

Research may help rescue antibiotics' effectiveness in the face of drug-resistant bacteria

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Bacteria—especially Gram-negative strains—are becoming increasingly resistant to current antibiotic drugs, and the development of new classes of antibiotics has slowed. Faced with these challenges, investigators are studying the potential of combination therapy, in which two or more drugs are used together to increase or restore the efficacy of both drugs against a resistant bacterial pathogen. Now new research indicates that such synergy may work even when bacteria become resistant to colistin, which is considered a treatment agent of last resort.

The findings are especially promising because recent evidence indicates the potential for rapid worldwide spread of colistin resistance. "For an infected patient, if the multidrug-resistant Gram-negative bacterial pathogen is resistant to colistin, then there is a big problem," said senior author James Kirby, MD, Director of the Clinical Microbiology Laboratory at BIDMC.

In their *Antimicrobial Agents and Chemotherapy* study, Kirby and his colleagues Thea Brennan-Krohn, MD and Alejandro Pironti, Ph.D. screened 19 different [antibiotics](#) for synergy with colistin. The team discovered several combinations where synergy was present and infections with [resistant pathogens](#) could potentially be treated with the [combination therapy](#).

Of particular interest, colistin demonstrated high rates of synergy with linezolid, fusidic acid, and clindamycin, which are protein synthesis inhibitor antibiotics that individually have no activity against Gram-negative bacteria. "It was remarkable to see two drugs, each of which is inactive on its own against these bacteria, inhibiting them in combination," notes Brennan-Krohn. "These findings suggest that colistin retains sub-lethal activity against colistin-resistant bacteria, which

may enable drugs like linezolid to reach their targets."

"Faced with highly resistant pathogens, clinicians often currently treat with multiple antibiotics without knowing the benefit the combinations may provide," said Kirby. "This study now provides some scientific underpinning for these choices and direction for future investigation." He added that combination therapy may also allow clinicians to use lower effective doses of [colistin](#) and other drugs, which would help avoid toxicities associated with the medications as well as slow the development of antibiotic resistance.

Provided by Beth Israel Deaconess Medical Center

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