause infections when they enter the body, often through medical devices like ventilators, intravenous catheters, urinary catheters, or wounds caused by injury or surgery.

Who is most likely to get an infection with CRE?

Healthy people usually don't get CRE infections. CRE primarily affect patients in acute and long-term healthcare settings, who are being treated for another condition. CRE are more likely to affect those patients who have compromised immune systems or have invasive devices like tubes going into their body. Use of certain types of antibiotics might also make it more likely for patients to get CRE.

Can CRE be treated?

Many people with CRE will have the germ in or on their body without it producing an infection. These people are said to be colonized with CRE, and they do not need antibiotics for the CRE. If

the CRE are causing an infection, the antibiotics that will work against it are limited but some options are often available. In addition, some infections might be able to be treated with other therapies, like draining the infection. Strains that have been resistant to all antibiotics are very rare but have been reported.

What are some things hospitals are doing to prevent CRE infections?

To prevent the spread of CRE, healthcare personnel and facilities can follow infection-control precautions provided by CDC. These include:

- Washing hands with soap and water or an alcohol-based hand sanitizer before and after caring for a patient
- Carefully cleaning and disinfecting rooms and medical equipment
- Wearing gloves and a gown before entering the room of a CRE patient
- Keeping patients with CRE infections in a single room or sharing a room with someone else who has a CRE infection
- Whenever possible, dedicating equipment and staff to CRE patients
- Removing gloves and gown and washing hands before leaving the room of a CRE patient
- Only prescribing antibiotics when necessary
- Removing temporary medical devices as soon as possible
- Sometimes, hospitals will test patients for these bacteria to identify them early to help prevent them from being passed on to other patients

What can patients do to prevent CRE infections?

Patients should:

- Tell your doctor if you have been hospitalized in another facility or country.
- Take antibiotics only as prescribed.
- Expect all doctors, nurses, and other healthcare providers wash their hands with soap and water or an alcohol-based hand rub before and after touching your body or tubes going into your body. If they do not, ask them to do so.
- Clean your own hands often, especially:
  - Before preparing or eating food
  - Before and after changing wound dressings or bandages
  - After using the bathroom
  - After blowing your nose, coughing, or sneezing
- Ask questions. Understand what is being done to you, the risks and benefits.

What if I have CRE?

Follow your healthcare provider's instructions. If your provider prescribes you antibiotics, take them exactly as instructed and finish the full course, even if you feel better. Wash your hands, especially after you have contact with the infected area and after using the bathroom. Follow any other hygiene advice your provider gives you.

I am caring for someone with CRE at home; do I need to take special precautions?

CRE have primarily been a problem among people with underlying medical problems, especially

those with medical devices like urinary catheters or those with chronic wounds. Otherwise healthy people are probably at relatively low risk for problems with CRE. People providing care at home for patients with CRE should be careful about washing their hands, especially after contact with wounds or helping the CRE patient to use the bathroom or after cleaning up stool. Caregivers should also make sure to wash their hands before and after handling the patient's medical device (e.g., urinary catheters). This is particularly important if the caregiver is caring for more than one ill person at home. In addition, gloves should be used when anticipating contact with body fluids or blood.

Is CRE infection related to medical care abroad?

A variety of enzymes produced by Enterobacteriaceae make them resistant to carbapenems. Several of these enzymes appear to be more common in other countries than they are in the United States. In the United States, patients infected or colonized with CRE have been identified from patients that received care in Greece, India, Italy, Pakistan, or Vietnam. None of these patients had gone to these countries specifically for a medical procedure (medical tourism), however, as with medical care in the United States, medical care abroad can be associated with healthcare–associated infections and/or resistant bacteria. Learn about those risks and how to minimize them. (/Features/MedicalTourism/)

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CRE: Carbapenem-Resistant Enterobacteriaceae

WHAT ARE THEY? A family of bacteria. These types of bacteria have developed ways to become very resistant to commonly used antibiotics. The resistance makes the bacteria very difficult to kill and infections harder to treat. There are 2 main types, *E.coli* (a common intestinal bacteria) and *Klebsiella pneumoniae.*

WHAT THE FACILITY DOES WHEN AN INDIVIDUAL HAS A CRE INFECTION:
To help protect everyone, special precautions called "Contact Precautions" will be started. There will be a small orange sign on your door. Staff members will wear gowns and gloves, and sometimes a mask and goggles when giving you direct care. You will have your own blood pressure cuff, thermometer and other items that will touch your skin directly.

