Unwanted impact of antibiotics broader, more complex than previously known

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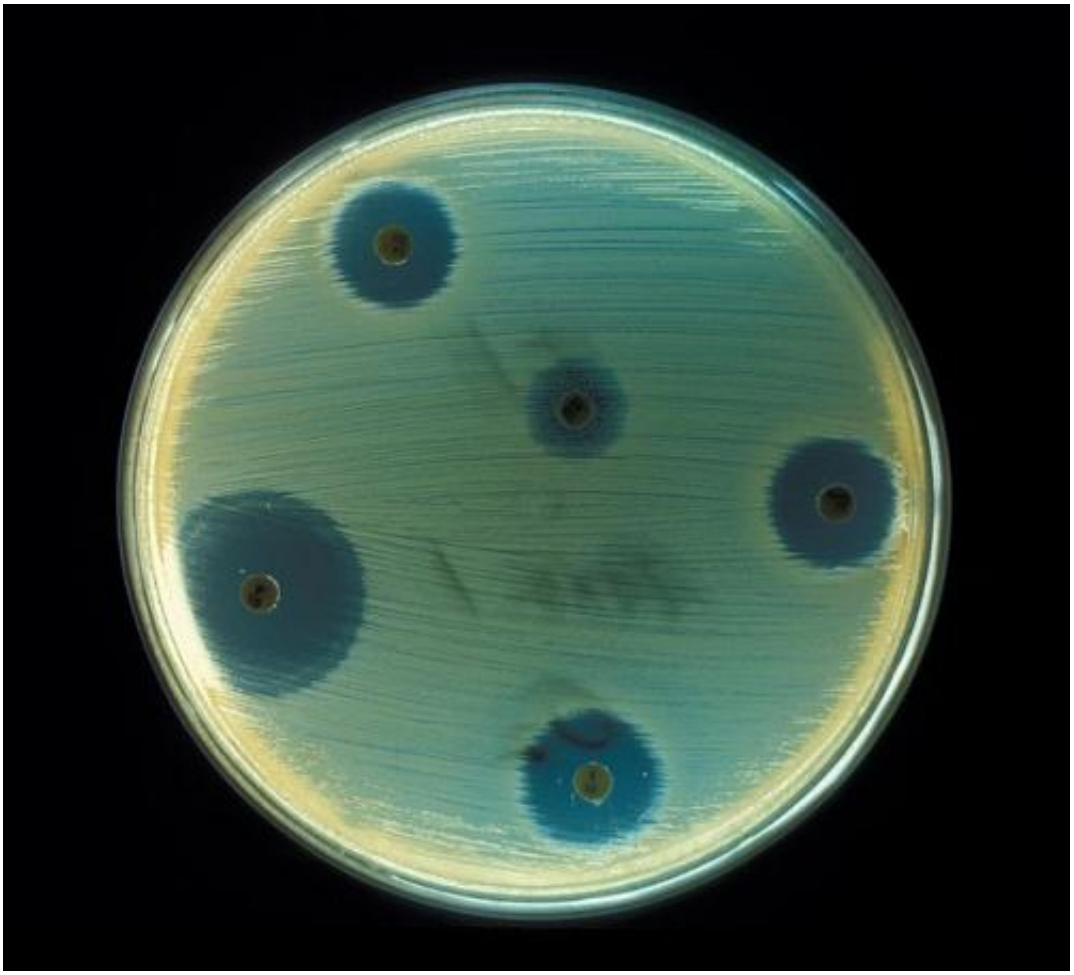

Staphylococcus aureus - Antibiotics Test plate. Credit: CDC

Researchers at Oregon State University have discovered that antibiotics have an impact on the microorganisms that live in an animal's gut that's

more broad and complex than previously known.

The findings help to better explain some of the damage these medications can do, and set the stage for new ways to study and offset those impacts.

The work was published online in the journal *Gut*, in research supported by Oregon State University, the Medical Research Foundation of Oregon and the National Institutes of Health.

Researchers have known for some time that antibiotics can have unwanted side effects, especially in disrupting the natural and beneficial microbiota of the gastrointestinal system. But the new study helps explain in much more detail why that is happening, and also suggests that powerful, long-term antibiotic use can have even more far-reaching effects.

Scientists now suspect that antibiotic use, and especially overuse, can have unwanted effects on everything from the immune system to glucose metabolism, food absorption, obesity, stress and behavior.

The issues are rising in importance, since 40 percent of all adults and 70 percent of all children take one or more antibiotics every year, not to mention their use in billions of food animals. Although when used properly antibiotics can help treat life-threatening bacterial infections, more than 10 percent of people who receive the medications can suffer from adverse side effects.

"Just in the past decade a whole new universe has opened up about the far-reaching effects of antibiotic use, and now we're exploring it," said Andrey Morgun, an assistant professor in the OSU College of Pharmacy. "The study of microbiota is just exploding. Nothing we find would surprise me at this point."

This research used a "cocktail" of four antibiotics frequently given to laboratory animals, and studied the impacts.

"Prior to this most people thought antibiotics only depleted microbiota and diminished several important immune functions that take place in the gut," Morgun said. "Actually that's only about one-third of the picture. They also kill intestinal epithelium. Destruction of the intestinal epithelium is important because this is the site of nutrient absorption, part of our immune system and it has other biological functions that play a role in human health."

The research also found that antibiotics and antibiotic-resistant microbes caused significant changes in mitochondrial function, which in turn can lead to more epithelial cell death. That antibiotics have special impacts on the mitochondria of cells is both important and interesting, said Morgun, who was a co-leader of this study with Dr. Natalia Shulzhenko, a researcher in the OSU College of Veterinary Medicine who has an M.D. from Kharkiv Medical University.

Mitochondria plays a major role in cell signaling, growth and energy production, and for good health they need to function properly.

But the relationship of antibiotics to mitochondria may go back a long way. In evolution, mitochondria descended from bacteria, which were some of the earliest life forms, and different bacteria competed with each other for survival. That an antibiotic would still selectively attack the portion of a cell that most closely resembles bacteria may be a throwback to that ingrained sense of competition and the very evolution of life.

Morgun and Schulzhenko's research group also found that one of the genes affected by antibiotic treatment is critical to the communication between the host and microbe.

"When the host microbe communication system gets out of balance it can lead to a chain of seemingly unrelated problems," Morgun said.

Digestive dysfunction is near the top of the list, with antibiotic use linked to such issues as diarrhea and ulcerative colitis. But new research is also finding links to obesity, food absorption, depression, immune function, sepsis, allergies and asthma.

This research also developed a new bioinformatics approach named "transkingdom network interrogation" to studying microbiota, which could help further speed the study of any alterations of host microbiota interactions and antibiotic impact. This could aid the search for new probiotics to help offset antibiotic effects, and conceivably lead to systems that would diagnose a person's microbiome, identify deficiencies and then address them in a precise and individual way.

Healthy microbiota may also be another way to address growing problems with antibiotic resistance, Morgun said. Instead of trying to kill the "bad" bacteria causing an illness, a healthy and functioning microbiota may be able to outcompete the unwanted microbes and improve immune function.

Provided by Oregon State University