

Combo of three antibiotics can kill deadly staph infections

September 14 2015, by Jim Dryden



Using three antibiotic drugs thought to be useless against MRSA infection -- piperacillin and tazobactam (bottle on left) and meropenem -- Washington University researchers, led by Gautam Dantas, Ph.D., have killed the deadly staph infection in culture and in laboratory mice. Credit: Robert Boston

Three antibiotics that, individually, are not effective against a drug-resistant staph infection can kill the deadly pathogen when combined as a trio, according to new research.

The researchers, at Washington University School of Medicine in St.

Louis, have killed the bug—methicillin-resistant *Staphylococcus aureus* (MRSA)—in test tubes and laboratory mice, and believe the same three-drug strategy may work in people.

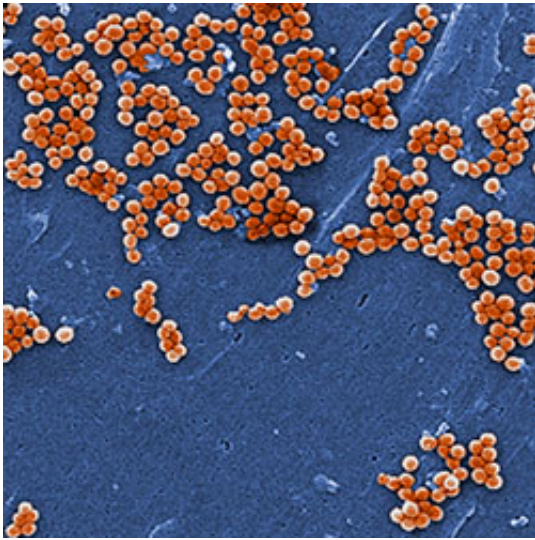
"MRSA infections kill 11,000 people each year in the United States, and the pathogen is considered one of the world's worst drug-resistant microbes," said principal investigator Gautam Dantas, PhD, an associate professor of pathology and immunology. "Using the drug combination to treat people has the potential to begin quickly because all three [antibiotics](#) are approved by the FDA."

The study is published online Sept. 14 in the journal *Nature Chemical Biology*.

The three drugs—meropenem, piperacillin and tazobactam—are from a class of antibiotics called beta-lactams that has not been effective against MRSA for decades.

Working with collaborators in the microbiology laboratory at Barnes-Jewish Hospital in St. Louis, Dantas' team tested and genetically analyzed 73 different variants of the MRSA microbe to represent a range of hospital-acquired and community-acquired forms of the pathogen. The researchers treated the various MRSA bugs with the three-drug combination and found that the treatments worked in every case.

Then, in experiments conducted by collaborators at the University of Notre Dame, the team found that the drug combination cured MRSA-infected mice and was as effective against the pathogen as one of the strongest antibiotics on the market.



Clumps of MRSA bacteria magnified more than 2,300 times by an electron microscope. Credit: Janice Haney Carr

"Without treatment, these MRSA-infected mice tend to live less than a day, but the three-drug combination cured the mice," Dantas said. "After the treatment, the [mice](#) were thriving."

Dantas explained that the drugs, which attack the cell wall of bacteria, work in a synergistic manner, meaning they are more effective combined than each alone.

The researchers also found that the drugs didn't produce resistance in MRSA bacteria—an important finding since more and more bacteria are developing resistance to available drugs.

"This three-[drug combination](#) appears to prevent MRSA from becoming resistant to it," Dantas said. "We know all bacteria eventually develop resistance to antibiotics, but this trio buys us some time, potentially a significant amount of time."

Dantas' team also is investigating other antibiotics thought to be ineffective against various bacterial pathogens to see if they, too, may work if used in combination with other drugs.

"We started with MRSA because it's such a difficult bug to treat," he said. "But we are optimistic the same type of approach may work against other deadly pathogens, such as *Pseudomonas* and certain virulent forms of *E. coli*."

More information: Gonzales PR, Pesesky MW, Bouley R, Ballard A, Biddy BA, Suckow MA, Wolter WR, Schroeder VA, Burnham C-AD, Mobashery S, Chang M, Dantas G. Synergistic, collaterally sensitive β -lactam combinations suppress resistance in MRSA. *Nature Chemical Biology*, published online Sept 14, 2015. [DOI: 10.1038/nchembio.1911](https://doi.org/10.1038/nchembio.1911)

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