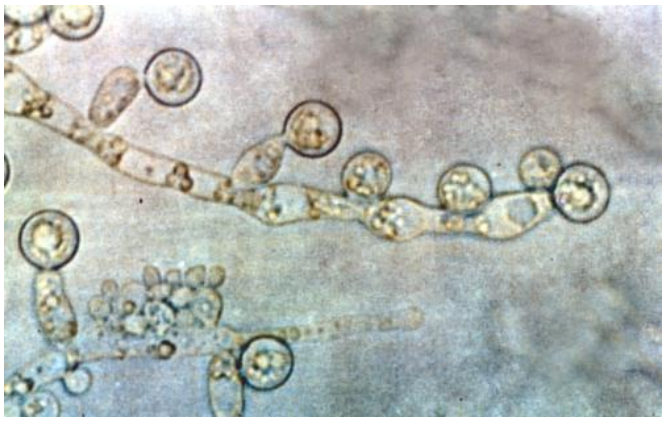
Stop antibiotics before resistance 'tipping point'

10 July 2018



Candida albicans. Credit: Wikipedia.

Treatments using antibiotics should stop as soon as possible to prevent patients passing the "tipping point" of becoming resistant to their effects, new research has shown.

A team of researchers, led by Professor Robert Beardmore from the University of Exeter, has uncovered new evidence that suggests reducing the length of the antibiotic course reduces the risk of resistance.

For the study, the researchers examined how microbial communities—groups of microorganisms that share a common living space in the body—reacted to different antibiotic cycling patterns, which sees the medication restricted or increased, under laboratory conditions.

They found that changes both in the duration and dose of antibiotics used and in sugar levels (which mimics the variable sugar levels in human patients) could push these microbial communities beyond a "tipping point—creating an irreversible shift to becoming drug resistant.

The researchers insist this new study demonstrates that resistant species can increase within the body even after an antibiotic is withdrawn—if a tipping point was unwittingly passed during treatment.

The study is published in leading journal *Nature Ecology & Evolution* on Monday, July 9th 2018.

Professor Beardmore, a mathematical biosciences expert from the University of Exeter, said: "It's a sensible idea that when you take an antibiotic away, resistance goes away too, but we wondered what kinds of antibiotic treatments don't behave like that. After all, in some clinical studies, resistance didn't disappear when the antibiotic did."

Antibiotic resistance occurs when microbes develop the ability to defeat the drugs designed to kill them, and so they multiply unhindered. Antibiotics are the most effective treatment for a wide-range of microbial infections, including strep throat and pneumonia.

For decades, patients have been instructed to complete courses of antibiotics because the perceived wisdom had been that taking too few tablets would allow bacteria to mutate and become resistant. However, more recently it has been suggested that the longer microbes are exposed to antibiotics, the more likely it is that resistance will develop.

Little research has been conducted to show how the length of a course of antibiotics impacts resistance, which, despite differences in patients, for example in their blood sugar levels, are recommended to be the same for all.

In the new study, the researchers examined how microbial communities containing Candida albicans and Candida glabrata reacted to different doses of an antimicrobial when fed with sugar.

Both species are commonly found together in healthy people, but are also opportunistic pathogens which can cause infection.

The study showed that as the antimicrobial was introduced, the communities were reduced, while the removal of the treatment allowed them to flourish again.

Crucially, the researchers showed that if sugar levels dropped in the community, it could reach a "tipping point" whereby resistance would persist even after the antimicrobial had stopped being used.

The new research opens up the possibilities for further studies to better understand when the best time would be to stop antibiotic treatment, to prevent resistance occurring.

Co-author Professor Ivana Gudelj added: "Our body is a mother ship for microbial communities but we've still expected to understand drug resistance by studying microbial species one at a time, in the lab.

"We show this can be misleading because microbes have intricate relationships that the drugs make even more complicated, and yet our theories of antibiotic resistance have ignored this, until now. So that's the first surprise: even sugars can affect antibiotic resistance."

'Drug-mediated metabolic tipping between antibiotic resistant states in a mixed-species community' appears in *Nature Ecology & Evolution* online on Monday, July 9th 2018.

More information: Robert E. Beardmore et al, Drug-mediated metabolic tipping between antibiotic resistant states in a mixed-species community, *Nature Ecology & Evolution* (2018). DOI: 10.1038/s41559-018-0582-7