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Bacterial Persistence and Resistance: Why Antibiotics Will Stop Working

In 1928, Dr. Alexander Fleming returned to his experiment to find mold growing in his Petri-dish. This moldy dish led to the invention of penicillin, the first antibiotic, almost 20 years later. Although Fleming discovered a bacteria-killing substance in his Petri-dish in 1928, his peers took little interest, believing the situation to be a lost cause and nearly impossible to use for medicinal purposes. The discovery went largely ignored until 1937, when Howard Florey and Ernst Chain began testing to attempt to purify penicillin. In 1940, the lab saw its first successful animal test, curing streptococci bacteria in mice. Although the substance became difficult to produce due to the large amounts of mold broth required to produce small amounts of penicillin, by 1946, following several breakthroughs in what formulas could produce the drug, penicillin became widely available and applicable on a commercial scale (Science Museum UK, 2021). 80 years ago, penicillin killed almost all bacteria with which it came into contact. However, due to genetic and epi-genetic changes in bacteria, certain strains of bacterial infections can no longer be treated with current antibiotics because they have become partially or fully resistant.

Certain bacteria have genes that create full resistance to penicillin, but even those that provide partial resistance still mean that a higher percentage of these resistant bacteria will survive against antibiotics. Antibiotics destroy DNA by preventing reproductive processes in bacteria, stopping the production of essential proteins, and/or surrounding the cell walls of the bacteria (Healthline, 2023). Known as antimicrobial resistance, resistant bacteria are a result of

common exposure to antibiotics among a population and the spread of the germs with certain resistance mechanisms. The presence of antibiotics within a system will kill all non-resistant bacteria, leaving only that which is resistant to reproduce. As a result, among each generation, the percentage of bacteria with some form of antimicrobial resistance increases as time passes due to evolution. However, full resistance largely differs from partial resistance in terms of the mechanisms used by the bacteria to survive antibiotic stress (CDC, 2022).

When bacteria is fully resistant to antibiotics, these germs develop the ability to destroy or otherwise get rid of antibiotics before the antibiotic would be able to kill the bacteria. Even when bacteria is only resistant to one drug used to treat the infection, the use of second and third line drugs to treat the infection could result in serious side effects. Certain medical advances, including treatments for cancer therapy, asthma, and diabetes, require the use of antibiotics that an infection could kill. Additionally, certain bacterial infections only have one discovered medical response, making successful treatment nearly impossible, if not entirely (CDC, 2022). If cases of full resistance spread across large populations, the medical system would lose an entire line of defense.

Partial antimicrobial resistance, a much more recently discovered phenomenon, rather than destroying the antibiotic, means that the bacteria will inhibit essential functions—force certain functions into dormancy during antibiotic stress. Thus, following a course of antibiotics, surviving cells can reproduce and symptoms of infections will return to a patient despite the treatment plan. The cell, known as a persister, will maintain all essential functions until antibiotic stress has diminished, before proceeding to reactivate said functions and repair any proteins

damaged by the treatment (Amato et al, 2014). Similar to full antimicrobial resistance, persisters allow bacterial infection to maintain its presence in a patient's system in spite of antibiotics, albeit through different mechanisms.

According to the World Health Organization, "Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality" (WHO, 2020). Since antimicrobial resistance reduces the effectiveness of many treatments against infection, resistant bacteria kills approximately 35,000 people every year in the United States alone according to the Center for Disease Control (CDC, 2022). In the future, rates will only increase as bacteria evolve to gain more resistance to current treatment options. Unless a treatment can be found for antimicrobial resistance, scientists will need to find an alternate solution to many medical advancements and the entire treatment for bacterial infection.

Bibliography

Amato, S. M., Fazen, C. H., Henry, T. C., Mok, W. W., Orman, M. A., Sandvik, E. L., Volzing, K. G., & Brynildsen, M. P. (2014). The role of metabolism in bacterial persistence. *Frontiers in microbiology*, *5*, 70. https://doi.org/10.3389/fmicb.2014.00070

CDC. (2022, October 24). *How do germs become resistant?* Centers for Disease Control and Prevention. https://www.cdc.gov/drugresistance/about/how-resistance-happens.html

CDC. (2022, October 5). *What exactly is antibiotic resistance?* Centers for Disease Control and Prevention. https://www.cdc.gov/drugresistance/about.html

How do antibiotics work? How long they take to work & more. (2018, May 4). Healthline. https://www.healthline.com/health/how-do-antibiotics-work

How was penicillin developed? (n.d.). Science Museum. Retrieved May 17, 2023, from https://www.sciencemuseum.org.uk/objects-and-stories/how-was-penicillin-developed