

NEW INFECTION TREATMENTS CAN HELP AVOID AMPUTATIONS



Dreamstime/TNS

The rising incidence of “superbugs,” which have evolved to resist human-made antibiotics, is driving renewed interest in phage therapy. Modern phage researchers and entrepreneurs now have the tools to rapidly analyze the genomes of bacteria and phages, and machine-learning may aid in finding the perfect match.

Battling ‘superbugs’

■ With antibiotic-resistant bacteria a growing problem, medical researchers are experimenting with treatment using phage, the most common organism on Earth with potent properties for killing bacteria that frequently infect humans

By Joe Carlson
Star Tribune (Minneapolis)

MINNEAPOLIS — John Haverty was ready to have his leg amputated. Haverty, 62, of Brownsville, Minnesota, had 17 surgeries over a decade to rid his right leg of a stubborn infection that lingered after knee-implant surgery. He had no way of knowing his eventual cure lay in a bacteria-killing virus known as a “phage,” found writhing in a sewer treatment plant.

In February, before Haverty knew anything about phages, his doctor at the Mayo Clinic leveled with him: Antibiotics were proving ineffective against the *klebsiella pneumoniae* bugs causing Haverty’s infection, and he would probably grow so weary of surgeries that he would eventually opt to have the leg removed at the hip. “You are going to tell me when you want your leg amputated,” Haverty recalled his doctor telling him. “We’re not going to tell you.”

Haverty and his wife soon went shopping for a post-amputation wheelchair, but he kept looking for answers online.

Many leads went nowhere. Then, one day, a response email arrived from a company called Adaptive Phage Therapeutics in Gaithersburg, Maryland. The email would trigger a series of events that would prevent Haverty’s planned amputation, by getting rid of the infection.

Haverty, it turned out, was just the 14th person worldwide treated with a phage (rhymes with “rage”) selected by Adapative Phage Therapeutics (APT). He was also the first patient treated in the nascent phage-therapy program at the Mayo Clinic in Rochester.

The rising incidence of “superbugs,” which have evolved to resistant human-made antibiotics, is driving renewed interest in phage therapy. Researchers say phage are the most common organism on the planet. Experimental efforts a century ago to

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harness phage for infections faded from mainstream science partly because antibiotic drugs worked so well and were relatively cheap.

Modern phage researchers and entrepreneurs now have the tools to rapidly analyze the genomes of bacteria and phages, and machine-learning may aid in finding the perfect match.

Haverty’s procedure, approved by the Food and Drug Administration as a compassionate use of an unapproved therapy, was described by APT as “pioneering” because Haverty was one of the first people to have a prosthetic joint infection treated with a phage selected by the company.

“You have to realize that the standard of care when antibiotics have failed, like in the case of John Haverty, often involves amputation and, sometimes, extended time in an intensive care unit. And too often, (it) results in death,” APT CEO Greg Merrill said. “We can deliver (phage) therapy extremely fast, and at price points well below the current standard of care for dealing with these infections.”

APT is an early-stage operation that is in the business of precisely matching a person’s infection with the specific bacteria-killing virus, known as a phage, that will treat it. The for-profit company acquired worldwide exclusive rights to phage technology developed by the U.S. Navy’s Biological Defense Research Directorate, and is now developing and refining its systems for identifying, storing and transporting phage therapies.

In Minnesota, Haverty’s doctors at the Mayo Clinic worked with APT to do genetic analysis of the infectious bacteria and its potential phage treatment. Infectious-disease physician Dr. Gina Suh, one of the Mayo doctors who has treated Haverty, said

she couldn’t discuss specifics about Haverty’s procedure before publication in a medical journal.

But, in general, she noted the benefits of phage aren’t limited to targeting bacteria with genetic resistance to traditional antibiotics. Phage therapy is also believed to be highly effective at penetrating “biofilm” that grows on infected implants. Once biofilm covers a metal implant, it becomes vastly more difficult to treat the infection, even if the bacterium isn’t totally resistant to antibiotics.

“Phage can play a role in biofilm infections. Prosthetic joint infection is one. Other examples of this would be, if someone has plates and screws, fracture-fixation devices that become infected, spinal hardware that becomes infected, indwelling brain devices called VP shunts, cardiac devices such as ICDs (implantable cardioverter defibrillators),” Suh said. “The list goes on and on.”

A phage is a virus that can only kill a bacterium. It has a head like a 20-sided die from a role-playing game, mounted on a thin body with tiny fibers at the bottom that look like spider legs. An animation from the National Institute of Allergy and Infectious Diseases shows a phage dropping onto a bacterium like a moon lander and injecting its phage DNA into the bacterium to “hijack” the host’s genetics. Eventually, umpteen new phage spawn inside and obliterate their bacterial host as they break free, restarting the phage life cycle.

Unlike other early-stage phage companies, APT is not genetically editing the phage it uses in its treatments.

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son of widely known phage expert, Dr. Carl Merrill, who was profiled in an extensive report about phage therapy in the biomedical publication *Stat* last year.

