

Create a Plan



Preparing for Carbapenem Resistant Enterobacterales
in Your Veterinary Practice



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CREATE
Carbapenem Resistant Enterobacterales Animal Testing and Epidemiology

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How to Recognize CRE

It is critical that veterinarians understand how to identify CRE in order to appropriately respond to infected or colonized patients. CRE are organisms that inhabit the gastrointestinal tract but may infect or colonize other sites. These may include, but are not limited to, the respiratory tract, urinary bladder, wounds, and the hepatobiliary tract.

Veterinary practitioners are most likely to encounter CRE when they are isolated by routine culture and susceptibility testing. A relevant culture would identify a gram-negative organism belonging to the bacterial order Enterobacterales (most commonly *Escherichia coli*, *Klebsiella pneumoniae*, or *Enterobacter* spp.) that is resistant to one or more carbapenem antibiotics.

Carbapenem antibiotics typically tested by microbiology laboratories include imipenem, meropenem, and ertapenem. Not all laboratories routinely test for resistance to carbapenem antibiotics and may only include them on extended panels. If an Enterobacterales isolate is resistant to most or all antimicrobial classes, and carbapenem has not been tested, it is prudent to request carbapenem testing regardless of potential treatment plans. If no interpretation (i.e., susceptible, intermediate, resistant) is provided by the laboratory, CRE should be suspected in isolates with a minimum inhibitory concentration (MIC) of 2 mcg/mL or greater for meropenem or imipenem and 1 mcg/mL for ertapenem. Exceptions to this include *Proteus* spp., *Morganella* spp., and *Serratia* spp., which have intrinsically higher MICs for imipenem in vitro.

A complete investigation also includes characterizing the mechanism of resistance for CRE. The most common and concerning mechanism of resistance is the production of a carbapenemase enzyme. Such enzymes hydrolyze carbapenem antibiotics and many other beta lactam drugs and fall into five main classes. These include: *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi Metallo-beta-lactamase (NDM), imipenemase (IMP), Verona integron encoded metallo-beta-lactamase (VIM), and OXA-48.

The genes that encode carbapenemases are often found on mobile plasmids and can be shared between different species and strains of bacteria. Laboratories can use phenotypic and genotypic testing to detect the presence of carbapenemases. Phenotypic tests identify the action of a carbapenemase enzyme through a number of distinct methods, including the modified carbapenem inactivation method (mCIM) and CarbaNP test. Genotypic tests identify carbapenemase genes via polymerase chain reaction (PCR) or whole genome sequencing (WGS). Those interested in learning more about these techniques should visit the LabCREATE section of the CREATE Project's website

It should be noted that not all CRE isolates will test resistant to a carbapenem with in vitro susceptibility testing. Phenotypic or genotypic testing for a carbapenemase, as described above, should be requested for carbapenem intermediate isolates or if CRE is suspected due to therapeutic failure. Veterinarians have a wealth of responsibilities—one of which is to protect the health of patients, staff, and clients. The ability to rapidly recognize CRE is instrumental in this endeavor, as the prevalence of these organisms is likely to increase in coming years.

Create a Plan

**Steps to take
BEFORE you have
a case of CRE in
your vet hospital.**

- 1 Determine if CRE is reportable in your region
- 2 Identify stakeholders for your CRE response team
- 3 Identify sources of funding for a response
- 4 Develop a system to flag positive animals in the medical record
- 5 Ensure a good foundation of infection control policies
- 6 Use antibiotics responsibly in your practice

Having these key structures and systems in place allows a response to be implemented quickly and may help prevent the spread of CRE in your practice.

Determine if CRE is Reportable in your Region

Currently, there are no specific federal regulations that require reporting of CRE isolated from animals. Requirements for reporting vary from state-to-state and may even differ between local public health jurisdictions. Should you always report a CRE case? The answer is currently unclear. For example, CRE are reportable in the City of Philadelphia but not in the State of Pennsylvania. CRE may not be reportable in your region. However, many jurisdictions require veterinarians to report unusual clusters of disease or pathogens of high consequence or concern. If you are unaware of your state or local reporting requirements, you should always contact your state or local public health department for clarification. Some public health departments may make recommendations regarding fecal screening of owners and hospital staff.

Identify Stakeholders for your CRE Response Team

Facilities should have a response-team structure in place in case of CRE in order to promote a rapid, effective response. Internal stakeholders should include practice management, clinicians that oversee the most vulnerable cases (i.e. ICU clinicians, internists etc.), nursing leadership, and environmental services. It may be helpful to include representatives from external partners such as your public health department and your diagnostic laboratory. Each team member will play an important role in the response. Contributions may address areas such as infection control practices, environmental management, medical records, and client and press communication. You should preemptively designate an individual to make definitive, time-sensitive decisions should the need arise.

Identify Sources of Funding for a Response

The costs associated with a single CRE case are considerably lower than that of an outbreak. The latter often imposes a significant cost on the affected facility; the outbreak at PennVet cost over \$200,000.00 to control. The amount spent will depend on the extent of the outbreak and available resources. Costs can include testing, environmental surveillance, and cleaning, particularly if external services are required. Although significant, the cost associated with CRE response is profoundly less devastating than potential damage to a practice's reputation or effects of legal recourse if the problem is ignored.

