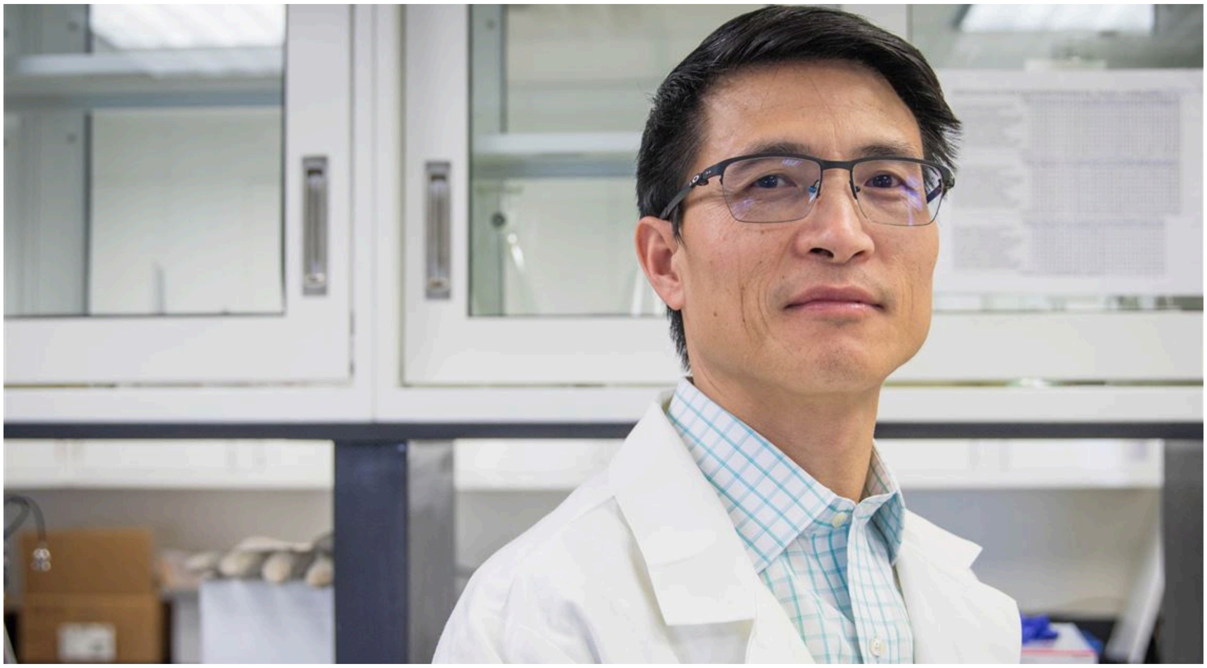

WVU researchers take a cue from the past to tackle antimicrobial resistance

Supported by a $1.9 million grant, the team honed in on the significant challenges posed by open fractures and their increased risk of infection

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Antimicrobial resistance is one of the most pressing challenges in global health today, and it threatens to reverse the progress made since the discovery of penicillin. Often called the "miracle drug," penicillin transformed health care, but now the effectiveness of it and other antimicrobials are under threat.

Antimicrobial resistance (AMR) occurs when bacteria and viruses adapt and no longer respond to antibiotics or antivirals. That means medicines, including penicillin, no longer work as well as they should. AMR is a natural evolutionary process, but the misuse and overuse of antimicrobials are accelerating that process, making infections more challenging to treat and increasing the risk of severe illness.

The World Health Organization considers AMR to be one of the top threats to global health, estimating it contributed to 4.95 million deaths in 2019. WHO and the National Institutes of Health agree that novel technologies must be developed to address and prevent the spread of such resistance.

One approach is occurring just across the Pennsylvania border: Bingyun Li, a professor at the West Virginia University School of Medicine, and his team are turning to a centuries-old treatment to pursue a “new” innovative approach involving silver, and their work shows significant promise.

