Antibiotic resistance may be dangerous—but it's hardly new

Gonorrhea has joined the list.

No, not on a roster of answers from high school sexual education class, but on a list that's more frightening: The sexually transmitted disease that infected 468,514 Americans in 2016 is now yet another bacterium which can resist antibiotics, according to the U.S. Centers for Disease Control and Prevention.

The CDC found that *Neisseria gonorrhoeae* could resist the popular Z-pak antibiotic (formally known as azithromycin). The degree of *N. gonorrhoeae*'s reduced susceptibility to the drug was 2.5 percent; the year before, it was just 0.6. Fortunately, for now, the other drug against gonorrhea, ceftriaxone, doesn't quite show the same decrease in effectiveness (the two drugs are given together to treat the disease).

But the finding shows that more common diseases are resisting antibiotics, and even new-generation drugs are joining penicillin, tetracycline, and Cipro along the path to resistance to antibiotics.

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This illustration shows a computer-generated image of drug-resistant Neisseria gonorrhoeae, the bacterium that causes gonorrhea.
Image credit: CDC/James Archer

A tarnish on the Golden Age

This is nothing new. Even if the *Los Angeles Times* announced in a 2016 series that "The golden age of antibiotics is over." According to the Times:

> The golden age of antibiotics appears to be coming to an end, its demise hastened by a combination of medical, social and economic factors. For decades, these drugs made it easy for doctors to treat infections and injuries. Now, common ailments are regaining the power to kill.
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> Harvard University infectious disease epidemiologist William P. Hanage cautions that "we will not be flying back into the dark ages" overnight. Hospitals are improving their infection control, and public health experts are getting better at tracking new threats. But in a race against nature, he said, the humans are losing ground.
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> We're seeing more drug-resistant infections," Hanage said. "And people will die.

One thing the Times didn't overhype, however, was the role of genetics in antibiotic resistance. In fact, the series cites the case of a woman with a urinary tract infection that stubbornly held on despite multiple antibiotic treatments. The culprit was finally found: a gene named mcr-1, which helped the bacteria resist treatment.

Antibiotics and resistance—a package deal from the beginning

Resistance to antibiotics has been an issue from the first use of antibiotics. In the 1930s, when sulfonamides were introduced, they were hailed as a medical breakthrough against previously fatal and incurable infections. But at the same time, resistance to sulfonamides was reported. Reports of resistance continued to arise with nearly every introduction of a new antibiotic. As time and research went on, it became clear that the mechanisms of resistance were genetic.

Most bacteria can acquire resistance. A bacterium with a resistance gene can easily share that gene with other bacteria, through lateral gene transfer. Bacteriophages and plasmids can also carry resistance genes, and be taken up and shared (again) by bacteria, thus building the population of resistant bugs.

And there are probably 20,000 resistance genes, divided into 400 types, pointed out Dorothy and Julian Davies, microbiologists at the University of British Columbia, in a recent review article. For example, there are 200 different varieties of the beta-lactamase gene alone–which chemically cleave penicillin and cephalosporin, rendering them useless. As to the question, which came first? The antibiotic or the resistance? The answer is probably "both."

While public health specialists and governments urge doctors to reduce antibiotic use, urge patients to avoid taking antibiotics, and use the complete dosage regimen if they do, and for hospitals and public facilities to use more stringent cleaning methods, it may be the enormous diversity of resistance genes that could eventually turn the tide of this growing health threat:

- New databases have been developing that can use next generation sequencing data to create a more detailed picture of the antibiotic resistome (yes, another 'ome'), classifying genes in pathogens and environmental microbes, identifying new genes behind new antibiotic resistant isolates, detailing horizontal gene transfer of those genes, all with the goal of being able to predict antibiotic resistance form a genotype. The Comprehensive Antibiotic Resistance Database (CARD) is one of these new databases, created by Canadian and British government and university researchers.
- After a prolonged period of stagnation, pharmaceutical companies are showing fresh interest in developing new antibiotics that could overcome resistance. This effort has paid off in the discovery by Northeastern University scientists of the first new antibiotic in 30 years, Teixobactin, a compound found in soil microbes like most other antibiotics. And another possible new class of antibiotics, lugdunin, was discovered by two scientists at the University of Tuebingen in Germany, by examining interactions in the microbes of the human nose.

Maybe there will be a better list to review, even a new golden age. Though, there's no reason to believe these new antimicrobials won't create resistance; in many ways, it's the nature of the beast.

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