Kentucky Antimicrobial Stewardship Innovation Consortium

Educational Pearl

Proteus, *Morganella*, & *Providencia* spp.: CRE or Nah?

Carbapenems are a beta-lactam class of antibiotics with broad-spectrum gram-negative activity. Specific carbapenems include meropenem, imipenem, and ertapenem. Carbapenem-resistant Enterobacteriaceae (CRE) are enteric gram-negative bacteria that are resistant to carbapenems and have been deemed an urgent threat by the Centers for Disease Control and Prevention (CDC).[1] CRE are typically resistant to many other antibiotics, resulting in limited options in treating CRE infections. However, some Enterobacteriaceae may be resistant to imipenem, yet not actually classified as CRE. Which bacteria are these? What options are available to manage infections due to these organisms?

Which Enterobacteriaceae have inherent limited susceptibility to imipenem?
Proteus spp., *Morganella* spp., and *Providencia* spp. are inherently less susceptible to imipenem due to non-carbapenemase mechanisms (e.g., altered target binding site, porin mutations, efflux pumps).[2] The 2015 CDC definition for CRE notes that these organisms must be resistant to a carbapenem other than imipenem (i.e., meropenem or ertapenem) to be classified as CRE.[3]

What antibiotics should be used for infections due to *Proteus* spp., *Morganella* spp., and *Providencia* spp.?
Ertapenem and meropenem may still be used to treat infections due to these organisms, if they test susceptible. However, narrower spectrum antibiotics should be utilized, if available, to preserve the broader spectrum of carbapenems.

Morganella spp. and *Providencia* spp. are chromosomal AmpC producing gram-negative bacteria but considered only a moderate risk for clinically significant AmpC expression (i.e., moderate risk for becoming resistant while on treatment). The 2024 IDSA Guidance on Resistant Gram-negative Infections suggests that antibiotic treatment be guided by susceptibility testing. However, in infections with a high bacterial burden and limited source control (e.g., endocarditis, central nervous system infections) the IDSA notes that it is reasonable to select cefepime over ceftriaxone, even if the isolate test susceptible to ceftriaxone.[4]

Key Takeaway: *Proteus* spp., *Morganella* spp., and *Providencia* spp. that test non-susceptible to imipenem but susceptible to meropenem and ertapenem are NOT CRE. Antibiotic treatment should be guided by susceptibility testing and severity of infection.

References:.

1. CDC. Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2019.
2. Clinical and Laboratory Standards Institute. M100: performance standards for antimicrobial susceptibility testing. 35 ed. 2025
3. CDC. Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE), 2015. Atlanta, GA: U.S. National Center for Emerging and Zoonotic Infectious Diseases (U.S.). Division of Healthcare Quality Promotion, CDC;2015
4. Pranita D Tamma, Emily L Heil, Julie Ann Justo, Amy J Mathers, Michael J Satlin, Robert A Bonomo, Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections, Clinical Infectious Diseases, 2024;, ciae403, https://doi.org/10.1093/cid/ciae403

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