WHAT SHOULD YOU DO BEFORE YOU LEAVE YOUR ROOM?
Make sure you have

- ☐ Clean Hands (15-30 second hand wash or hand sanitizer)
- ☐ Clean Clothes
- ☐ Clean Canes, Walkers and Wheelchairs and other equipment
- ☐ Covered Wounds
- ☐ Contained Drainage
- ☐ No signs or symptoms of a respiratory infection such as sneezing or coughing
- ☐ We may teach you to use special disinfecting wipes so that you can help to keep your environment clean

WHAT SHOULD FAMILY/VISITORS DO? **Use common sense and come visit**

- ☐ Wash hands before and after leaving the room
- ☐ Eat and drink outside the room in an activity area
- ☐ Visitors and family should not use your toilet or your towels
- ☐ If visitors are helping provide personal care for you, they should ask for gowns, gloves and masks, the same as the staff.
- ☐ If you are sneezing and/or have a productive cough, visitors should wear gown gloves and a mask when coming close to you.
- ☐ Your family and visitors may also be trained to utilize the special disinfecting wipes so that everyone can help to keep your environment clean

WHEN DO THE SPECIAL (Contact) PRECAUTIONS STOP? We may keep you on Contact Precautions for the duration of your stay. You may have Contact Precautions discontinued if the team feels it is appropriate.

QUESTIONS? Please contact your primary care provider or ask to speak to the nurse or infection preventionist. Thank you.

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High C's of
Infection Prevention and Control

Residents/patients should have the following before leaving their rooms:

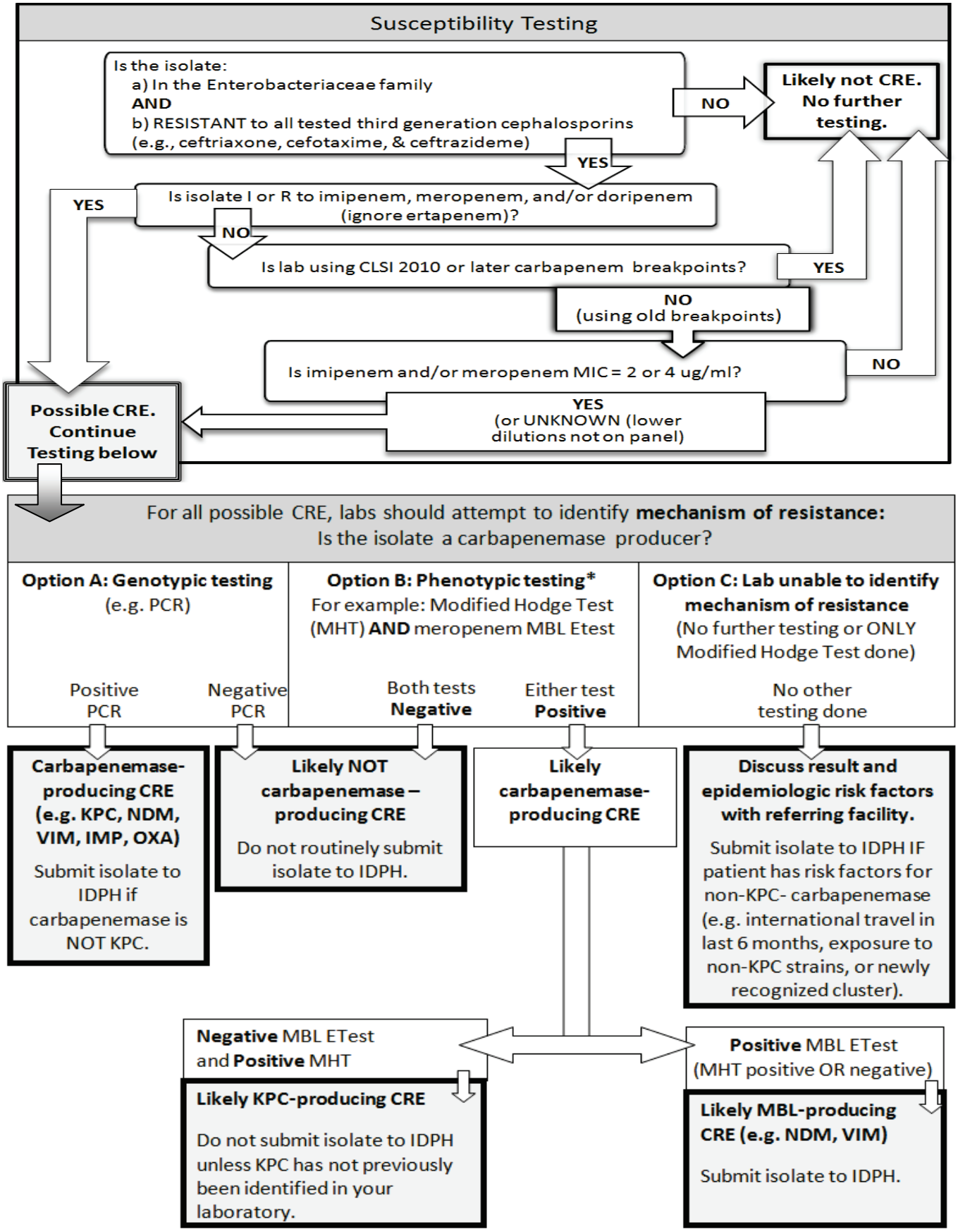
Clean Hands
Clean Clothes
Clean Equipment and Environment
Contained Drainage
Covered Wounds

