The War against Superbugs

DePaul Biologist Studies Deadly Bacteria in Their Environment

Joanna Brooke works with student researchers Margaret Johnson and Ramneek Mangat. They are trained in biosafety, and "we run a very tightly regulated lab," Brooke says.

Joanna Brooke's lab is filled with mutants. But don't worry—they can't get out. And even if they could, they may be more vulnerable to antibiotics, due to genetic alterations engineered by Brooke and her students.

Brooke, an associate professor of biological science who teaches microbiology, biotechnology and medical bacteriology, studies *Stenotrophomonas maltophilia*, a bacterium that infects people with weakened immune systems. According to a recent article in the International Journal of Antimicrobial Agents (elsevier.com/locate/ijantimicag), this bacterium is a "newly emerging superbug."

The death rate is as high as a frightening 70 percent, partly because *S. maltophilia*, or "Steno," as Brooke and her students call it, is so clever at eluding antibiotics. It produces antibiotic-attacking enzymes, changes the surface of its cells so that the drugs can't get in, and alters its own genome by borrowing DNA from other species.

by Elizabeth Gardner

"It's an interesting organism because it's ubiquitous in the environment—in lakes, streams, rivers, wherever there's water," she says. "You and I will come into contact with it through tap water, but our immune systems are strong enough that we're not susceptible. But we're running out of drugs that will work on it, and the mortality rates are going up. It has the potential to become a superbug."

Brooke has spent the past five years as principal investigator for a study funded by the National Institutes of Health on how *S. maltophilia* forms "biofilms" on the surfaces of medical equipment in hospitals and implanted devices in patients. A biofilm is a tough protective layer made out of polysaccharides, proteins and DNA. Some types of bacteria can form biofilms around themselves when enough of them cluster together, making a barrier that antibiotics can't breach. *S. maltophilia* biofilms can cause pervasive, persistent and deadly hospital-acquired infections because they can lurk in nebulizers, catheters, and other moist environments.

Part of Brooke's research is to create genetic variants of the bacteria. Some of them lack the ability to form biofilms, or form only very weak ones, while others are extra good at it. The idea is to figure out exactly how the films work and how to stop them. She and her students replace certain "gene targets" with different genetic sequences and study what effect the change has on biofilm formation. They find those targets partly by using gene databases put together by other researchers. In turn, they contribute their own information to those databases.

Altering the organism's genes could also make it more directly susceptible to antibiotics, Brooke says. "Steno has the ability to make enzymes that break down antibiotics, so drug therapy might be more effective if you combined different antibiotics that target different parts of the cell."

Brooke fell for biofilms as an undergraduate at the University of Guelph in Ontario, Canada, when she took her first microbiology course and her mentor introduced her to them via an electron microscope. She went on to earn a master's degree and a Ph.D. at the University of Western Ontario and was a postdoctoral fellow at the University of Texas Southwestern Medical Center, where she studied diphtheria toxin receptors.

Studying individual bacteria is only part of the story, and not the most important part, Brooke believes. "An organism may be sensitive to an antibiotic in a test tube, but not in a patient," she says. That's where a second component of her research comes in: studying how bacteria survive on surfaces and sometimes work together to thwart their human adversaries. For example, Brooke says several studies have shown that *S. maltophilia* can work together with some strains of *Pseudomonas*, using its enzymes to fight penicillin that would otherwise kill the *Pseudomonas*.

And it's not just different species of bacteria that team up: Brooke says researchers have discovered examples of bacteria and fungi working together to create biofilms. "It comes down to being willing to consider the context of the microenvironment," she says. Carbohydrates, proteins and lipids can interact even when they're produced by unrelated organisms.

Finding where bacteria gather, and why, is an essential step in fighting infection. A 2009 paper published by Brooke and her group in the Journal of Environmental Health looked at bacteria on 70 surfaces around a university: telephone mouthpieces, water fountain drains, computer keyboards, photocopiers, and elevator and vending machine buttons. The team found *S. maltophilia* in 60 percent of fountain drains, and *Staphylococcus aureus*, a common cause of infections, on just about everything. None of the bacteria they found were antibiotic-resistant strains, but the findings were of no comfort to the germ-phobic.

"Given the rise in community-acquired infections, we wanted to see what's happening on surfaces: which bacteria are present, how many, and do they have the potential to cause infection?" Brooke says. Next, she wants to find out how the numbers compare with those in hospital environments, and whether doing a more effective job of disinfecting surfaces would significantly reduce infection rates. The group published a related paper in the same journal testing three different disinfectants on public telephone mouthpieces. (A cleaner with 1.84 percent sodium hypochlorite wiped out 100 percent of the bacteria, beating both isopropyl alcohol and ammonia-based cleaners.)

Brooke also is interested in the question of where the bacteria originate. "Are they coming from patients and being spread to surfaces, or is it the other way around?" She's interested in tracing the movement of bacteria using molecular analysis to differentiate among the many strains.

"I teach that it's not good enough to look at one organism in pure culture on a Petri plate," Brooke says. "Microbial infections in patients are often communities—not just one genetic system."

Brooke says the fight against microbes has two fronts: prevention and cure. She's glad to see growing worldwide appreciation of simple strategies like handwashing, disinfecting surfaces, and not crowding patients together in hospital wards, as well as outside-the-box thinking on how to thwart bacteria once they're in the body. For example, some researchers are studying the protein pathways that allow microbes to produce enzymes that break down antibiotics. If those pathways can be disrupted, the bacteria may be crippled. Other discoveries are coming directly from nature, like a chemical compound from the eastern red cedar tree that was recently shown to kill methicillin-resistant *S. aureus* (MRSA).

Will mankind win the war against superbugs? "I don't know if we can ever say we've won, because these organisms have such an ability to adapt and evolve," Brooke says. "We're just trying to stay ahead of what's going to happen next."

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