Bacteria's appetite may be key to cleaning up antibiotic contamination

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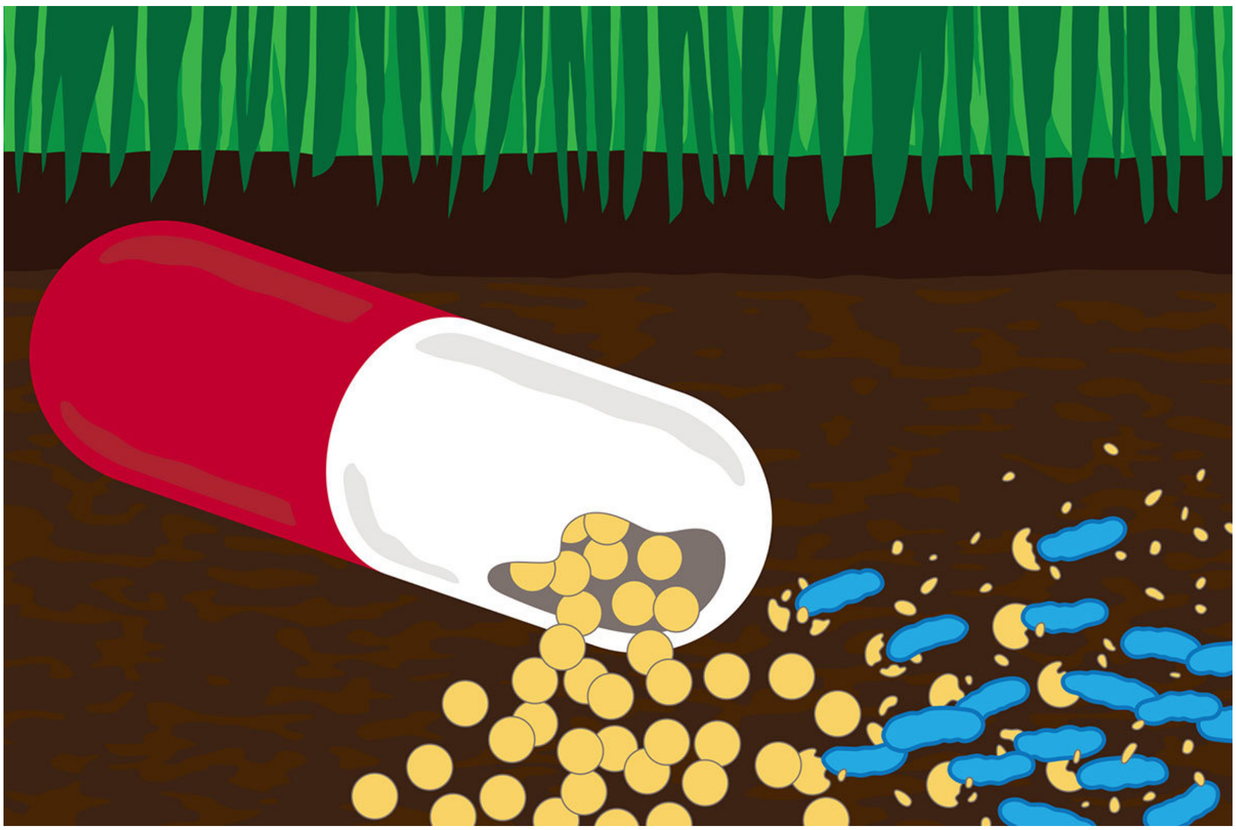

Antibiotics in the environment contribute to drug resistance. But researchers at Washington University School of Medicine in St. Louis have figured out how some soil bacteria turn the drugs into food. The information could lead to new ways to clean up antibiotic-contaminated soil and waterways. Credit: Michael Worful

Antibiotics can be lifesaving for people suffering from serious bacterial infections such as pneumonia and meningitis. The drugs are lethal to bacteria—but some bacteria fight back by developing resistance to antibiotics, and a few not only resist the onslaught, but turn the lethal drugs into food.

Scientists have understood little about how bacteria manage to consume antibiotics safely, but new research from Washington University School of Medicine in St. Louis illuminates key steps in the process.

The findings, published April 30 in *Nature Chemical Biology*, could lead to new ways to eliminate antibiotics from land and water, the researchers said. Environmental antibiotic contamination promotes drug resistance and undermines our ability to treat bacterial infections.

"Ten years ago we stumbled onto the fact that bacteria can eat antibiotics, and everyone was shocked by it," said senior author Gautam Dantas, PhD, an associate professor of pathology and immunology, of molecular microbiology, and of biomedical engineering. "But now it's beginning to make sense. It's just carbon, and wherever there's carbon, somebody will figure out how to eat it. Now that we understand how these bacteria do it, we can start thinking of ways to use this ability to get rid of antibiotics where they are causing harm."

Drug resistance is a serious and worsening problem that threatens to set medical care back to a time when antibiotics were not yet discovered and infectious disease was the number one cause of death worldwide.

Modern industrial and agricultural practices are hastening the rise of antibiotic resistance by saturating the environment with active drugs. In India and China, which together produce the vast majority of the world's antibiotics, pharmaceutical factories sometimes dump antibiotic-laden waste into local waterways. In the United States, some farmers add antibiotics to their animal feed to help their livestock grow, which produces waste loaded with the drugs.

Bacteria easily share genetic material. So when antibiotics infiltrate the water and soil, resident bacteria respond by spreading antibiotic resistance genes through the community.

Dantas, postdoctoral researcher and first author Terence Crofts, PhD, and colleagues wanted to understand how some environmental bacteria not only withstand antibiotics, but feed on them. They studied four distantly related species of soil bacteria that all flourish on a diet of penicillin alone. Penicillin was the first antibiotic discovered, but it has fallen out of favor because of resistance. Other members of the penicillin family such as amoxicillin and ampicillin are still effective and widely prescribed to treat bacterial infections.

The researchers found three distinct sets of genes that became active while the bacteria ate penicillin but inactive while the bacteria ate sugar. The three sets of genes correspond to three steps bacteria take to transform a lethal compound into a meal.

All of the bacteria start by neutralizing the dangerous part of the antibiotic. Once the toxin is disarmed, they snip off a tasty portion and eat it.

Understanding the steps involved in converting an antibiotic into food could help researchers bioengineer bacteria to clean up soil and waterways contaminated with drugs and thereby slow the spread of drug resistance. The soil bacteria that naturally eat antibiotics are finicky and difficult to work with. But a more tractable species such as E. coli potentially could be engineered to feed on antibiotics in polluted land or water.

Crofts and Dantas showed they could give E. coli the ability to survive and thrive on penicillin. The bacterium normally requires sugar, but with some genetic modification and the addition of a key protein, it flourished on a sugar-free diet of penicillin.

"With some smart engineering, we may be able to modify bacteria to break down antibiotics in the environment," Crofts said.

Any such bioengineering project would have to include a plan to speed up the antibiotic-eating process. The way soil bacteria naturally remove antibiotics from the environment is effective but slow. They couldn't possibly handle the amounts of antibiotics near pharmaceutical factories and in sewage facilities.

"You couldn't just douse a field with these soil bacteria today and expect them to clean everything up," Dantas said. "But now we know how they do it. It is much easier to improve on something that you already have than to try to design a system from scratch."

More information: Terence S. Crofts et al, Shared strategies for β-lactam catabolism in the soil microbiome, *Nature Chemical Biology* (2018). DOI: 10.1038/s41589-018-0052-1

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