Healthcare workers should consider the following actions:

Careful Assessment
Careful Use of Antimicrobials
Collaborative Approach
Communication

(Deb Burdsall ©2013)

Recommended Laboratory Procedures for Testing Carbapenem-Resistant Enterobacteriaceae (CRE)



*Other phenotypic tests are available and may be used; this two-step process is most common.

IDPH
Illinois Department of Public Health

Revised 11/2014

Carbapenem-Resistant Enterobacteriaceae (CRE): Submitting Samples to the Illinois Department of Public Health

IDPH and CDC want to prioritize sample submission of CRE isolates **other than KPC** for further (genotypic) testing.

At a *minimum*, prior to submission, laboratories should confirm the identification of the organism, ensure pure cultures, and **repeat resistance testing** on isolates, with a different method if possible, to confirm resistance patterns.

Submit **likely MBL-producing CRE isolates**:

1) Must exhibit carbapenem resistance (I or R to imipenem, doripenem, or meropenem using updated breakpoints) and resistance (R) to all third-generation cephalosporins tested (e.g., ceftriaxone, cefotaxime, and ceftazidime)

   AND

2) Must have phenotypic testing suggesting MBL (e.g., + MBL Etest or +multi-disk test) OR, if phenotypic testing not done, be isolated from a patient with international travel in last 6 months or epidemiologic link to a patient with non-KPC CRE.

<u>Additional Recommended Trainings</u>

Sentinel Labs TRAIN courses: www.train.org

- Sentinel220 Transportation Security Awareness (20 minutes)
- Sentinel221 Packaging and Shipping Infectious Substances (1.5 hours)

IDPH
ILLINOIS DEPARTMENT OF PUBLIC HEALTH

Revised 11/2014

IDPH
ILLINOIS DEPARTMENT OF PUBLIC HEALTH

Pat Quinn, Governor
LaMar Hasbrouck, MD, MPH, Director

825 North Rutledge Street • Springfield, Illinois 62702-4910 • www.dph.illinois.gov

TO: Hospital Laboratories, Laboratory Directors, Sentinel Laboratories

FROM: Bernard T. Johnson
Chief, Division of Laboratories

Mary Driscoll
Chief, Division of Patient Safety and Quality

DATE: December 2, 2014

SUBJECT: Confirmation of Carbapenem-Resistant Enterobacteriaceae (CRE) Isolates Reported to the Illinois Extensively Drug-Resistant Organism (XDRO) Registry

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The Illinois Department of Public Health (IDPH) Divisions of Laboratories (DOL) and Patient Safety and Quality (DPSQ) request your assistance in confirming CRE isolates that you are reporting in the Illinois XDRO registry.

According to current Illinois surveillance criteria, CRE are Enterobacteriaceae with one of the following laboratory test results:

1. Molecular test (e.g., polymerase chain reaction [PCR]) specific for carbapenemase; or
2. Phenotypic test (e.g., Modified Hodge) specific for carbapenemase production; or
3. Susceptibility test (**for *E. coli* and *Klebsiella spp* only**): non-susceptible (intermediate or resistant) to ONE of the following carbapenems (doripenem, meropenem, or imipenem) AND resistant to ALL of the following third-generation cephalosporins tested (ceftriaxone, cefotaxime, and ceftazidime). *Note: ignore ertapenem for this definition.*

To ensure that CRE isolates identified in Illinois and entered in the XDRO registry meet this definition, and to better characterize isolates being reported based on susceptibility testing and/or phenotypic testing, the IDPH has engaged in a program with Rush University to confirm and further characterize reported CRE isolates.

IDPH asks that your facility please submit up to five (5) CRE isolates to the IDPH Laboratory in Chicago between now and July 31, 2015.

