

## SCIENCE

# Antibiotic-Resistant Germs, Lying in Wait Everywhere

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MATTER

The Lechuguilla Cave in New Mexico is a network of chambers stretching 1,600 feet underground. The bacteria that grow on the walls of its most remote recesses have been living in complete isolation for more than four million years.

In 2010, Gerry Wright, a microbiologist at McMaster University in Ontario, ran an experiment on those long-lost bacteria. He and his colleagues doused them with antibiotics, the drugs that doctors have used for the past 70 years to wipe out bacterial infections.

But many of the Lechuguilla bacteria would not die.

“Most of them were resistant to something,” said Dr. Wright. Some strains, he and his colleagues found, could resist 14 commercially available antibiotics.

Dr. Wright’s discovery didn’t fit the conventional story of antibiotics. Antibiotics were introduced in the mid-1900s. Each time a new drug was introduced, it would take years before bacteria that could resist it became common.

In the decades since, this trend has turned into a crisis. Last week, the World Health Organization reported that antibiotic resistance is now a major threat to public health across the entire planet. “We will soon hit the wall,” warned Joseph Nisbet, a microbiologist at the University of Lyon in France.

At first, the antibiotics crisis seemed like a simple story of evolutionary cause and effect. Whenever bacteria reproduce, there’s a tiny chance that a mutation will emerge that lets them resist an antibiotic. When we take that antibiotic, the mutant microbes can thrive while susceptible bacteria die.

If that were all there was to the story, the Lechuguilla Cave bacteria should

have been easy targets. Cut off from the world, they never had a chance to evolve resistance to our drugs.

But Dr. Wright discovered that they were already prepared. They had many genes that allowed them to survive what should have been a fatal dose of antibiotics.

Their resistance hinted that antibiotic-resistance genes were not just the product of modern medicine, but an ancient part of nature.

Now a new study from Mr. Nesme and his colleagues reveals just how widespread resistance is.

To carry out their study, Mr. Nesme and his colleagues took advantage of the fact that many teams of scientists are gathering huge amounts of DNA from all over the world. They've cataloged millions of genes, and made them available in online databases.

Mr. Nesme and his colleagues searched the databases from 71 of those places — everywhere from Antarctic ice to the bottom of the ocean. They looked for genes that were similar to the ones that disease-causing bacteria use to resist antibiotics.

As the authors report in the journal *Current Biology*, they hit the jackpot. "We find them in all environments," said Mr. Nesme.

Dr. Wright, who was not involved in the research, said that Mr. Nesme's study confirms the work that he and his colleagues have been doing. "This paper reinforces that resistance is everywhere," he said.

Scientists are puzzled about why resistance genes should be so old and so widespread. If the genes didn't evolve recently to fight against modern medicine, what are they doing in other bacteria?

They're probably doing a lot of things. Bacteria make their own antibiotics, for example, which they sometimes use to fend off competitors. Some of their competitors have evolved ways to resist those deadly molecules.

In addition, some resistance genes can be found in antibiotic-producing bacteria themselves. These bacteria can defend against their own poisons. "Otherwise, they make antibiotics once and commit suicide," said Dr. Wright.

But a number of studies suggest that bacteria use resistance genes for jobs that have nothing to do with antibiotics.

Last week, for example, Dr. Wright and his colleagues published a study they had conducted on bacteria that live in soil. They found a gene in these bacteria that provides resistance to an antibiotic called rifamycin.

Or rather, it would provide resistance if the bacteria actually used the gene. But when Dr. Wright and his colleagues exposed the bacteria to rifamycin, the gene remained silent and the bacteria died.

Dr. Wright suspects that the soil bacteria use the rifamycin-resistance gene to perform a different job. But what that job is, he has no idea.

The global supply of resistance genes that scientists are uncovering appears to be fueling the antibiotics crisis. That's because disease-causing bacteria can pick up resistance genes from other species and use them to fight our drugs.

Resistance genes can move between different species of microbes in many ways. Viruses, for example, can pick up DNA from one microbial host and then ferry it to another.

In some cases, disease-causing bacteria are simply borrowing genes that other bacteria were already using to resist antibiotics in nature. In the 1980s, for example, doctors saw an abrupt rise of bacteria resistant to the antibiotic vancomycin. Dr. Wright and his colleagues later discovered the source of their genes. They came from the very bacteria that make vancomycin in nature.

In other cases, Dr. Wright suspects, disease-causing bacteria pick up genes that other microbes used for different jobs. It just so happens that those genes can also make bacteria able to withstand to a particular antibiotic.

"All of a sudden you get something we recognize as resistance," said Dr. Wright.

It's sobering to realize that we're up against a planet's worth of resistance genes. But understanding our enemy is better than ignorance. Dr. Wright thinks that new antibiotics should be tested not just against the bacteria that live inside of us and make us sick. They should also be tested on bacteria living in the soil or the ocean. Scientists would discover the resistance genes that will someday threaten the usefulness of a new drug.

"It would be an early warning system, so you could at least be on the lookout," he said.