

# Physicians slow to use effective new antibiotics against superbugs

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New, more effective antibiotics are being prescribed in only about a quarter of infections by carbapenem-resistant Enterobacteriaceae (CRE), a family of the world's most intractable drug-resistant bacteria, according to an analysis by infectious disease and pharmaceutical scientists at the University of Pittsburgh School of Medicine and

published today by the journal *Open Forum Infectious Diseases*.

This sluggish uptake of such high-priority [antibiotics](#) prompted the researchers to call for an examination of clinical and pharmaceutical stewardship practices across U.S. hospitals, as well as behavioral and economic factors, to see if the trend can be reversed before lackluster sales lead the pharmaceutical industry to stop developing much-needed antibiotics.

"The [infectious diseases](#) community spent the past decade saying, 'We need [new antibiotics](#), this is a top priority,' and now we're at risk of sounding like the boy who cried wolf," said lead author Cornelius J. Clancy, M.D., associate professor of medicine and director of the mycology program and XDR Pathogen Laboratory in Pitt's Division of Infectious Diseases. "We have a responsibility to learn why it takes so long for antibiotics to be adopted into practice and figure out what we need to do to ensure the best antibiotics quickly reach the patients who desperately need them."

The U.S. Centers for Disease Control and Prevention has classified CRE as urgent threat pathogens and calls them the "nightmare bacteria." The World Health Organization and Infectious Disease Society of America have designated CRE as highest priority pathogens for development of new antibiotics. At the time of those declarations, polymyxins were the first-line antibiotics against CRE, even though they failed to work in about half the cases and carried a significant risk of damaging the kidneys.

Since 2015, five antibiotics against CRE have gained U.S. Food and Drug Administration (FDA) approval: ceftazidime-avibactam, meropenem-vaborbactam, plazomicin, eravacycline and imipenem-relebactam. Studies, including those conducted at UPMC, have shown that the first three of these antibiotics are significantly more effective at

fighting CRE and less toxic than polymyxins (eravacycline and imipenem-relebactam are still too new for conclusive data).

Clancy and his colleagues surveyed hospital-based pharmacists in the U.S. to gauge their knowledge of the new antibiotics and their willingness to use them. The drugs were classified as the "first-line" choice against CRE blood infections by 90% of the pharmacists, pneumonia by 87%, intra-abdominal infections by 83% and [urinary tract infections](#) by 56%.

"Clearly hospital-based pharmacists are aware of these antibiotics and believe they are the best choice for the vast majority of CRE infections," said Clancy.

But when the team estimated the number of CRE infections nationwide and used national prescription data to calculate the proportions of old vs. new antibiotics used to treat those infections, they found that from February 2018 through January 2019, the new antibiotics were used only about 23% of the time. Their use likely started to exceed that of polymyxins only in December 2018, nearly four years after the first of the new antibiotics was approved by the FDA. Even after accounting for CRE infections in which new antibiotics might not be first-choice agents, the team found that use was only about 35% of what was expected based on positioning by hospital-based pharmacists.

Allergan and The Medicines Company, developers of two of the new antibiotics, have sought to exit the antimicrobial field since introducing their drugs because of insufficient returns on investment. Achaogen declared bankruptcy months after attaining FDA approval for a third new antibiotic.

The researchers suggest several reasons for the slow uptake of the new antibiotics, starting with cost. A 14-day course of the new antibiotics

costs between \$13,230 and \$15,070, compared to \$305 to \$784 for the old drugs.

"Cost is a limitation, but I'm not convinced it is the sole cause of our findings," said Clancy. "Clinicians may not be prescribing the new drugs due to concerns about accelerating antibiotic-resistance or because initial studies on their effectiveness were relatively small. We need to get at the root causes of the disconnect between what the doctors prescribe and what the pharmacists we surveyed believe they should be prescribing, and then find a solution."

**More information:** Cornelius J Clancy et al, Estimating the Treatment of Carbapenem-Resistant Enterobacteriaceae Infections in the United States Using Antibiotic Prescription Data, *Open Forum Infectious Diseases* (2019). [DOI: 10.1093/ofid/ofz344](https://doi.org/10.1093/ofid/ofz344)

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