- Submit isolates on slants (see shipping and contact information below). If your facility's testing methods are different for clinical versus screening isolates, submit a mix of these isolates up to a total of 5. Please indicate whether the submitted isolate is a clinical or screening isolate.
- Submit the standard IDPH test requisition form.
- Indicate the CRE genus and species.
- Indicate the test/methods used to determine that the isolate is a CRE and any further characterization done at your facility. Please be specific about the methods employed in your facility, e.g. ,
    - "Susceptibility testing only"
    - "Susceptibility testing and Modified Hodge"
    - "Modified Hodge and MBL (E test)"
    - "Molecular testing"
    - "Other—provide details"
- Please provide results of all CRE testing that was done.

Isolates will be sent to Rush University laboratory, where conventional methods will be used to confirm the isolate as CRE as defined above. Once confirmed, the laboratory will use molecular methods to detect the *Klebsiella pneumoniae* carbapenemase (bla_{KPC}) and/or New Delhi metallo- β -lactamase (bla_{NDM}) genes. Organisms that produce a carbapenemase other than these may be shipped to the CDC for further molecular characterization.

The IDPH DOL will send you test results from Rush University and the CDC (if referred).

Based on the results, the DPSQ may follow up with your facility to change the results entered in the XDRO registry. Results will also be used for future educational workshops.

NOTE: **After your facility has submitted the 5 isolates for this confirmation program,** return to the routine practice of only submitting CRE isolates that have undergone phenotypic or molecular testing suggesting they are producing a carbapenemase **other than KPC** (e.g., metallo-β-lactamase-producing isolates). Return to your regular algorithm and submit only these isolates to IDPH for further testing by CDC.

Ship specimens meeting the criteria above to:

Illinois Department of Public Health
Clinical Microbiology Laboratory
2121 West Taylor Street
Chicago, IL 60612

If you have any questions for the Division of Laboratories about specimen submission procedures, please call the Clinical Microbiology Laboratory at (312) 793-4760. If you have general questions about this project, please call the Division of Patient Safety and Quality at (312) 814-3143.

CDC Vitalsigns™
March 2014

Making Health Care Safer

Antibiotic Rx in Hospitals: Proceed with Caution

1 in 2

More than half of all hospital patients receive an antibiotic.

3x

Doctors in some hospitals prescribed 3 times as many antibiotics as doctors in other hospitals.

30%

Reducing the use of high-risk antibiotics by 30% can lower deadly diarrhea infections by 26%.

Antibiotics save lives, but poor prescribing practices are putting patients at unnecessary risk for preventable allergic reactions, super-resistant infections, and deadly diarrhea. Errors in prescribing decisions also contribute to antibiotic resistance, making these drugs less likely to work in the future.

To protect patients and preserve the power of antibiotics, hospital CEOs/medical officers can:

◇ Adopt an antibiotic stewardship program that includes, at a minimum, this checklist:

1. **Leadership commitment:** Dedicate necessary human, financial, and IT resources.
2. **Accountability:** Appoint a single leader responsible for program outcomes. Physicians have proven successful in this role.
3. **Drug expertise:** Appoint a single pharmacist leader to support improved prescribing.
4. **Act:** Take at least one prescribing improvement action, such as requiring reassessment within 48 hours, to check drug choice, dose, and duration.
5. **Track:** Monitor prescribing and antibiotic resistance patterns.
6. **Report:** Regularly report to staff prescribing and resistance patterns, and steps to improve.
7. **Educate:** Offer education about antibiotic resistance and improving prescribing practices.

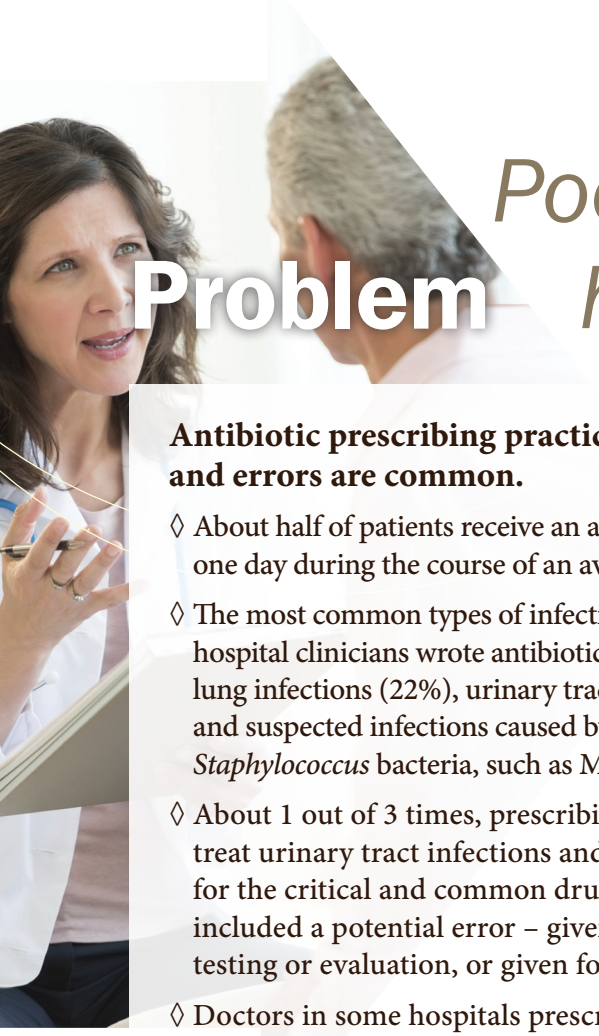
◇ Work with other health care facilities to prevent infections, transmission, and resistance.

