"The Case Against Antibiotics"

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INTRODUCTION

In Nevada, a woman in her 70s was returning from a long trip to India when she noticed pain in her right hip seroma after getting treatment for a broken femur. When she went to the doctors in Reno, they told her it was infected and gave her a typical bombardment of antibiotics to cure it, assuming that the infection would subside (CDC, 2017). Unfortunately, her infection was resistant to all 26 antibiotics that can treat bacterial infections available in the United States. This included "last resort" antibiotics: treatments that doctors only use in grave cases if a bacterium becomes antibiotic resistant. The woman died a month later of septic shock (Brink, 2017).

The case in Nevada isn't isolated. A Chinese study took 374 H. Pylori strains from patients who went through an intestine viewing procedure and tested their resistance to antibiotics over a period of nine years (Gao et al., 2010a). The clarithromycin antibiotic resistance rate rose from 14.8% to 65.4%. The fluoroquinolone antibiotic resistance rate increased from 27.1% to 63.5%. This alarming trend continued throughout the study (Gao et. al., 2010b).

Antibiotic-resistant bacteria are called "superbugs". The one that the woman from Nevada had is specifically called a "nightmare superbug", because they resist even last resort antibiotics. Some estimates suggest that nearly 700,000 people die each year from drug-resistant infections, a figure projected to increase to one superbug-related death every three seconds by 2050 (WHO, 2019).

To understand the superbug crisis, we must explore what antibiotics are, how they work, and what they can do. Antibiotics work by disrupting vital processes in bacteria. In penicillin, it was breaking down the bacterial cell wall, killing them. In others, it could mean stopping the bacteria's ability to reproduce, directly killing the nucleus, or some other disruptive force (American Academy of Pediatrics, 2022). When penicillin was created in 1928, it saved billions of lives. But soon after its invention, many bacteria became resistant to penicillin and another medicine was created to stop this new strain: methicillin. Now, even that has been compromised (Ventola, 2015a). The race against bacteria has continued throughout humanity's existence and will continue as long as we exist. Our most vital asset in this race has been antibiotics. Just 100 years ago, the average life expectancy in America was 53.2 years old (O'Neill, 2024). Now, with antibiotics and other

medical advancements that enhance the lives of the elderly, our life expectancies are closer to 80 years (Ventola, 2015b).

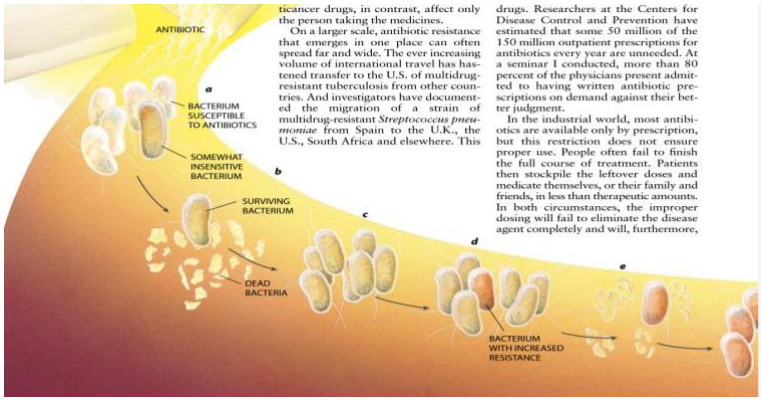
CREATION OF SUPERBUGS

But how do bacteria become superbugs? They might be randomly mutated and selected or grown in a lab. Since bacteria are so plentiful, they experience random mutations regularly, resulting in many strains that are slightly different. Some mutations are negative, but bacteria with them die off due to natural selection. Some mutations are positive and allow bacteria to live longer by possessing a more optimized skill set for their environment. One such mutation is antibiotic resistance. Specifically, some bacteria have developed biochemical "pumps" that can remove an antibiotic before it reaches its target, while others have evolved to produce enzymes that "inactivate" the antibiotic (Missouri Department of Health and Sciences, 2022).

The mutations bacteria gain can also be passed onto other species, both related and unrelated to the original. This process happens through DNA exchange. If a bacterium that possesses an antibiotic-resistant characteristic exchanges DNA with one that doesn't have that trait, they both now share that trait.

Figure 1

The Process by Which Bacteria Become Resistant to Antibiotics (Levy, 1998a).



