**Preventative Measures and Alternatives to Fight Antibiotic Resistant Bacteria (ARB)**

Author: Maria A Vazquez Sanchez
Major: Microbiology/ Cell and Molecular biology
Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

**Key Words:**

**Antibiotic, antibiotic resistance,**

**Antibiotic Resistance is a topic acquiring popularity internationally; one reason for this is that bacteria are constantly evolving and becoming resistant to antibiotics faster than antibiotics are being developed. (Ragheb et al 2019). Antibiotic resistance represents a current problem that will only worsen; if not addressed right now, antibiotic resistance could soon become the biggest threat to humanity. In other words, humans are at risk of experiencing another pre-antibiotic era where any infection will result in death. Bacteria will continue evolving; therefore, it’s necessary to take different approaches to this problem. Antibiotic resistant bacteria are present in the environment and in humans. In this review the author will discuss some alternatives to decrease antibiotic resistance in bacteria by analyzing the alternatives that have been researched up on, to reduce the evolution of antibiotic resistant bacteria (ARB). In addition, the author will propose a plan for the general public to become aware of the problem, and how everyone can help by using antibiotics more responsibly. Antibiotic resistance should be public concern as much as other issues such as politics or economics. This article will also emphasize the importance of collecting data regarding antibiotic resistance in different environments that could be breeding grounds for antibiotic resistant bacteria, this includes cities and rural areas.**

**Introduction**

The definition of antibiotic resistance according to Ashbolt et al, “an antimicrobial resistant microorganism has the ability to multiply or persist in the presence of an increased level of an antimicrobial agent compared with a susceptible counterpart of the same species.” (2013) Antibiotic resistance in human pathogens has been observed and it’s believed that antibiotic misuse has contributed largely to this issue; therefore, antibiotics access is being regulated in many countries like the US. Although regulating human use of antibiotics could be helpful in preventing resistance, it is necessary to realize that antibiotics are also used in the farming industry, one example of this is the use of antibiotics in beef in the US; some of these antibiotics end up in the soil after the cows excrete them. This causes a problem because the bacteria that lives in this soil can mutate and develop antibiotic resistance.

**Recent Progress**

A solution to the antibiotic resistance problem was proposed in a research study published on January 2019. The study focuses on reducing mutagenesis of bacteria through identifying and inhibiting the components that promote mutations to slow down bacterial evolution. (Mark N. Ragheb et al). Although good antibiotics are being developed, bacterial genes have been observed to develop resistance at alarming rates, despite humans developing new antibiotics; in other words, bacteria are winning the antibiotic war.

The researchers experimented with bacterial cells lacking Mfd, which is believed to influence mutagenesis, given that it regulates DNA translocation, repairs damaged DNA and encodes protein function (Ragheb et al, 2019).

To test if Mfd played a role on bacterial evolution, Ragheb et al did several experiments. The first experiment was done to measure the evolving rates of bacteria cultured in rifampicin. The following strains were cultured in antibiotic containing media using the “Luria-Delbruck fluctuation analysis’ (e3): Bacillus subtilis wild type and Bacillus subtilis with Mfd deletion, Salmonella typhimurium wild type and S. typhimurium with Mfd deletion, and Pseudomonas aeruginosa wild type and P. aeruginosa with Mfd deletion. Mutation rates were determined to be higher in the wild type compared to the ∆Mfd type for all three bacterial samples.

From these results it was determined that removing Mfd from cells influenced mutagenesis; therefore, “DNA translocase Mfd protein” had an effect in ARB evolution (158)

Another experiment was done to determine if Mfd deletion had an effect in ARB of an infected model, they used “CACO-2 epithelial cells with a clinical isolate of S. typhimuriumand subsequently measured mutation frequency using resistance to 5-fluorocytosine (Richardson et al., 2009)” (159). The results showed that the removal of Mfd reduced mutagenesis by ~5 fold in an infected E. coli culture, compared to the ~2-~4 fold, observed in broth, figure 1.(159)

Another interesting finding in this study was the correlation of Mfd and mycobacterium tuberculosis (Mtb) and ARB. The antibiotics rifampicin ethambutol, and ciprofloxacin. Were used to test antibiotic resistance in Mtb cells lacking Mfd, and Mtb wild type cells. The results shown that ARB was observed to be “up to 100-forld greater” in wild type bacteria than in Mfd lacking bacteria. (159) this information could be used in other clinical studies in order to develop better treatments for Mtb infections.

**Discussion**

These results confirm that Mfd influence bacterial evolution and it has an effect in ARB (158); therefore, the identification of Mfd as an evolving factor that influences ARB could be used in clinical settings. Moreover, treatments could be developed where Mfd removal in bacteria could be combined with antibiotic treatment. This research study provides bases to develop other strategies to treat ARB in the environment and in hosts. Thus, more studies should be done in different bacteria, to determine how Mfd influences mutagenesis.

Another approach to prevent or reduce ARB could be the use of environmentally friendly methods to remove antibiotics from places like water sources and soil. This could be achieved with the help of local authorities in charge of waste water treatments and by limiting the antibiotic use in animals only to cases where antibiotics are needed for illness or surgical procedures. Educating the general public about ABR, and how does misuse of antibiotics can impact our environment, this can also and pose a threat to human health and well a how to use antibiotics responsibly, could also help decrease the risks of antibiotic resistant illness (Ashbolt et al, 2013).

As previously mentioned, the use of antibiotics in beef farms in the US is not being regulated as much as the use of antibiotics in humans; consequentially, the antibiotics that end up in the cattle manure are spread out in the environment. These same antibiotics could end up in water sources and unknowingly ingested by humans. It has been proven that bacteria will develop resistance to the antibiotics that these are exposed to, although some of the bacteria in the environment is nonpathogenic, these bacteria could transfer its resistant genes to other bacterial cells that are pathogenic via horizontal transfer, (Ashbolt et al, 2013). Considering that some bacteria in the environment could acquire antibiotic resistance through plasmid DNA uptake, it is imperative to start collecting data about bacterial population and pathogenicity, from beef farms and other places in the environment where antibiotics are present as a consequence of human activity. Considering the environmental factors that promote antibiotic resistance, it is important to come up with a solution to regulate the use of antibiotics in animals as well as in humans.

Antibiotic resistance seems like a new topic; however, it has been happening since the first antibiotics were developed. Ragheb et al mention that “Estimates suggest that at least 700,000 people die annually from drug-resistance infections; this number could rise to 10 million by 2050, far surpassing cancer as the major cause of death worldwide (O’Neill, 2014).” Therefore, we must act before it’s too late.

**References**

[Mark N. Ragheb, Maureen K. Thomason, Chris Hsu, Patrick Nugent, John Gage, Ariana N. Samadpour, Ankunda Kariisa, Christopher N. Merrikh, Samuel I. Miller, David R. Sherman, Houra Merrikh, *“Inhibiting the Evolution of Antibiotic Resistance,”*

Molecular Cell,Volume 73, Issue 1, 2019,Pages 157-165.e5,

Ashbolt, Nicholas & Amézquita, Alejandro & Backhaus, Thomas & Borriello, Peter & Brandt, Kristian & Collignon, Peter & Coors, Anja & Finley, Rita & Gaze, William & Heberer, Thomas & Lawrence, John & Larsson, Joakim & Mcewen, Scott & J Ryan, James & Schönfeld, Jens & Silley, Peter & Snape, Jason & Van den Eede, Chris & Topp, Edward. (2013). *“Human Health Risk Assessment (HHRA) for Environmental Development and Transfer of Antibiotic Resistance. Environmental health perspectives.”* 121. 10.1289/ehp.1206316.