**Antibiotic Resistance in the Environment: a Link to the Clinic?**

**Abstract:** Antibiotic resistance in microbes is starting to become a bigger deal daily, due to the incredibly fast rate of microbial genetic evolution. It is because of recent research that scientists now know that bacteria out in the environment have a broad range of antibiotic resistance to multiple antibiotics. In aquatic environments these organisms develop their resistance because of human activities. Horizontal Gene Transfer is used in isolating these genes and inserting them into plasmids. Further research has discovered that there are bacteria that develop resistance to multiple antibiotics without being introduced to any human involvement to affect their genome.

**Introduction:** Antibiotics are distinctive in that their use precipitates their obsolescence by selecting for resistant microbes. Challenges include difficulty in identifying suitable bioactive chemical matter that can traverse microbial membranes. These challenges have conspired to make new antibiotic discovery a low priority for the pharmaceutical industry despite a growing clinical need.

Antibiotic resistance not restricted to pathogenic bacteria was discovered by Davies in 1973. Antibiotic producing bacteria or opportunistic pathogens such as *Pseudomonas aeruginosa* are often very drug resistant in comparison to the bacteria typically associated with disease. A vast majority of bacteria on the planet are not pathogenic.

One gram of soil can contain 4,000-10,000 species. Actinobacteria, producers of bioactive compounds, can contain 580 species of its own. Therefore, environmental microbes are embedded in an environment rich in chemical diversity. Fossilized stromatolite mats and terrestrial plants are exceptional producers of these chemicals. Such compounds produced are drivers of natural selection which as a result plays a key role in the evolution of microbial genetics. Genome sequencing has shown all bacteria have genes dedicated to protection and nutrition. These genes do a multitude of things including immunity elements, transporting proteins etc. It is the chromosomal genes that give these bacteria their resistance to antibiotics.

**Recent Progress**

**The Environmental Antibiotic Resistome**

The resistome consists of all antibiotic resistance genes including those circulating in pathogenic bacteria, antibiotic producing, and benign non-pathogenic organisms found either free living in the environment or as commensals of other organisms.

**Results:** 480 strains of bacteria isolated from various soils vs. 21 different antibiotics representing a broad range of chemical classes of drugs which include natural products and their semi-synthetic derivatives. Regardless of what antibiotic was used, resistance was observed in all antibiotics. Furthermore all strains were multi-drug resistant in this experiment. Expanding on the same research, many of these organisms were found to have intrinsic multi-drug resistance phenotypes. This discovery proved there could be a reservoir for new resistance mechanisms. Another study designed to investigate whether antibiotic resistant genes in plants were at risk of increasing the resistance gene burden of soil microbes.

Culture-based surveys of environmental bacteria is that they only same sample a small fraction of total microbial diversity. Functional metagenomics is used to bypass limitations that require prior knowledge of sequences that include genes of interest. Another method used is isolating and expressing genes of interest followed by the screening on various antibiotics. The downfall of this method is that gene expression is necessary.

Graham and his colleagues then started on analyzing soils from 1940 to 2008. They found that there was an increase in all resistance genes in the bacteria over this time frame. They also found the genes that encode for CTX-M extended spectrum Beta-lactamase in soils before they emerged as a major clinical problem.

Aquatic environments, just like soil, have shown an increase in antibiotic resistant bacteria. On the contrary to soil bacteria that gained resistance naturally, aquatic bacteria have gained their resistance more because of human activity. Antibiotics used in soils that run off to nearby lakes as well as contamination of water are the main culprits in making to deal with organisms such as *E.coli* and Salmonella much more difficult. Resistance in culturable bacteria is likely associated with normal aquatic microbes rather than pathogens. In an independent study, blaTEM-harboring microbes in sewage were seen to be enriched following treatment. Resistance in terrestrial bacteria pale in comparison to those that are sub-surface. Based on the sub-surface bacteria isolated, they found that the majority of these bacteria are multi-drug resistant. Interestingly, these bacteria are believed not to have been effected by human activities.

Several studies have shown that antibiotic resistant bacteria can be isolated from multiple animals, acquired either by scavenging on or by exposure to human associated material. A couple of studies have shown that commensal microbes harbor a large number of antibiotic resistance elements. Numerous reports have linked the use of antibiotics on swine, beef, and poultry to the increase in antibiotic resistant microbes. The same can be said about the fruits as well, due to the processes of food handling, irrigation resistant microbes. The same can be said about the fruits as well, due to the processes of food handling, irrigation and manufacturing. Agricultural practices play a key role in the global resistome. Diminished use of antibiotics in organic farming has not been conclusively deduced to decrease antibiotic resistance rate of bacteria.

**Limiting antibiotics:** Bacteria and viruses are two methods of contracting a disease. Antibiotics are used against bacteria only, but the issue this causes is that most colds, flus, and sore throats. However, tens of millions of prescriptions of antibiotics are written for viral diseases. There are 2 issues with this: 1) It has no effect on viral diseases and 2) increases the likelihood of acquiring drug resistant bacteria.

To decrease both demand and overprescribing, the FDA and the CDC have launched antibiotic resistance campaigns aimed at health care professionals and the public. A nationwide ad campaign developed by the FDA's Center for Drug Evaluation and Research emphasizes to health care professionals the prudent use of antibiotics and offers them an educational brochure to distribute to patients.

**Conclusion:** It is clear that in the environment there are many resistant organisms that exist. They are part of the resistome, which is a collection of all antibiotic resistance genes in pathogenic and non-pathogenic bacteria. Most of these resistance genes are isolated through horizontal gene transfer using plasmids. There is growing evidence that these resistance genes come from the environmental resistome. CTX-M extended spectrum appears to have come from chromosomal genes of environmental genus Kluyvera. The qnrA gene associated with aquatic bacteria comes from the aquatic bacterium *Shewanella algae.* These finds clearly show a direct correlation in resistance in the environment with the clinic.

Exposure to antibiotics definitely are a contributing factors but there may be many more. The next challenges might include the conditions of which HGT is satisfied and the role it plays in resistance genes from the environment to the clinic. Another study could discuss why certain resistance genes are more successful in certain pathogens than others.

**References**

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