These superbugs may also come about synthetically as a byproduct of Gain of Function (GoF) research. Gain of Function refers to the process of giving a virus or bacteria an evolutionary trait that it did not previously have to monitor its performance in different environments. Some argue that this can help prepare us for a public health crisis in the future. But critics say that this argument doesn't hold water, as synthetic viruses have very different characteristics than natural viruses, and don't react in the same ways. These research experiments have devastating outcomes if leaked to the general population. In 2020, Boston University conducted one such GoF study of

the COVID-19 Omicron variant, combining it with the original COVID-19 variant to analyze the outcome. This created a superbug that was resistant to everything in our antibiotic arsenal and could have spread through humans easily (Cruickshank, 2022a). Biomedical engineers from Johns Hopkins University and other universities are now calling for an end to Gain of Function research (Cruickshank, 2022b).

HOW SUPERBUGS SPREAD

The true danger of superbugs lies not just in their creation, but also their proliferation. Their severe threat to humans has come about due to four major factors: the overprescription of antibiotics, the extensive use of antibiotics in agriculture, the limited production of new antibiotics, and the abuse of antibiotics by patients.

Overprescription has allowed bacteria to build up resistance against antibiotics. Some doctors incorrectly prescribe antibiotics for a variety of reasons, including time constraints involved in diagnosis (using antibiotics as a blanket solution to get the diagnosis over with), fatigue in repeated diagnoses, and uncertain diagnoses with little differentiation between different bacterial infections (Hyun, 2017a). To combat this issue, some hospitals created posters outlining a commitment to reduce antibiotic prescription, which has resulted in less antibiotics use in those hospitals (Hyun 2017b). This indicates that reminders of a commitment have encouraged doctors to be more thorough in their differentiation of disease as well.

In agriculture, farmers often pump their cattle with antibiotics to keep them healthy and plump year-round. As we know, this comes in tandem with the evolution of antibiotic-resistant bacteria. When humans eat the cattle, those antibiotics and antibiotic-resistant bugs are ingested as well. This vector of disease transmission allows superbugs to spread even faster than through only human interaction (Levy, 1998b).

On top of this, finding new antibiotics is incredibly expensive and time-consuming. A prospective antibiotic sample must first be repeatedly tested on a medium full of different bacteria, measuring bacterial death. Then, it's converted into a biochemically favorable compound until it is finally synthesized into a vaccine that humans may be able to take. Finding the sample alone is extraordinarily difficult to do in nature. Even assuming one is found, most fail after being tested on BSL-2 bacteria.

The proliferation of superbugs is also caused by patients themselves. It has been reported that patients and their families pressure doctors for prescriptions of antibiotics even when they are not necessary (Hyun, 2017c). The deadly combination of overprescription, agricultural misuse, difficulty of antibiotic discovery, and patient pressure has led to the public health crisis of today. Not only will superbugs lead to millions of deaths in the future if left unchecked, they also "increase [the number of] severe diseases, the length of disease, the risk of complications, the mortality rate, healthcare costs," and many more negative consequences (Llor and Bjerum, 2014).

FUTURE STEPS

So how can we stop the growth of superbugs? A version of a drug that we've already invented, Polymyxin B, seems to show promise as a last-line defense against gram negative (thin peptidoglycan membrane) superbugs. Polymyxins are incredibly antibacterial, but their major side effect is nephrotoxicity: they kill our kidneys and thus limit the dose that doctors can give to patients (Velkov et. al., 2016). Also, as a conventional antibiotic, it is victim to the four negative effects we've explored.

A more likely solution is the development of new antimicrobial materials that can be used in hospitals and other high-risk environments. Students at the University of Nottingham's School of Pharmacy have developed a polymer that is coated with chlorhexidine, a compound normally reserved for pre-surgical sanitization (Icke, 2023a). This polymer has been shown effective at killing microbes, eradicating their proliferation within 30 minutes without spreading into the environment. It was effective against SARS-COV-2 and even killing chlorhexidine-resistant strains of bacteria (Icke, 2023b). Researchers are looking into using them as the outer coating of commonly contaminated areas, such as surgical beds and surgery equipment. Research into creation of more biocompatible and antimicrobial polymers is pivotal in the fight against superbugs.

The most ideal long-term solution is using bacteriophages, the "natural predators of bacteria." Bacteriophages are viruses that infiltrate bacteria and use them as hosts to create more viruses. Unlike antibiotics which must be found and purified for human use regularly, bacteriophages evolve alongside bacteria so human adaptation isn't necessary past invention. If we could invent a bacteriophage that poses little to no threat to a human and attacks bacteria effectively without spilling into human cells, it could be the world's first smart drug (The Economist Newspaper, 2023).

The stage of bacteriophage invention is the one that we are in right now. Universities across the nation have been given millions of dollars in research funding to combat this rising issue. Johns Hopkins, University of Wisconsin-Madison, and Stanford are among the largest beneficiaries of this research. Specifically, JHU has been given 16 million dollars to improve antibiotic use (Polyniak, 2016).

In the meantime, we can all work together to use less antibiotics and understand more about the evolutionary war that our bodies fight every day to keep all of us protected.

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