

Daily dose of antibiotics helps bacteria develop multi-drug tolerance

March 7 2016



Escherichia coli. Credit: Rocky Mountain Laboratories, NIAID, NIH

Antibiotics do not easily eradicate the gut bacteria *Escherichia coli*, as some bacteria survive treatment in a dormant state. Once treatment is stopped, these dormant cells can become active again and recolonize the

body. Researchers from KU Leuven, Belgium, have shown that the more frequently bacteria receive antibiotics, the more of them survive. What is more, these survivors have evolved into bacteria with multi-drug tolerance.

Antibiotics are essential in the fight against bacterial infections and save countless lives. However, due to the overconsumption and frequent misuse of [antibiotics](#), resistant [bacteria](#) are increasingly common. But even when no [resistant bacteria](#) are involved, infections sometimes flare up again after a seemingly successful course of antibiotics.

To examine this phenomenon in detail, scientists from the KU Leuven Centre of Microbial and Plant Genetics treated the gut bacteria *Escherichia coli* with daily antibiotic doses in the lab. Even though most bacteria were initially killed, some bacteria found a quick way to adapt with minimal changes in their genetic material.

The result was the rapid development of many persister [cells](#). These cells are in a dormant state, and, as a result, are insusceptible to the antibiotic treatment. These survivors are not resistant - meaning that they cannot continue growing during an antibiotic treatment - but tolerant: they survive the antibiotic treatment and can resume their reproduction after the treatment.

"These tolerant cells can just sit out treatment", says professor Michiels. "On the first day of treatment, they are already present, albeit in small numbers. They ensure that the population is not wiped out and that it can be reconstituted after the antibiotic treatment. Eventually, you end up with an entire population that is tolerant to several antibiotics."

The research team of Professor Michiels showed that the number of tolerant cells in a population increases as bacteria are exposed to antibiotics more often: daily doses have a bigger impact than weekly

doses. Fortunately, the number of cells with multi-drug tolerance decreases again as soon as the [antibiotic treatment](#) ends.

"It is common practice to screen for resistance during antibiotic treatments, but not for tolerance. And yet, tolerant bacteria can go on to develop antibiotic resistance, which adds to the global antibiotic crisis: the development of new antibiotics cannot keep pace with the growing [antibiotic resistance](#) of bacteria. Therefore, figuring out how and why more bacteria develop antibiotic tolerance is important to improve future therapies and thus save lives", Michiels concludes.

The KU Leuven team is currently examining whether other pathogens show a similar increase in tolerance and whether the same process of genetic adaptation takes place during the treatment of infections in human beings.

More information: Frequency of antibiotic application drives rapid evolutionary adaptation of Escherichia coli persistence, [DOI: 10.1038/nmicrobiol.2016.20](#)

Provided by KU Leuven

Citation: Daily dose of antibiotics helps bacteria develop multi-drug tolerance (2016, March 7) retrieved 10 April 2024 from <https://phys.org/news/2016-03-daily-dose-antibiotics-bacteria-multi-drug.html>

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