→ See page 4

Want to learn more? Visit

www www.cdc.gov/vitalsigns

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion



Problem Poor antibiotic prescribing harms patients

Antibiotic prescribing practices vary widely and errors are common.

◊ About half of patients receive an antibiotic for at least one day during the course of an average hospital stay.

◊ The most common types of infections for which hospital clinicians wrote antibiotic prescriptions were lung infections (22%), urinary tract infections (14%), and suspected infections caused by drug-resistant *Staphylococcus* bacteria, such as MRSA (17%).

◊ About 1 out of 3 times, prescribing practices to treat urinary tract infections and prescriptions for the critical and common drug vancomycin included a potential error – given without proper testing or evaluation, or given for too long.

◊ Doctors in some hospitals prescribed up to 3 times as many antibiotics as doctors in similar areas of other hospitals. This difference suggests the need to improve prescribing practices.

Poor prescribing puts patients at risk.

◊ Although antibiotics save lives (for example, in the prompt treatment of sepsis, a life-threatening infection throughout the body), they can also put patients at risk for a *Clostridium difficile* infection, deadly diarrhea that causes at least 250,000 infections and 14,000 deaths each year in hospitalized patients.

◊ Decreasing the use of antibiotics that most often lead to *C. difficile* infection by 30% (this is 5% of overall antibiotic use) could lead to 26% fewer of these deadly diarrheal infections. These antibiotics include fluoroquinolones, β-lactams with β–lactamase inhibitors, and extended-spectrum cephalosporins.

◊ Patients getting powerful antibiotics that treat a broad range of infections are up to 3 times more likely to get another infection from an even more resistant germ.

Every time antibiotics are prescribed:

1. Order recommended cultures before antibiotics are given and start drugs promptly.

2. Make sure indication, dose, and expected duration are specified in the patient record.

3. Reassess within 48 hours and adjust Rx if necessary or stop Rx if indicated.

Specific recommendations for common prescribing situations:

Rx for urinary tract infections

- Make sure that culture results represent true infection and not just colonization.
  - Assess patient for signs and symptoms of UTI.
  - Make sure that urinalysis is obtained with every urine culture.
- Treat for recommended length of time and ensure that planned post-discharge treatment takes into account the antibiotics given in the hospital.

Rx for pneumonia

- Make sure that symptoms truly represent pneumonia and not an alternate, non-infectious diagnosis.
- Treat for the recommended length of time and ensure that planned post-discharge treatment takes into account the antibiotics given in the hospital.

Rx for MRSA infections

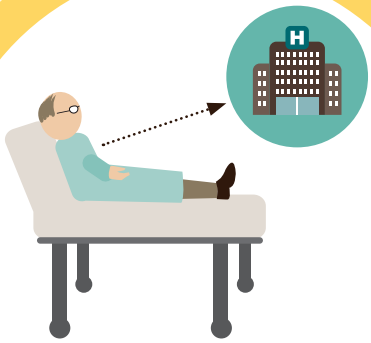
- Verify that MRSA is growing in clinically relevant cultures. Do not use vancomycin to treat infections caused by methicillin-susceptible staph (and not MRSA).

SOURCE: CDC Vital Signs, 2014

Improving antibiotic prescribing in hospitals

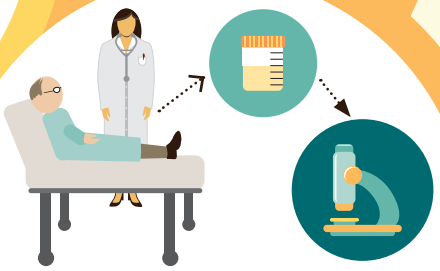
Key moments for improving the cycle of antibiotic prescribing practices

1



While in the hospital for surgery, George develops a fever and feels pain when he urinates.

2



The doctor thinks George has a urinary tract infection (UTI). Following the hospital's UTI guideline, the doctor orders urine cultures to see if George has bacteria in his urinary tract (bladder, kidneys).

3

At the same time, the doctor prescribes antibiotics and includes the dose, duration, and indication in the patient record.