Haverty says the specific bacteria-killing virus used in his case was culled from gunk found in sewage treatment plant. That icky location doesn’t surprise him or medical experts, since viruses that kill bacteria tend to live in bacteria-rich environments.

Haverty said the treatment from APT was free to him, since it’s not yet approved by the FDA. (He declined another phage therapy, partly because the center wanted to charge him \$10,000.) The FDA is interested in facilitating the “development and rigorous clinical assessment” of phage products, and in 2017 the agency held a two-day meeting to highlight the goal.

Today, numerous phage organizations exist, including 28 private entities like APT and 54 phage labs worldwide listed on the open-source research website Phage Directory.

APT’s Greg Merrill said the company plans to recruit patients in up to four different clinical trials at 10 sites in 2020. The company has nearly 1,000 phages meticulously cataloged and stored, and is targeting eight common types of bacterial infections.

“It’s like having many arrows in your quiver — we should be able to have an arrow that takes out the target,” said APT chief operating officer Subhendu Basu.

For John Haverty, a doctor’s stark assessment has given way to a life of renewed vigor. Recent photos show Haverty and his wife taking a walk among the red rocks of Arches National Park on a car trip through Utah.

“I’m like a kid again. I’ve gone back 10 years in age,” he said. “I can see myself as an old man now walking my dogs down the road again, whereas before, I didn’t have much of a lifespan in mind at all.”

Options aplenty for tracking blood pressure

By Barb Gonzalez
For The (Bend) Bulletin

Uncontrolled high blood pressure can lead to stroke, heart disease, aneurysm, vascular dementia, chronic kidney disease and erectile dysfunction. As there are usually no symptoms to indicate high blood pressure, measuring it is essential to find your numbers.

Technology has become a great helper in monitoring your health with several devices that can measure and track your blood pressure and other vitals.

According to the Central Oregon Health Council, half the people living in the area have high blood pressure. The Centers for Disease Control and Prevention has created a new guideline that indicates normal blood pressure is 120 (systolic pressure or the pressure in your arteries when your heart is contracting) over 80 (the blood pressure measurement between heartbeats). You are considered to have stage 1 hypertension if your numbers are higher than 130 over 89. As these new guidelines are lower than previously recommended, the CDC encourages everyone to monitor blood pressure at home. Check with your insurance company for possible coverage of a blood pressure device.

Many blood pressure monitors (BPMs) are available that sync with a smartphone app to record, track and create a document to send to your health care professional. From full blood pressure cuffs that can also monitor your heart to a smartwatch, you can easily monitor your heart health at home.

Withing Blood Pressure Cuffs

I’ve been using a blood pressure cuff for a few years. It’s helped my doctor and I dial in a plan to regulate my blood pressure. It is clinically validated and has proven to be reliable and accurate when compared to the measurements taken in my doctor’s office. I’m happy to see that Withings has made the newest version of the BPM Connect (\$100) more compact. A soft cuff that can wrap around a 6-inch long core, so it easily fits into a purse or backpack. The core appears to be solid white until you press the start button, which reveals LED lights that shine through to indicate functions and display the results.

As many as eight people can use the same BPM Connect. When starting the measurement, users can choose between taking a single measurement or average three consecutive measurements for a more accurate reading. A light shines green for healthy blood pressure levels, yellow for slightly elevated or red for critically high — time to get to the doctor. Previous generations of the BP Connect cuff required a phone to take measurements. Because of the core display, the new Connect can take a measurement without a phone, show you the results, then sync the data to the Withings HealthMate app later.

The Withings HealthMate app also syncs with the company’s wireless scales and Pulse fitness trackers to track your activity, calories, sleep, weight and environment. HealthMate coordinates info with Apple Health, My Fitness Pal (for calorie intake) and other compatible apps.

I was also able to test the Withings BP Core blood pressure cuff (\$250) that measures all aspects of heart health. Currently, it is only available in Europe. But Withings expects FDA approval and a U.S. release in 2020.

Hot Yoga lowers my blood pressure significantly. As I feel dizzy after class, I wanted to know if it was because of a drop in blood pressure (It was. It went down to 98/65). The MocaCuff (\$45) comes with a hard-shelled travel case. It conveniently takes the blood pressure measurement using a wrist band, so I don’t have to fuss with wrapping a big cuff around my sweaty arm. It is crucial with a cuff device to keep it at heart height for accurate measurements. The MocaCuff displays your results on the device along with a color-coded indication of normal to critically high hypertension. It also syncs with the MocaCare phone app that can export results to share with your healthcare professional.

Blood pressure from a smart watch

The Samsung Watch Active (\$200) and Active2 (\$300) make it even easier to track your BP using the smart watch you are already wearing. Currently, it is only available as part of an opt-in study with the University of California, San Francisco, through the My BP Lab app on GS 9 or newer Galaxy phones. It requires an accurate recent blood pressure measurement as a baseline then uses the app to track changes to that baseline, estimating a readout of your current blood pressure numbers.

These are just a few of the blood pressure monitors available. Be sure that any device you use is FDA approved and follow directions to get the most accurate measurement possible.