Five rules to tackle antibiotic resistance

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Current efforts to tackle antibiotic resistance are "not nearly radical enough", a leading scientist says.

Dr. Ben Raymond, of the University of Exeter, says relying too heavily on reducing antibiotic use and discovering new drugs could lead to "disaster".

In a new study, he proposes five rules for "sustainable use". These include acting to protect new drugs before resistance becomes a problem, using more diverse antimicrobials to reduce long-term use of single drugs, and using data to design management plans for particular superbugs.

The World Health Organisation says antibiotic resistance is rising to dangerous levels worldwide, and warns of "a post-antibiotic era in which common infections and minor injuries can once again kill".

Dr. Raymond, of the Centre for Ecology and Conversation on the University of Exeter's Penryn Campus in Cornwall, said: "People think the best way to tackle antibiotic resistance is to give out fewer antibiotics and find new drugs.

"Those are important steps, but this approach alone is not nearly radical enough.

"Even if we can keep finding new drugs, disaster will follow if we use them in the same way as we use current ones.

"No drug yet discovered is evolution proof, and the typical practice of using single drugs at once, in unprotected 'monotherapies' is unsustainable.

"This 'business as usual' approach can be disastrous, as exemplified by the history of resistance in gonorrhoea and the emergence of untreatable infections.

"Resistance to new antibiotics can become widespread in two or three years, so new drugs must be partnered with more sustainable patterns of use."

The study's five rules are:

1. Prevention. "Resistance is easier to deal with before it becomes severe," Dr. Raymond said. "Antibiotics can be protected by the way you use them, for example by avoiding heavy use of single drugs for extended periods of time, as using drugs in this manner creates more 'selection pressure' - the conditions microbes need to evolve resistance."

2. Don't rely on "fitness costs". Some plans depend on stopping use of a drug, in the hope that resistant bacteria suffer a "fitness cost—dying out because they carry resistance genes that are no longer useful. This can work, but Dr. Raymond warns that resistance to a drug does not necessarily go away just because use of that drug stops.

3. Limit supply of mutations. One way to do this is to use combinations of antibiotics, as microbes rarely develop resistance to multiple antibiotics at once. Dr. Raymond also says it's "madness" from a resistance management perspective to build up a massive supply of resistance genes in the environment. Resistance in the environment can come from waste water and use of antibiotics in animals. "As an individual you are very unlikely to have acquired an antibiotic resistance microbe from an animal, but it's highly likely that environmental contamination has helped some of the microbes in your body acquire resistance," he said.

4. Low doses don't work, short courses might. A much greater pool of mutations can give microbes resistance to low doses of antibiotics, so such doses might help resistance evolve. Short, intensive courses of antibiotics might help patients without giving microbes the opportunity to evolve.

5. Information is power. "If you don't know what kind of resistance is around among patients or in your hospital, you could give people the wrong drug at the wrong time," said Dr. Raymond. "The more data you have, the better you can design your resistance management programmes. Resistance management programmes should target specific microbes or groups of microbes, rather than resistance in general."

Dr. Raymond warns that broader lessons of resistance management from other disciplines are "not widely appreciated" among microbiologists; while evolutionary biologists and clinicians need to talk to each other much more often.

The study, partly funded by the Medical Research Council, calls for a "new philosophy in which usage is tied to a long-term commitment to sustainability".

Dr. Raymond added: "Some humility in the face of natural selection can ensure that human creativity keeps pace with evolutionary innovation."

The paper, published in the journal *Evolutionary Applications*, is entitled: "Five rules for resistance management in the antibiotic apocalypse, a road map for integrated microbial management."

More information: Ben Raymond, Five rules for resistance management in the antibiotic apocalypse, a road map for integrated microbial management, *Evolutionary Applications* (2019). DOI: 10.1111/eva.12808

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