4

In keeping with the antibiotic stewardship policy, the doctor reassesses the prescription 2 days later. Based on test results and patient exam, she puts George on a better antibiotic for a shorter time.

5

The doctor's clear notes showing dose, duration, and indication give other doctors and nurses information they need to provide George with the best medical care.

SOURCE: CDC Vital Signs, 2014

What Can Be Done

The Federal government is

◊ Expanding the National Healthcare Safety Network to help hospitals track antibiotic use and resistance.

◊ Sharing prescribing improvement recommendations and tools with clinicians and administrators.
www.cdc.gov/getsmart/healthcare

◊ Supporting networks testing new prescribing improvement strategies.

◊ Helping hospitals and health departments create regional programs to improve antibiotic prescribing.

◊ Improving health care for veterans by launching antibiotic stewardship programs in Veteran's Health Administration hospitals.

◊ Providing incentives for development of new antibiotics.

State and local health departments can

◊ Gain an understanding of antibiotic stewardship activities in the state or area.

◊ Facilitate efforts to improve antibiotic prescribing and prevent antibiotic resistance.

◊ Provide educational tools to facilities to help prescribers improve practices.

Hospital CEOs/medical officers can

◊ Adopt an antibiotic stewardship program that includes, at a minimum, this checklist:

1. **Leadership commitment:** Dedicate necessary human, financial, and IT resources.
2. **Accountability:** Appoint a single leader responsible for program outcomes. Physicians have proven successful in this role.
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5. **Track:** Monitor prescribing and antibiotic resistance patterns.
6. **Report:** Regularly report to staff prescribing and resistance patterns, and steps to improve.
7. **Educate:** Offer education about antibiotic resistance and improving prescribing practices.

◊ Work with other health care facilities to prevent infections, transmission, and resistance.

Doctors and other hospital staff can

◊ Prescribe antibiotics correctly – get cultures, start the right drug promptly at the right dose for the right duration. Reassess the prescription within 48 hours based on tests and patient exam.

◊ Document the dose, duration and indication for every antibiotic prescription.

◊ Stay aware of antibiotic resistance patterns in your facility.

◊ Participate in and lead efforts within your hospital to improve prescribing practices.

◊ Follow hand hygiene and other infection control measures with every patient.

Hospital patients can

◊ Ask if tests will be done to make sure the right antibiotic is prescribed.

◊ Be sure everyone cleans their hands before touching you. If you have a catheter, ask each day if it is necessary.

For more information, please contact
Telephone: 1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348
Web: www.cdc.gov
Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Publication date: 3/4/2014

www www.cdc.gov/vitalsigns

www www.cdc.gov/mmwr

CS245773B

Antibiotic use in nursing homes

Get Smart About Antibiotics Week
November 18-24, 2013

Did you know?

1. Antibiotic resistance is one of the world's most pressing public health threats.
2. Antibiotics are the most important tool we have to combat life-threatening bacterial diseases, but antibiotics can have side effects.
3. Antibiotic overuse increases the development of drug-resistant germs.
4. Patients, clinicians, healthcare facility administrators, and policy makers must work together to employ effective strategies for improving antibiotic use – ultimately improving medical care and saving lives.

Scope of the problem in nursing homes

- Antibiotics are among the most commonly prescribed medications in nursing homes.
- Up to 70% of long-term care facilities' residents receive an antibiotic every year.
- Estimates of the cost of antibiotics in the long-term care setting range from $38 million to $137 million per year.
- Among the antibiotic-resistant organisms most commonly found in nursing home populations are multidrug-resistant Gram-negative bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant enterococci (VRE).

Antibiotic resistance in long-term care is associated with:
- Increased risk of hospitalization
- Increased cost of treatments
- Increased risk of death

Why focus on nursing homes?

