

Preventing “Nightmare Bacteria” from Becoming Nightmare Outbreaks

A Diagnostics First Publication

In early 2015, carbapenem-resistant *Enterobacteriaceae* (CRE) became a household term when a high-profile outbreak — including two deaths — at a California hospital were linked to contaminated medical scopes.¹ But these multidrug-resistant pathogens have been a growing problem for at least a decade. CRE infections increased five-fold from 2008 to 2012, reaching 48 states by 2012.² In 2012, the U.S. Centers for Disease Control and Prevention (CDC) reported that approximately 4% of acute care and 18% of long-term acute care hospitals in the U.S. reported at least one patient with a CRE infection during the first half of that year.³

Now, in 2017, an *Infection Control and Hospital Epidemiology* study of 16 healthcare facilities in the Washington, D.C. area reported a surprisingly high 5.2% prevalence rate.⁴ That’s only one metropolitan area of the U.S., but it’s certainly not unique.

Former CDC head Thomas Frieden, MD, MPH, once called CRE “nightmare bacteria.”² That’s because CRE are both highly resistant to antibiotics and often lethal. Up to 50% of patients with CRE bacteremia (bloodstream infections) die.⁵ These bacteria can also cause urinary tract infections and pneumonia. In healthcare settings, they colonize devices such as catheters, ventilators and central lines.⁶

Carbapenems are considered the antibiotics of last resort — if an *Enterobacteriaceae* infection is resistant to the carbapenems, it’s resistant to most other antibiotics too. One particularly concerning type of resistance is caused by carbapenemases, enzymes that inactivate carbapenems. The carbapenemase-producing CRE (*Klebsiella pneumoniae* carbapenemase [KPC], for example) are genetically coded on plasmids rather than chromosomes, which makes them highly transmissible in addition to mediating high-level resistance.

▾ Surveillance

The best way to stop the spread of CRE in a healthcare facility is to know exactly where they are hiding.⁷ Many hospitals are implementing active surveillance programs, testing patients with rapid molecular technologies that detect the genes responsible for producing carbapenemases.

A study presented at the annual meeting of the Association for Professionals in Infection Control and Epidemiology in June 2017 by researchers at St. Jude’s Children’s Hospital found that colonization

with CRE strongly correlates with development of bacteremia. Thus, screening patients for CRE, although they are typically asymptomatic, could help prevent the spread of infections and identify patients at risk of developing serious disease.⁸

At Sanford Health in Bismarck, North Dakota, that’s the responsibility of Kenneth Irmen, PhD, technical director of the microbiology laboratory. He and his team develop new infection detection tests, validate new tests, and implement them. They are on the front lines of detecting — and therefore preventing the spread of — CRE and other highly infectious and multidrug-resistant pathogens.



CRE are more prevalent in areas of denser population, particularly in large urban areas on the coasts of the U.S. But CRE rates are creeping higher in the middle of the country,

Irmen said. A 2014 CRE outbreak at a long-term care facility in Bismarck prompted the infection control committee at Sanford Health to increase its vigilance. Today, all patients newly admitted to the intensive care unit (ICU) at Sanford Health are screened — rectal swabs are collected and analyzed for carbapenemase-producing CRE by Irmen’s team with the help of Cepheid’s Xpert® Carba-R* test. “We know that CRE lurk in our community because a case or two pops up now and then,” Irmen said, “but screening our ICU patients helps us sleep at night.”

* For *In Vitro* Diagnostic Use.

Nicholas Moore, PhD, is assistant director of the Clinical Microbiology Lab at Rush University Medical Center, a large medical center in the heart of Chicago that provides tertiary care for a range of patients, including some of the most chronically and critically ill. Many of these patients have had multiple admissions at Rush and other healthcare facilities, putting them at high risk for both being colonized and infected with multidrug-resistant organisms.

Moore's lab staff work up clinical cultures and advise clinicians on antimicrobial therapy 24 hours a day, seven days a week, 365 days a year. They actively survey all patients transferred to Rush from other healthcare providers, which includes community hospitals and acute and long-term care facilities, for CRE colonization. Thanks in part to that vigilance, CRE prevalence is relatively low at Rush, at approximately 1 to 3%. In contrast, a 2013 study found CRE prevalence of 30 to 54% in long-term acute care facilities in the Chicago area.⁹

