Heavy Metals May Contribute to Antibiotic Resistance in Bacteria

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SWEDEN - A new study at Uppsala University shows that very low concentrations of heavy metals and antibiotics contribute to resistance.

New Swedish research shows that plasmids containing genes that confer resistance to antibiotics can be enriched by very low concentrations of antibiotics and heavy metals. These results strengthen the suspicion that the antibiotic residues and heavy metals (such as arsenic, silver and copper) that are spread in the environment are contributing to the problems of resistance. These findings have now been published in the highly regarded journal, *mBio*.

Antibiotic resistance is a growing medical problem that threatens human health worldwide. Why and how these resistant bacteria are selected is largely unknown, although it is known that the primary selection takes place in humans and animals treated with antibiotics. Another contributory factor is that roughly half of the antibiotics used in treating humans and animals are, in unchanged and active form, excreted in the urine.

Professor Dan I. Andersson, at Uppsala University, who headed the study, said: "These antibiotics then disperse, usually in very low concentrations, through sewerage systems into water and soil, where they can remain active in the environment for a long period and so contribute to the enrichment of resistant bacteria."

Besides antibiotics massive quantities of biocides and heavy metals are also present in the environment. This is due partly to various natural sources (such as heavy metals in groundwater), but also to contamination caused by human activities.

Biocides and heavy metals are used mainly to prevent growth of various microorganisms in different contexts. For example, they promote growth in animal production (pigs and poultry), serve as ingredients in anti-fouling paint for boat hulls and as disinfectants for industrial, domestic and hospital use, and are found in products.

Plasmids (small extra fragments of DNA that can be transferred between bacteria) can contain not only antibiotic resistance genes but also genes conferring resistance to biocides and heavy metals, such as arsenic, copper, silver, lead and mercury.

Professor Andersson continued: "When these chemicals spread in the environment, bacteria with resistant plasmids will be selected. This indirectly results in antibiotic resistance increasing as well. What's more, in most environments there are complex mixtures of antibiotics, biocides and heavy metals that, together, have intensified combination effects."

In the study in question, the researchers performed very sensitive competition experiments in a laboratory environment. They allowed two different strains of bacteria, one susceptible to antibiotics and one resistant with a plasmid, to grow together in a culture with small amounts of antibiotics and heavy metals present. The results show that very low concentrations of both heavy metals (such as arsenic) and antibiotics, separately or in combination, were able to enrich the resistant plasmid-bearing bacteria.

Professor Andersson added: "These results are worrying and suggest that substances other than antibiotics that are present in very small quantities in the environment can drive development of resistance as well. The results underline the importance of reducing the use of antibiotics, but also suggest that our high use of heavy metals and biocides in various contexts should decrease too."

Reference: Erik Gullberg et al. (2014) Selection of a Multidrug Resistance Plasmid by Sublethal Levels of Antibiotics and Heavy Metals*. mBio. DOI:10.1128/mBio.01918-14.*

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