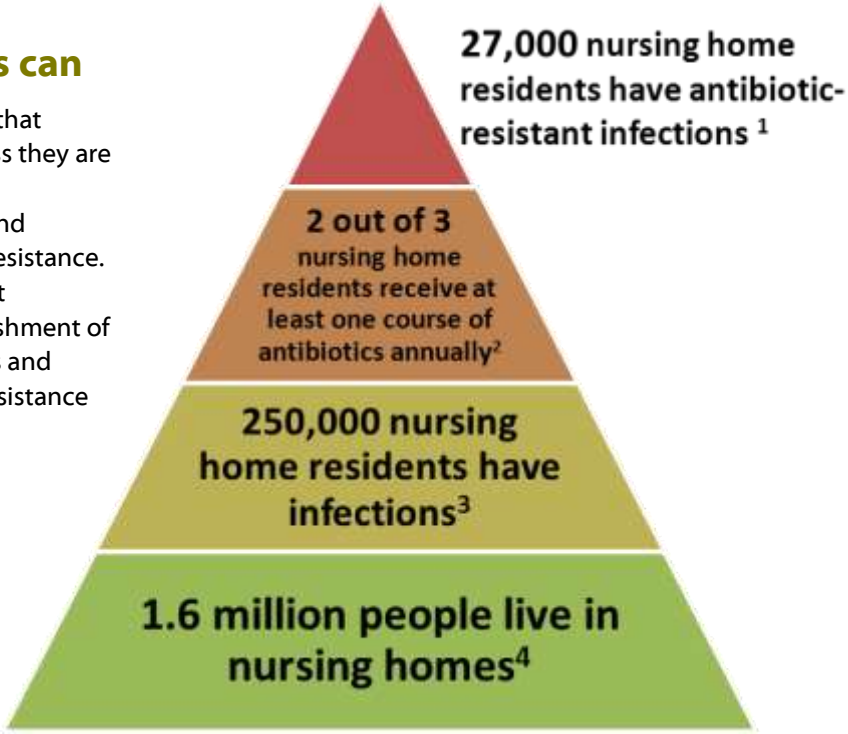
- Many long-term care residents can be "colonized" with bacteria, meaning that germs can live on the skin, wound surfaces or even in the bladder without making the person sick. Challenges with separating colonization from true infection can contribute to antibiotic overuse in this setting.
  - Studies have consistently shown that about 30%-50% of frail, elderly long-term care residents can have a positive urine culture even without any symptoms of a urinary tract infection. Unfortunately, many of these patients are placed inappropriately on antibiotics.
- Poor communication when patients transfer facilities, for example from a nursing home to a hospital, can result in antibiotic misuse.
- Antibiotic-related complications, such as diarrhea from *C. difficile,* can be more severe, difficult to treat, and lead to more hospitalizations and deaths among people over 65 years. Long-term care facility residents are particularly at risk for these complications.

Nursing homes administrators can

- Have clear policies and practices to ensure that patients are not started on antibiotics unless they are needed.
- Review the facility's microbiology reports and antibiogram to detect trends in antibiotic resistance.
- Implement policies that encourage prudent antimicrobial prescribing, including establishment of minimum criteria for prescribing antibiotics and review of antibiotic appropriateness and resistance patterns.

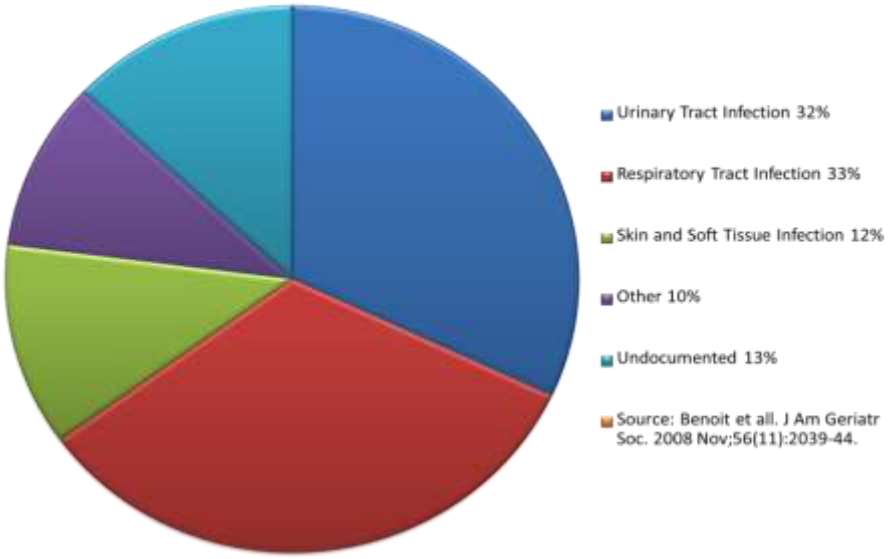
Nursing home providers can

- Obtain microbiology cultures prior to starting antibiotics when possible so antibiotics can be adjusted or stopped when appropriate.
- Remember that treatment with antibiotics is only appropriate when the practitioner determines, on the basis of an evaluation, that the most likely cause of the patient's symptoms is a bacterial infection.
- Use antibiotics only for as long as needed to treat infections, minimize the risk of relapse, or control active risk to others. Antibiotics are generally not indicated to treat colonization.
- Avoid use of antibiotics to treat viral illnesses such as colds, influenza, and viral gastroenteritis.
- Engage residents and their family members in addressing the need to improve antibiotic use in your facility.



