

How viruses beat a superbug—and saved a man after 9 months of near-certain death

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In the end, it was viruses, not an antibiotic, that saved Tom Patterson's life after a superbug infection he suffered in Egypt left him hallucinating, comatose and near death for months.

Acinetobacter baumannii, a type of toxin-excreting bacteria ranked near the top of the U.S. government's threat list, had nearly destroyed the University of California, San Diego professor's kidneys. At that point, his wife, the infectious-disease specialist Steffanie Strathdee, decided to get creative.

Why not try infecting her husband with bacteria-hunting viruses called bacteriophages? After all, the medical literature showed that these ancient microbes can kill even germs that have evolved resistance to all antibiotics. But finding just the right bacteriophages would be a painstaking and risk-filled process.

With Patterson's condition deteriorating rapidly and seemingly no other way to save his life, his medical team at UC San Diego Health agreed to give the bacteriophages idea a try.

The team worked with the Navy, Texas A&M University, San Diego State University and AmpliPhi Biosciences, a local biotech company. They collected, concentrated and purified an army of bacteriophages picked for their ability to seek out and destroy the specific strain of bacteria that was multiplying out of control throughout Patterson's body.



There were fears that this experimental therapy, put together in only 20 days under an emergency exemption by the U.S. Food and Drug Administration, might actually prove toxic and kill the patient. Instead, the approach produced a miraculous turnaround for Patterson.

His case, which began in late 2015 and stretched for more than nine months, is believed to be the first instance of bacteriophages being used intravenously to treat a patient who was near death because of an infection caused by drug-resistant bacteria. The medical and research team's triumph was touted last week at a conference in Paris and in an announcement by AmpliPhi. It is also expected to be the subject of an upcoming report in a scientific journal.

Dr. Robert Schooley, Patterson's doctor and head of the infectiousdiseases division at UC San Diego, said he will never forget the moment when it became clear that his patient would survive.

"When he opened his eyes, it was a sense of elation I haven't had many times in my career," Schooley said. "Up until we tried the phages, it had just been a continuous downhill course no matter what we tried, and there was just not much hope left."

Schooley and others who helped treat Patterson cautioned against drawing broad conclusions from this dramatic turnaround, and they said much more analysis will be needed to turn this one case into a regimen of care for many other patients. Nonetheless, they agreed that Patterson's triumph represents an intriguing way to fight back against the scourge of superbugs - which is growing as the world struggles to develop new kinds of antibiotics.

Bacteriophage therapy is not new.

French microbiologist Felix d'Herelle and British bacteriologist



Frederick Twort are credited with identifying bacteriophages a century ago. Before the discovery of penicillin, bacteriophage treatment was common in America and Europe and has continued in Russia and Poland even though it has fallen out of favor in most countries.

The journey to this field of treatment for Patterson began on Nov. 28, 2015, just after he and Strathdee, who also works at UC San Diego, visited Egypt for vacation.

Patterson woke up with severe abdominal pain followed by fever, nausea, vomiting and a racing heartbeat. The condition worsened as he arrived at a medical clinic, and he was soon evacuated to Germany, where doctors drained fluid from a cyst around his pancreas. Those physicians soon diagnosed him as being infected with the deadly superbug.

The toxins pumped by the bacteria into Patterson's bloodstream caused not only pain, but also hallucinations. He remembers perfectly lifelike scenes of wandering in a desert for 100 years, watching his wife disappear into asphalt and consulting with men in flowing white robes who kept stopping him from moving toward his destination because he had failed to eat a special leaf inside a wooden box within a prescribed time limit.

At one point, he said, he resolved to end it all by eating the sand under his feet in that psychedelic desert.

"I started to drink the sand, I looked down, and the sand was pouring out through my ribs. I couldn't even kill myself," he recalled thinking at the time.

Now, back from the edge of death and having completed a long course of physical therapy that has allowed him to return to his job as a



professor of comparative psychology, Patterson said the toxin was distorting his mind's ability to interpret the things around him.

"You create the most rational story you can from the bits and pieces that are feeding into your brain," he said.

Strathdee said arriving at the decision to try an experimental treatment on her husband was torture. "It was the craziest thing I have ever done and hopefully ever will do in my life," she said.

The gamble paid off. The moment Patterson awakened from his coma was a bit surreal, she recalled. In the hospital for nine months and hallucinating or in a coma for most of that time, there was some serious catching-up to do.

"He woke up and said, 'What's been going on?' And I told him, 'Donald Trump is the nominee for president, and we saved you with purified sewage from Texas,'" Strathdee said. "He looked at me and said, 'I'm hallucinating again.'"

That's right, sewage.

It turns out that if you're looking for bacteriophages capable of subduing bacteria that commonly infect people, then human wastewater is a great place to search. For years, scientists have been collecting, cataloging and freezing samples of these viruses after screening them for potentially dangerous traits.

When Patterson's medical team at UC San Diego agreed to pursue a bacteriophage treatment, it asked the FDA for special approval under the agency's Emergency Investigational New Drug program.

The regulators could not have been more accommodating, said Schooley,



the doctor for Patterson. They steered him toward the Navy, which has been using its network of ships to collect a comprehensive library of bacteriophage specimens for years.

On March 15, 2016, doctors infused a cocktail made up of four kinds of bacteriophages provided by Texas A&M and AmpliPhi Biosciences. Another round obtained from the Navy's Biological Defense Research Initiative was given on March 17. Patterson woke up from his coma on March 19.

Because no single bacteriophage can take out every permutation of Acinetobacter baumannii, it was necessary to use several versions. At one point, Patterson's team had exhausted all available types of bacteriophages.

Not to be deterred, the Navy turned to a new sewage sample and discovered a few more kinds that should prove effective.

Bacteriophage therapy has fallen out of favor in many countries partly because in decades past, science had not progressed enough to precisely match particular viruses with the particular bacteria they prey on. Centrifuges also were not yet powerful enough to purify bacteriophages to the level that is now possible.

Today, an increasing number of labs are working with bacteriophages. Yale University recently had great results treating a patient's drugresistant bacterial infection with a single type of bacteriophage isolated from a water sample taken from a lake.

Dr. Paul Turner, chief of ecology and evolutionary biology at Yale, said Patterson's case was more complicated than his team's because it required multiple strains of bacteriophages.



"These two cases nicely illustrate the promise as well as the challenges of phage therapy," Turner said.

He noted that broadening the use of this old but new treatment is very doable but not trivial.

"The challenge, of course, is which phages should be chosen to do the job? This will require a lot more research so that basic researchers and physicians can amass a next-generation drug arsenal," Turner said.

UC San Diego is considering whether to create its own <u>bacteriophage</u> center, complete with its own library of viral samples.

Meanwhile, the 70-year-old Patterson joined last month's March for Science in San Diego. The event was one of hundreds held around the nation to promote the value of science.

Patterson carried a sign that proclaimed: "Science saves lives."

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