Develop a System to Flag CRE Positive Animals in the Medical Record

All veterinary facilities should have a predetermined method for clearly identifying CRE patients in the medical record. At PennVet, we have developed a 'flag' that opens each time a positive patient's electronic medical record is accessed. If this level of customization is not available, the paper record and cages of a positive patient should be clearly labeled. Identification allows all responsible clinicians to ensure that adequate infection control is in place during each animal visit.

Ensure a Good Foundation of Infection Control Policies

There are often no clinical signs associated with CRE colonization, which means that CRE can spread rapidly and silently in veterinary hospitals. This is especially true in settings where patients are routinely immune compromised and receive antimicrobial therapy, such as an intensive care unit. In order to limit microbial spread, all veterinary practices should have a standard set of infection prevention policies and procedures. Key aspects of an infection control program to consider include: hand hygiene, personal protective equipment, environmental cleaning, and equipment reprocessing. All of these are best practices regardless of the target pathogen but are particularly salient in the context of CRE.

The single most important aspect of any veterinary infection prevention program is hand hygiene. Hands should be washed before and after handling a patient and before touching any other surfaces. Examples include medical charts, computers, and pens. Hand hygiene of non-visibly soiled hands can be performed with an alcohol-based hand sanitizer. Facilities should have an adequate number of dispensers. There should be multiple dispensers in each room, and they should be located close to patient care areas. Small bottles on carabiners can be purchased and clipped on the outside of populated patient cages for easy access. Visibly soiled hands must be washed with warm water and soap for a minimum of 20 seconds with all surfaces of the hand washed. Hospitals have a responsibility to teach and assess handwash hygiene among employees.

It is important to maintain a clean and clutter-free clinical environment. All facilities should have dedicated staff focused on and trained in cleaning and disinfection best practices. Cleaning (removal of gross debris) must always be performed prior to disinfection. Disinfecting an area without first cleaning it does not constitute appropriate sanitary practice. All disinfection products should be labeled for use in veterinary settings and used according to the manufacturer's instructions for use (i.e. wet contact time, dilutions). Specific standard operating procedures should be set for patient housing and clinical areas. *(Continued on Page 4)*

Ensure a Good Foundation of Infection Control Policies *(continued from page 3)*

Equipment that is reused and shared between patients should be cleaned and disinfected between uses. Non-critical devices (those that do not penetrate soft tissue or bone or come into contact with mucosal surfaces- i.e. stethoscopes and blood pressure cuffs) can be cleaned with appropriate disinfecting wipes or sprays unless otherwise noted. If an item is visibly soiled, it must be thoroughly cleaned before disinfection. For semi-critical devices (those that touch or penetrate mucosal surfaces- i.e. endoscopes), sterilization by autoclave/gas or high-level disinfection with a liquid disinfectant are necessary. Only trained staff should use high level disinfection products to ensure their safe and proper use. Critical devices (those that penetrate soft tissue or bone- i.e. surgical equipment) should be reprocessed and sterilized according to manufacturer instructions. They are most commonly autoclaved or gas-sterilized. Employees that perform these tasks should be adequately trained and routinely assessed. The reprocessing of consumable, or single-use, equipment is highly discouraged. In a study from the University of Pennsylvania (Lavigne et al. 2021), the re-use of endotracheal tubes for anesthesia was implicated in the spread of CRE.

Facilities should have defined policies for the use of personal protective equipment (PPE). Ideally, veterinary staff should wear gloves for examination and treatment of all sick patients (if not all patients). Lab coats should be worn over any street clothing when handling patients, and scrubs should only be worn in the hospital. Soiled clothing should always be changed immediately. Hospitals should always have an adequate supply of gloves, shoe covers, and gowns or coveralls.

Use Antibiotics Responsibly in your Practice

According to the American Veterinary Medical Association (AVMA), antimicrobial stewardship is “the collective actions taken to prevent the emergence and spread of strains of antimicrobial resistant bacteria.” Both robust infection prevention practices and the judicious use of antimicrobial drugs are considered key components of antimicrobial stewardship. The judicious use of antimicrobials is an important component in the battle against CRE but should not be the only strategy used for prevention. Even veterinary facilities that do not routinely use carbapenems are vulnerable to CRE introduction and spread. CRE are typically resistant to most antimicrobials. The use of any antimicrobial may make animals more susceptible to colonization with CRE.

Strategies for implementation of antimicrobial stewardship programs (ASP) are still developing in veterinary medicine. There are many actionable steps to refine antibiotic prescribing practices in hospitals, but it is best to start with simple steps that can have a big impact on overall prescribing. Your practice should identify areas with the most significant potential for improvement and devise a strategy to implement changes that demands accountability. Examples of such strategies include: developing a list of common surgeries and defining which should not receive prophylactic therapy, carrying an expanded range of topical therapeutic options, and lowering the overall cost of culture to make it more accessible to all owners.

Antimicrobial stewardship also requires veterinarians to consider the use of carbapenems in practice. Prescription of carbapenem antimicrobials should be a very rare occurrence, as they represent a critical final line of defense in the medical community. Some veterinarians argue that use of carbapenem antimicrobials should be limited to life-threatening cases, while others believe these drugs should never be used to treat animal patients. Regardless, all practices should have a clear set of guidelines to limit their use.

Veterinarians have a responsibility to promote the health and well-being of their patients and clients. Having a clear, defensible CRE response plan in place protects, not only an individual facility, but also the community it serves.