[1] Centers for Medicare and Medicaid Services, Long Term Care Minimum Data Set, Resident profile table as of 05/02/2055. Baltimore. MD.
[2] Loeb, M et.al. Antibiotic use in Ontario facilities that provide chronic care. J Gen Intern Med 2001; 16: 376-383.
[3] Centers for Disease Control and Prevention, National Center for Health statistics, 1999 National Nursing Home Survey. Nursing Home Residents, number, percent distribution, and rate per 10,000, by age at interview, according to sex, race, and region: United States, 1999.

Most common infections treated with antibiotics in nursing homes



Developed in partnership with the ***American Medical Directors Association***

Centers for Disease Control and Prevention
For more information please contact Centers for Disease Control and Prevention
1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-63548
Email: getsmart@cdc.gov Web: http://www.cdc.gov/getsmart/
Web: http://www.cdc.gov/getsmart/healthcare/

Healthcare-associated Infections HAI Elimination

ILLINOIS

Antimicrobial Stewardship Collaborative

The Illinois Antimicrobial Stewardship (AMS) Collaborative engaged 5 Chicago area hospitals in working to improve antimicrobial use, identify common challenges and strategies for success, and ultimately enhance patient safety and quality of care by decreasing resistant HAIs and *C. difficile*.

- In-depth assessments at each collaborative facility included a pre-collaborative survey of current AMS practices, a review of technical documents by expert consultants, and in-depth qualitative interviews with hospital leadership, pharmacists, front-line prescribers, microbiologists, information technology, and other key stakeholders.
- Based on site-specific assessments, each facility developed a goal for improving antimicrobial prescribing at their facility using a variety of strategies including:
  - Formation of formal AMS committees
  - Antibiotic "time outs" during rounds to review "dose, duration, indication"
  - Changes to Information Technology infrastructure
    - e.g., mandated indication for selected agents in Prescription Order Entry
  - Tracking Pharmacy interventions
  - Enhanced communication between pharmacy & prescribers, including post-prescription review
  - Development/revision of antimicrobial guidelines with inclusion of de-escalation strategies
- The collaborative created the term "**Antimicrobial Mindfulness**" as an umbrella concept for various methods employed to systematically assess and re-assess the appropriateness of antimicrobial therapy.

Antimicrobial mindfulness: regularly think through the 5 Ds of Antimicrobial Stewardship*

right **Diagnosis:**
- Does this patient have an infection or something else?

right **Drug selection:**
- for the diagnosis, the institution, AND for the patient

right **Dose:**
- adjusted for size & renal function

right **Duration:**
- harms minimized by shortest effective duration

right **De-escalation:**
- narrowest spectrum, least invasive, lowest cost

*Developed by Ramesh Patel, PharmD & David Schwartz, MD

For more information contact: erica.runningdeer@illinois.gov

Inter-facility Infection Prevention Transfer Form

When transferring patient/resident, please complete to the best of your ability to assist with care transitions.

Patient Information

Last Name _____ First Name _____

Date of Birth _____/_____/_____

Isolation Precautions

The patient currently requires the following type(s) of isolation precautions.

- ☐ Contact precautions. Reason: _____
- ☐ Droplet precautions. Reason: _____
- ☐ Airborne precautions. Reason: _____

☐ The patient DOES NOT require isolation.

Infection/Colonization History (check all that apply)

☐ MRSA (Methicillin-resistant *Staphylococcus aureus*)

☐ VRE (Vancomycin-resistant enterococci)

☐ *Clostridium difficile*

☐ Any MDRO gram-negative bacteria (multidrug-resistant). If known, please also specify:

- ☐ Carbapenem-resistant *Enterobacteriaciae* (examples: *Klebsiella* or *E. coli* with KPC, NDM-1)
- ☐ *Acinetobacter*, multidrug-resistant
- ☐ ESBL (extended spectrum beta-lactamase) bacteria
- ☐ *Pseudomonas aeruginosa*, multidrug-resistant

☐ Respiratory Illness (influenza, adenovirus, etc., suspected or confirmed) — Droplet Precautions

☐ Respiratory Illness (tuberculosis , etc., suspected or confirmed) — Airborne Precautions

☐ Any other pathogen requiring isolation. Please list: _____

Sending Facility Information

Facility Name _____ Unit_____

Address _____ Phone _____

Person Completing Form

Name/Title _____

Phone _____

Email/Fax _____

Infection Prevention Designee

Name _____

Phone _____

Email/Fax _____

Please send copies of any relevant microbiology cultures, medication administration record (MAR) or physician order sheet (POS), and immunization documentation.

This resource is provided as part of the Illinois CRE Detect and Protect Campaign, which is funded by an Affordable Care Act award from the U.S. Centers for Disease Control and Prevention.