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Resisting the Resistance: How the Environment is Impacting Antibiotic Resistance

Hannah Hinrichs

Upon their discovery, antibiotics were known as "wonder drugs" due to their ability to cure serious bacterial infections. While antibiotics are still revolutionary in healthcare today, the emergence of antibiotic resistance is a growing threat to public health. Antibiotic resistance is simply a normal adaptive response where bacteria evolve over time. However, overuse of antibiotics, sub-optimal treatment regimens, and environmental exposures create optimal conditions for antibiotic resistance to develop and spread. Common ways antibiotics enter the environment are via wastewater and agricultural use. Even with properly functioning wastewater treatment systems, full removal of resistant bacteria may not be possible as many have been found in natural bodies of water. Within the agricultural ecosystem, bacteria exhibiting antibiotic resistance may be pathogenic to humans. The growing issue of antibiotic resistance demonstrates that addressing environmental exposures now is imperative for the future prevention of development and halting the spread of resistant strains.

Keywords: *environmental exposure, infections, antibiotics resistance*

A "Wonder drugs." This is how antibiotics were described when they were first discovered thanks to their ability to cure serious bacterial infections that no other medications were able to. Even to this day, they are a revolution in the healthcare system.[1] However, like most things in life, a good thing can quickly turn bad when used in excess. Antibiotic resistance develops when bacteria are able to defeat the "wonder drugs" designed to kill them.[2] As a result of widespread antibiotic use, more bacteria exhibiting resistance to antibiotics are being discovered, which is leading to treatment failures and deaths across the globe.[1] Currently, the issue of antibiotic resistance poses a major public health threat, as it has been detected in all regions of the world. The year 2019 saw close to five million deaths associated with antimicrobial resistance worldwide. Each year in the United States, 2.8 million infections exhibiting antimicrobial resistance are diagnosed with at least 23,000 deaths occurring annually.[2,3] This global issue jeopardizes positive treatment outcomes, and the consequences go beyond the clinical setting. In nature, antibiotics find their way into the environment via reservoirs such as wastewater and animals. While optimizing drug treatment regimens and utilizing patient education strategies can minimize the emergence of resistance, addressing antibiotic resistance in the environment will prevent the development and halt the spread of dangerous future strains from developing.

Antibiotic resistance is simply a normal adaptive response, and clear example of bacteria evolving over time.[3] When a person is diagnosed with a bacterial infection, they will be prescribed an antibiotic that is designed to attack and kill the specific bacteria. The bacteria, in turn, may try to avoid this attack through mechanisms that allow them to evolve. Bacterial evolution may lead to resistance against that specific antibiotic, meaning that it would likely not be as effective in the future. The four main mechanisms bacteria use for resistance include modification of the antibiotic, prevention of the antibiotic from reaching its target, production of a change or bypass in the antibiotic's target site, and resistance to global cell adaptations. Bacteria can chemically modify or destroy antibiotics to render them inactive. A classic example of this mechanism is when bacteria produce an enzyme known as beta lactamase, which destroys antibiotics of the beta lactam class, such as penicillin. Decreasing entry into the bacteria and increasing efflux of the drug out of the bacteria are mechanisms that prevent the antibiotics from reaching their target and producing their effect. Bacteria may also avoid an antibiotic's action by protecting or modifying the antibiotic's target site, which decreases binding affinity. Lastly, over time, bacteria have adapted to survive harsh environments, including the human body. Due to environmental stress, antibiotics have made adaptations to overcome these stressors. Antibiotic resistance was named one of the most important threats of the 21st century by the World Health Organization, and, over time, more deaths and losses to the global economy will occur as a result. Although the mechanisms of resistance are well understood, continuous research studying the patterns of antibiotic resistance and drug development should be prioritized to tackle this ever-evolving problem. By studying these trends, clinicians can be aware of the current and up-and-coming resistance mechanisms to treat bacterial infections accordingly.[3]

Looking outside of healthcare facilities is another important area to explore in the development and spread of antibiotic resistance. One of the ways in which antibiotics enter the environment is via wastewater. Incorrect use of antibiotics, excretion of poorly metabolized antibiotics, and improper disposal of antibiotics are ways that these medications wind up in water sources.[4] Wastewater treatment plants clean water coming from homes, commercial buildings, schools, and street gates, so that it can later be returned to the environment and reused.[5] The water treatment process goes through multiple stages in which the water is screened several times and, each time, more particles are removed through a series of physical, biological, and chemical processes. For instance, chlorine is added during the process to kill bacteria and is effective against many of them. After treatment, the water is then ready to be reintroduced into the environment.[4,6] However, even with the use of properly functioning wastewater treatment systems, full removal of resistant bacteria may not be possible as many have been found in streams, rivers, lakes, and oceans. Often, these bacteria can be traced back to the waste of households, healthcare facilities, communities, farms, and sewage systems.[7] Wastewater treatment plants are among the main sources of environmental antibiotic release, serving as a reservoir for antibiotic-resistant bacteria.[8,9] Data from 13 countries showed that sulfamethoxazole, trimethoprim, and ciprofloxacin were frequently found leaving wastewater treatment plants, and were detected at concentrations of up to 1 µg/L.[10] While the levels found in the water were well below the therapeutic concentrations needed to treat infections in clinical practice, bacteria are still able to develop resistance to these antibiotics.[8] This further illustrates the importance of inhibiting any amount of antibiotics from entering the wastewater—no matter how small of an amount it may be—in order to halt the emergence of resistance.[11]

Antibiotic use within and beyond the agricultural ecosystem is another factor contributing to the public health concern, and it is vital to understand how organisms transfer between environments and species.[12] Antibiotic-resistant bacteria associated with animals may be pathogenic to humans. These organisms can be directly transmitted to humans either directly through physical contact with animals and the food chain, or indirectly via farm waste. Antibiotic-resistant bacteria move from the animals and enter the environment through soil, water, and crops. Then, from the environment, they may spread to municipal facilities and eventually make their way to households and hospitals.[13,14] Usage of antibiotics is thought to alter the microflora of host animals in such a manner that they may obtain nutrients from food that they consume; not only does this provide a better-quality food-animal, but it also provides an appreciable economic advantage. Upon review of the 2013 United States domestic sales of antibiotics for use in food-producing animals, roughly 62% of antibiotics were considered medically important for human antibiotic therapy. Like humans, animals can develop antibiotic resistance when regimens are not complete or optimal for the treatment of infection. Using the same antibiotics in animals and humans pose a major risk, as antibiotic resistance can spread from animals to humans. In animals, the development of resistance is especially prevalent, because they are often placed in cramped quarters and occasionally treated prophylactically with antibiotics.[15] A collaboration between farmers, veterinarians, pharmacists, researchers, and governmental organizations is needed to address and mitigate the spread of antibiotic resistance in agriculture.

A danger to the community arises when antibiotic resistant infections occur, as initial treatments fail and options then become limited.[4] Antibiotic resistance spreads throughout the environment via water sources, animals, humans, and healthcare facilities, but no matter the origin or cause, the risk on public health is still immense. Mitigating the development and spread of antibiotic resistance should be a priority and collaborative effort of government organizations, healthcare professionals, and researchers alike. In healthcare, proper use and disposal of antibiotics should be emphasized to everyone, and the indiscriminate use of antibiotics in farming animals should be avoided.[14] Understanding and studying the trends of antibiotic resistance in the environment is important, as it can lead to better outcomes for public health around the world. Should this issue not be addressed now, healthcare may face a much larger problem in the future.

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