

Combining antibiotics, researchers deliver one-two punch against ubiquitous bacterium

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By combining two well-established antibiotics for the first time, a scientific team led by Case Western Reserve University School of Medicine and Louis Stokes Cleveland VA Medical Center has delivered a "double whammy" against the pervasive *Pseudomonas aeruginosa*, a potentially deadly form of bacteria that is a major source of hospital-based infections.

In a recent *Journal of Infectious Diseases* study, investigators showed using two [antibiotic drugs](#) to fight *P. aeruginosa* in mouse models was significantly more effective than either antibiotic alone. The antibiotics were ceftazidime-avibactam, a combination drug used to treat a wide variety of serious bacterial infections, and fosfomicin, used to primarily treat infections of the urinary tract.

"By successfully combining these two drugs against this widespread form of bacteria, we hope to lay a foundation for eventually eradicating the [infection](#)," said the study's lead author Krisztina M. Papp-Wallace, Ph.D., an assistant professor of medicine at the School of Medicine and a research scientist at the Cleveland VA Medical Center. "These findings have significant implications for further studies directed at clinical applications and could bring benefits to numerous patients worldwide."

Immunocompromised patients, such as those with cancer or [cystic fibrosis](#), burn victims and patients on ventilators, are at particular risk from the bacterium, which can be spread by the hands of health-care workers or contaminated equipment.

Bacteria and other microorganisms have increasingly developed resistance to antibiotics, making infections harder to treat and expanding the risk of contamination to others. As a result, health-care costs are also growing. Microorganisms that develop antimicrobial resistance are sometimes referred to as "superbugs." While such resistance typically occurs naturally over time, usually through spontaneous genetic changes, the misuse and overuse of antibiotics in humans and animals is accelerating this process.

The new approach described in the paper is directed at destroying enzymes in the cell wall of the bacterium. Homing in on a particular strain of *P. aeruginosa* known as CL232, the researchers found that, after 24 hours, the ceftazidime-avibactam-fosfomycin combination was much more effective in reducing the presence of the bacterium than the medications individually.

"Dr. Papp-Wallace's insight about combining the two [antibiotics](#) proved to be right on target," said the study's senior author, Robert A. Bonomo, MD, professor of medicine, pharmacology, molecular biology and microbiology at the School of Medicine and chief of the medical service at the Cleveland VA Medical Center. "This is superb bench-to-bedside science and has positive implications for future patients worldwide."

More information: Krisztina M Papp-Wallace et al, Ceftazidime-Avibactam in Combination With Fosfomycin: A Novel Therapeutic Strategy Against Multidrug-Resistant *Pseudomonas aeruginosa*, *The Journal of Infectious Diseases* (2019). [DOI: 10.1093/infdis/jiz149](https://doi.org/10.1093/infdis/jiz149)

Provided by Case Western Reserve University

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