"It's very exciting that they’re discovering other ways to fight infection — basically re-engineering old techniques to make them safer for cells,” said Holly Johnson, an orthopedic surgeon and associate professor at Weill Cornell Medical School, New York, who is not a part of the research team.

Long before we understood that germs caused sickness, silver was used as an antimicrobial agent. Ancient Greeks and Romans relied on it to disinfect water and preserve food supplies, and it was frequently used as a wound dressing, treating burns and open injuries to prevent infection. While ancient cultures learned through experience of silver’s almost magical protective properties, today we know that this is because silver is toxic to bacteria and viruses.

Silver began to be replaced by antibiotics as a primary treatment in the 1900s — penicillin came into mass production around 1945 — but has in recent years resurfaced as a potential solution to the growing problem of antimicrobial resistance.

Supported by a $1.9 million grant from the NIH, Li and his team honed in on the significant medical challenges posed by open fractures, with their increased risk of infection, to investigate how silver might help.

To improve silver’s germ-fighting ability, Li and his team had to go small — very small. They created carbon nanotubes that could deliver silver nanoparticles directly to the sites of infection. These nanoparticles are extremely small, between 1 and 100 nanometers wide. To put that into perspective, a single nanometer is one-billionth of a meter — much smaller than the width of a human hair and undetectable to the human eye. As its name suggests, the nanotube is a cylindrical nanostructure that acts as a precise delivery system for the silver nanoparticles.

Orthopedic surgeon and research team member Matthew Dietz describes that technology as “like shoving a pool noodle full of different-shaped, marble-sized balls that then get delivered through the tubes to the site of the infection.” The team developed a protocol that delivers silver directly to infection sites by combining silver nanoparticles with carbon nanotubes.

Toxic to microbes, silver can also be harmful to human cells — albeit in significantly higher doses. The research team found that combining silver nanoparticles with carbon nanotubes created a “synergistic effect,” where the two substances together were more effective than either alone. Using less silver reduces toxicity while maintaining its germ-killing power.

“With this new formulation,” Li said, “we can use much less silver and get higher antimicrobial properties, reducing the concern of toxicity and potentially adding an alternative for future antibiotics.”

Antimicrobial resistance is poised to make common surgeries and minor infections more dangerous, undoing much of the progress we've come to rely on in modern medicine. While minor, localized infections such in the ear or superficial skin abscesses can lead to severe complications, they are typically manageable when addressed properly. As antimicrobial resistance continues to increase, these will be harder to address.

Even today, there are serious infections that are difficult to treat. Infections that arise from acute trauma, such as open bone fractures, or ones that result from implanting foreign bodies, such as artificial joints or pacemakers, can lead to devastating complications, including chronic pain, prolonged hospital stays, the need for additional surgeries and even life-threatening infections. Li and his team are striving to address these pressing issues.

Dietz is particularly excited about the team Li has put together. He finds the team component particularly refreshing. “[Li’s] so smart and mechanistically focused on things,” Dietz said, “but he is willing to listen to the surgeon who is saying, ‘Hey, we've got this problem.’ and Li responds ‘Yep, how can we try and fix it?’”

What are some of the problems surgeons are dealing with? Open tibial fractures, for one. Unlike many other bones, the tibia, the weight-bearing bone in the lower leg, is located just beneath a thin layer of skin, making it highly vulnerable to trauma that can result in an open fracture. The likelihood of infection escalates once the bone is exposed to the outside.

Open fractures frequently need to be treated surgically, rendering the tissues more vulnerable to infection. This is a problem Li thinks can be solved with silver nanotechnology. “With this new formulation, we can use much less silver and get higher antimicrobial properties,” Li states.

The WVU team envisions the technology they have developed being used in instances beyond fractures. Dietz references the military setting as an example: “We have war fighters that are involved in terrible accidents, and we are able to save their lives, but they are coming home with these terrible infections, and presently we don't have a great solution for them.”

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