# Scientists discover key to restricting antibiotic resistant bacteria

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Antibiotic resistance poses a significant threat to human health on a global scale. It has been predicted that resistant infections will cause 10 million deaths per year by 2050. Given that antibiotics are crucial in many areas of medicine, it is important to understand how antibiotic use influences the likelihood that resistance will emerge in response to

treatment.

Researchers from the University of Oxford's Department of Zoology have discovered that moderate doses of antibiotics restrict the emergence of antibiotic-resistant bacteria. This constraint arises because antibiotic exposure harms resistant cells, limiting the ability of individual resistant cells to establish successful populations.

The scientists' findings, published in *PNAS*, have two major implications:

1. The conventional paradigm for antibiotics has been to treat bacterial infections very aggressively with large doses of antibiotics. This research suggests that using more moderate doses of antibiotics may be a good way to prevent the emergence of resistance during treatment whilst minimizing the deleterious side-effects of aggressive antibiotic treatment.
2. The research highlights the importance of studying the impacts of antibiotics on individual bacterial cells; it is only by understanding the impact of antibiotics on individual cells that we can understand how antibiotic exposure influences the emergence of resistance.

Prof. Craig MacLean at the Department of Zoology, University of Oxford, and lead author of the study, says: "Our research has been trying to figure out how the intensity of antibiotic treatment influences the emergence of antibiotic resistant populations of bacteria. Other researchers have studied this problem, but we took a unique perspective that involved studying the emergence of resistant populations from individual bacterial cells."

The scientists obtained the results published today by using large-scale lab experiments where they measured the ability of individual antibiotic-

resistant cells to establish successful populations. Their focus on individual bacterial cells allowed them to understand how the effects of antibiotics of the growth and death of individual cells can restrict the emergence of resistant populations of bacteria.

Prof. Craig MacLean says: "The work was challenging, because bacteria are so small (1 millionth of a meter long), but there were two big surprises during this project. First, I was surprised by the fact that even low doses of antibiotic can have very detrimental effects on individual resistant cells. Second, I was surprised by how much variability exists in how individual cells respond to antibiotics, and how this scales up to influence the growth of bacterial populations."

The scientists are hopeful that their work will pave the way for future clinical work examining how antibiotic dose influences the emergence of resistance in systems that have direct clinical relevance.

They note that this research has examined resistant bacteria in isolation and that in reality, pathogenic bacteria are often embedded in complex communities, such as the gut microbiome. The next step will be to understand how these bacteria influence the emergence of resistance.

**More information:** Helen K. Alexander et al. Stochastic bacterial population dynamics restrict the establishment of antibiotic resistance from single cells, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.1919672117

https://phys.org/news/2020-07-scientists-key-restricting-antibiotic-resistant.html