In addition to the obvious benefits to public health, there's an economic incentive for active surveillance, even in places where CRE are not all that common. Research suggests that when the prevalence of CRE is 0.3% and above, the cost savings in preventing CRE spread outweigh the cost of universal screening for hospital inpatients.¹⁰ That's because a single CRE infection can cost a hospital more than \$66,000 due to increased length of hospital stays and the need for contact precautions and private rooms. Additionally, a CRE infection can cost an insurance company or other third-party payer as much as \$31,000, and cost society up to \$83,000 in lost work days, wages and life expectancy.¹¹

"Surveillance is tricky, because it's not reimbursed[^]," Moore said. "Labs or hospitals have to absorb the cost, but it's important to do. That doesn't mean you need to screen everyone, but you have to think about risk to your facility. The risk is that colonizing organisms can spread from asymptomatic patients to high-risk patients."

▼ Precautions and interventions

All new carbapenemase-producing CRE cases at Sanford Health in Bismarck are first detected by Irmen's team in the microbiology lab. Once that information is entered in their system, CRE, like other reportable diseases, triggers an automatic and immediate alert to the hospital's Infection Control team. They initiate a protocol that includes patient isolation and heightened hand washing. Similarly, at Rush University Medical Center, once Cepheid's Xpert[®] Carba-R test comes back positive for carbapenemase-producing CRE, Moore's team makes two calls — one to recommend contact precautions to the physician caring for that patient and one to the Infection Control Department, who will ensure contact precautions are enforced for the duration of the patient's hospitalization.

The CDC recommends the following 12 key interventions once carbapenemase-producing CRE are detected in a healthcare facility.⁵

- 1 **Notify quickly**
lab personnel must notify clinical staff of a confirmed case within four to six hours 
- 2 **Require handwashing**
not just by policy, but monitoring and reporting adherence rates and giving staff immediate feedback on non-compliance 
- 3 **Use contact precautions**
wash hands before putting on a gown and gloves, before entering an infected patient's room, and removing them before exiting the room 
- 4 **Minimize and properly use devices**
minimize use of medical devices such as central venous catheters, endotracheal tubes and urinary catheters, which increase the risk of infection 
- 5 **Practice antimicrobial stewardship**
use the narrowest spectrum antimicrobial agents necessary, and only for appropriate indications and duration 
- 6 **Bathe high-risk patients with 2% chlorhexidine**
daily while in high-risk settings, such as the ICU 
- 7 **Clean environment**
clean and disinfect colonized patient rooms and equipment daily 
- 8 **Cohort patients and staff**
house carbapenemase-producing CRE patients in single rooms and dedicate staff to care for them and not non-CRE patients 
- 9 **Screen contacts of carbapenemase-producing CRE patients**
particularly roommates of previously unrecognized CRE patients 
- 10 **Practice active surveillance**
screen everyone admitted to a facility or only high-risk patients, even if not directly linked to known CRE patients 
- 11 **Educate staff**
on the importance of these precautions, as well as the proper donning and doffing of gowns and gloves and device use 
- 12 **Communicate with other facilities**
facilities transferring colonized or infected patients must notify the receiving facility so the interventions above can be swiftly put in place 

[^] when performed for infection control purposes.

There is evidence that many of these interventions work. A 2016 review of seven studies concluded that there is benefit to isolating colonized patients, cohorting infected patients, wearing gloves, enhanced environmental cleaning, handwashing, and educating staff to ensure compliance with all of the above. However, compliance rates and the time it took to get an outbreak under control varied.¹²

▼ Patient perspective

The number of CRE outbreaks is increasing in the U.S. and many other regions globally, as are the number of studies confirming the efficacy of surveillance, prevention methods, and interventions. But few consider the organism truly at the center of the issue: the patient.

In a survey of CRE patients, an Irish hospital discovered that most felt confused by what was happening to them and felt treated like “lepers.” The study concluded that better communication and

patient education is needed when it comes to CRE — and likely other multidrug-resistant infections — in order to potentially lessen patient anxiety, improve satisfaction with their care, and ease future interactions with healthcare providers.¹³ “Listening to the voices of those receiving our care is just the beginning,” the authors wrote. “The challenge is to use these narratives to improve practice and the patient experience.”

One way to do this may be to boost surveillance testing and decrease the turnaround time on test results so that patients can be triaged appropriately and infection control precautions can be implemented as soon as possible to best protect other patients and reduce the number who experience CRE infections.

As CRE continue to expand their geographic footprint, hospitals must be able to quickly identify colonization in order to effectively deploy limited infection control resources. Fortunately, new molecular diagnostic tools have made this rapid detection of CRE a reality in modern healthcare.

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