Safe thresholds for antibiotics in sewage needed to help combat antibiotic resistance

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New research reveals current understanding of safe antibiotic levels in rivers may not prevent evolution of antibiotic resistance and fully protect human health. The study suggests the need to introduce thresholds to help fight the spread of resistant bacteria.

Around 70 percent of the antibiotics we take as medicine end up in the natural environment, through flushed waste and discarded medicines, among other sources. These antibiotics interact with bacteria that are also present in the water, which can evolve resistance within these environments. The bacteria can then transfer resistance to human-associated bacteria, meaning antibiotics are less likely to work.

Antibiotic resistance is recognized by the World Health Organisation as one of the greatest health threats of our time. By 2050, up to 10 million deaths each year could be caused by antibiotics, and other antimicrobial drugs, no longer working to treat common diseases, including respiratory tract, sexually transmitted and urinary tract infections. The threat of resistance could also increase the risk of contracting infection after basic surgical procedures.

To prevent the situation being worsened via evolution of resistance in aquatic environments, a lot of research has attempted to determine safe concentrations of antibiotics in waste water that do not contribute to resistance. However, new research by the University of Exeter and AstraZeneca, published in *Communications Biology*, indicates that current thresholds may not be sufficient to prevent evolution of resistance.

The research team conducted laboratory experiments testing five antibiotics grouped within three commonly-used classes of antibiotics—macrolide (azithromycin, clarithromycin and erythromycin) fluoroquinolone (ciprofloxacin) and tetracycline. The macrolides and ciprofloxacin were included on the European Commission Water Framework Directive's Priority Substances Watch List in 2018, due to concerns about their toxicity to aquatic life. The team investigated the lowest concentrations at which resistance to antibiotics evolved in complex communities of bacteria present in wastewater. The team found that fluoroquinolone concentrations similar to those found in the environment did drive increased antibiotic resistance, whereas macrolides did not, confirming the need to set thresholds specific to the type of antibiotic.

Furthermore, the team found that resistant bacteria persisted in water at concentrations below the current threshold used to determine when mitigation strategies may need to be implemented. This presents a greater risk of human exposure to antibiotic resistant bacteria in the environment, and a greater chance that increased resistance could evolve over time.

Dr. Isobel Stanton, of the University of Exeter, said: "Antibiotic resistance is a grave international threat to life. While much attention has focussed around reducing use in clinical environments, we also need to urgently curb evolution and transmission of bacteria that are resistant to antibiotics through the natural environment. Our research indicates that current thresholds proposed may still be too high, and may not completely remove the risk posed by antibiotics present in aquatic environments."

Professor Will Gaze, of the University of Exeter, said: "Our work has helped to increase understanding of the extent to which rivers, streams and oceans contribute to the spread of antibiotic resistance in humans. We now need action to ensure waste water contains safe levels of antibiotics, to slow the increase in antibiotic resistance which threatens society."

More information: *Communications Biology* (2020).
www.nature.com/articles/s42003-020-01176-w

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