

Texas A&M center confronts antibiotic crisis with potential new bacterial treatment

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Dr. Jason Gill, program director, Center for Phage Technology, examines lab work in progress. Credit: Texas AgriLife Research photo by Kathleen Phillips

It's been called "the trots," "Montezuma's Revenge," "the runs" and worse. But no matter the name, when it strikes, victims wish for a medicine that could go straight to the offending bacteria to quickly knock it dead.

That wish will ultimately come true if work by Texas A&M University scientists stays on target at the Center for Phage Technology in College Station.

A "medicine that grows" is how the phage concept was described by Dr. Ryland Young, a professor of biochemistry and biophysics who was



instrumental in establishing the center.

"Phage is a word that simply means viruses that grow on bacteria," Young said. "They are harmless to humans, harmless to animals, harmless to plants. The only things they attack are bacteria. And every kind of bacteria that are involved in the disease process has bacteria phages that will attack them. So if you are a bacterial cell, your enemy is the bacterial virus."

Young said new technology to fight bacterial diseases – of which there are many in addition to "the trots" — is critically important because people and animals have become increasingly resistant to antibiotics currently on the market. And yet, he said, there is no major U.S. pharmaceutical company currently trying to develop new antibiotics.

"There is not enough money in it," he said. "You can't blame them. They are companies and they are there to make money. They can make a lot more money making pain drugs and lifestyle drugs. Antibiotics are not a particularly attractive investment."

When antibiotics work, he explained, people get well and don't need drugs any more. Yet bacterial illnesses at a minimum cause lost productivity in the workplace and schools, and some bacteria, such one commonly called MRSA, or methicillin-resistant Staphylococcus aureus, can be deadly.

"There is kind of a worldwide crisis right now in human medicine because for some bacteria such as MRSA, we are down to only one antibiotic that works," Young said. "Bacteria have this very pronounced characteristic of being able to very rapidly become drug-resistant. And that's a problem. There is a need for alternatives to antibiotics."

So serious is the issue, that the Interagency Task Force on Antimicrobial



Resistance was initiated in 1999 following a congressional hearing on the topic, according to the Center for Disease Control and Prevention. Ten federal agencies are participating in the effort. A transatlantic effort on the topic was formed between the U.S. and Europe in 2009.

"People infected with antimicrobial-resistant organisms are more likely to have longer, more expensive hospital stays, and may be more likely to die as a result of the infection," the CDC notes on its website.

Phages are not new to science. They were first described in 1915, before what Young called "modern biology." Years after the phage discovery, scientists began exploring molecular biology and the intricacies of DNA.

What researchers now know is that the phage, or bacterial virus, encounters a bacterial cell, absorbs to it, injects its DNA into it and "typically 30 minutes later, the bacteria cell explodes," Young explained. Several hundred new virus particles then continue on to eliminate other targeted bacterial cells, if any.

So, almost 100 years after their discovery, scientists can isolate bacteria phages, sequence their DNA and engineer them to be more effective against certain types of bacteria, he said.

"They are relatively cheap to produce," Young said. "All you need to grow them is a culture of the bacteria that you want to kill. You throw one bacterial phage particle in there, come back in a few hours and you have trillions of the bacteria phages, and the bacteria cells have all been killed. Phages grow themselves, that's the beauty of them."

However, regulation will play a role in future development, he noted, because U.S. Food and Drug Administration policies currently subject phage technology to the same criteria as chemical drugs.



"If I give you a chemical drug, that drug is likely to penetrate every tissue of your body — your ears, your eyes, your nose, your heart, your kidneys. And a chemical can have a different effect on every organ," Young explained. "And that is why drug testing is so important. I would not advocate lowering the barriers for chemical drugs at all.

"But bacteriophages are not going to go to your eyes, your ears, your brain. And even if they did, they can't do anything," Young said. "They're not capable of even recognizing human cells, and even if they could, the way genes are set up in bacteria phages are completely different than the way they are in humans, so they would not be recognized as genes."

The researcher said part of the center's plan is to educate policy makers so that the rules can be changed for approving phage-based medications for humans without subjecting them to the same type of requirements for chemical pharmaceuticals.

He said phages will likely first be used in veterinary medicine because the barriers for testing for animal use are a lot lower. Veterinary applications could be in use within 10 years, Young believes.

"Once we are successful in veterinary applications, there will be a lot of pressure to get phage therapeutics approved for humans," he said. Dr. Jason Gill, program director, Center for Phage Technology

Young said the center is midway through its five-year development plan and is hiring faculty with phage expertise to conduct research and assist other scientists with projects where phage technology might be introduced. Young expects the phage center to eventually have 15 scientists developing different phages to target different needs.

"This is translational research," he said, "which means taking the basic



research and translating it to practical applications as into commercial products. And we're the first such entity in the world."

"In the long run, we'd like to <u>bacteria</u> phages exploited to their fullest for human, animal husbandry and veterinary antibacterial uses," Young said.

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