"What Doesn't Kill Us…"

In 1929, a scientist studying fungi discovered one of nature's greatest secrets. Alexander Fleming found that his fungi produced an agent that killed bacteria. He had encountered the antibiotic penicillin, and for the next four decades humans were unstoppable against infectious bacteria (Rao 1). We created a variety of antibiotics, mass producing them and distributing them widely. But just as mankind thought it had seized victory, we suffered a crippling blow. Antibiotic resistance had begun to develop. "This situation was first documented in 1963, when increased levels of resistance in a particular strain of Salmonella Typhimurium were observed at several British feedlots; several resistant isolates were subsequently identified over a period of 3 years" (Khachatourians 2). Within forty years our greatest weapon had already begun to lose its efficiency. The prolific expansion of antibiotic use in factory farming and human medicine has added to their continuing loss of effectiveness. Since the advent of antibiotics, humans have shown irresponsibility with their use, and only through careful and innovative practices will we counter the damage that we have already dealt to our world.

Antibiotics have the ability to decimate bacteria populations. How can these instruments of destruction cause their own downfall? To understand the development of antibiotic resistance, we must first understand the theory of natural selection. Charles Darwin published this concept in 1859 in *Origin of Species*. His idea of natural selection suggested that in every species there lies some genetic variation. This genetic variation allows some of the species to have a better chance of survival based on environmental conditions and, over generations, these traits that improved chance of survival spread throughout the population. This idea, he believed, explained why species changed over time. We now know that natural selection applies not only in the macroscopic world but in the microscopic as well (Rao 2). Bacteria, much like any other organism, evolve based on their conditions. Bacteria naturally have obtained some antibiotic resistance because of exposure to antibiotic-

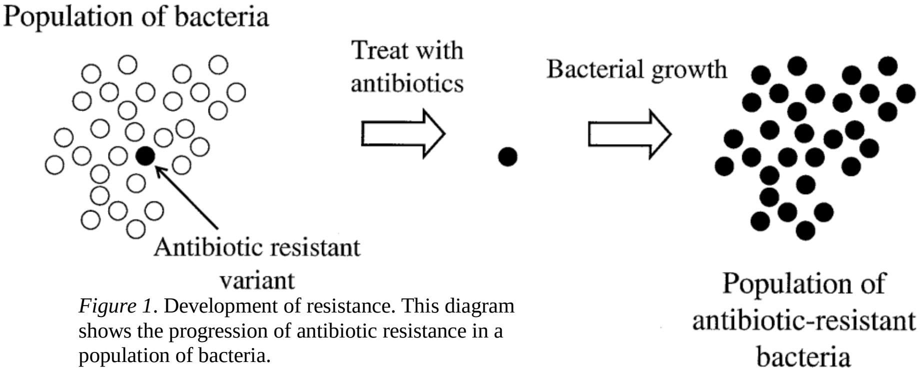

Figure 1. Development of resistance. This diagram shows the progression of antibiotic resistance in a population of bacteria.

producing fungi (Goldman 4). As human use of antibiotics became widespread, genes for resistance mutated in bacteria populations and resistance increased. Slight variations among billions of bacteria allow some of them to survive antibiotics. When antibiotics penetrate an area, selective eradication removes the non-resistant bacteria leaving empty space open to colonization by the resistant bacteria. Resistant bacteria's prevalence then makes the original antibiotic useless (Goldman 5). Over time the increase of resistance occurs to various kinds of antibiotics. Multi-drug resistant strains such as Methicillin-resistant Staphylococcus aureus (MRSA) cultivate. These strains have the possibility of becoming resistant to all current kinds of antibiotics (Goldman 1).

While disconcerting, other forms of resistance can develop much more quickly. Horizontal gene transfer passes antibiotic resistance among bacteria. Genes for resistance can form together in circular DNA molecules called plasmids (Goldman 6). These plasmids transferring between bacteria allow for the rapid exchange of resistance. Once a resistance develops in one bacterium, horizontal gene transfer spreads resistance among the whole population. Horizontal gene transfer does not rely upon the random genetic variation like natural selection, and extends resistance in a bacteria population without antibiotics destroying most of the bacteria. Horizontal gene transfer can occur between different types of bacteria as well. Plasmids classified as conjugative can transfer between different types of bacteria. Horizontal gene transfer can occur when antibiotics interact with bacteria causing their plasmids to transfer. Some plasmids have a special property called promiscuity. Promiscuity allows plasmids to transfer between bacteria regardless of the presence of antibiotics (Khachatourians 3). Plasmids with both promiscuity and conjugative properties can transfer resistance between multiple types of bacteria in a natural environment. This process has occurred in German water treatment plants where conjugation between bacteria has produced vancomycin resistant enterococci. These plants destroyed the bacteria but the threat of resistant bacteria persists (Khachatourians 6). Human mass production and use of antibiotics along with bacteria's own nature has helped to spread antibiotic resistance among bacteria.

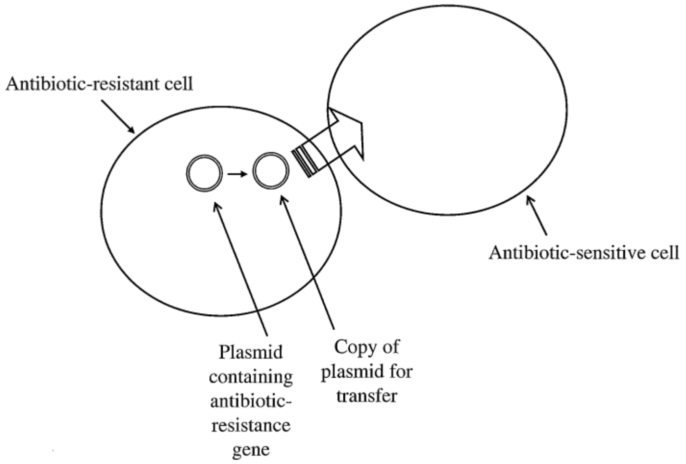

Figure 2. Horizontal gene transfer. Transfer of plasmids between bacteria.

No one person or group will take responsibility for antibiotic resistance, nor can they. The blame extends across many aspects of human society. A major contributor, factory farming, plays a major role in the development of antibiotic resistance. Factory farmers crowd animals together and feed them constantly. As with any kind of animal, large sedentary groups can serve as breeding grounds for bacteria. Possibly, the animals spread the contagion before the farmers realized the animals' condition. Or perhaps, farmers gave antibiotics only to animals that exhibited symptoms. When this system proved impractical and the disease spread to many animals before containment, farmers devised a way to combat this infectious cycle: they began to place antibiotics in the feed of all their animals. The antibiotics served as a prophylactic, an agent used to prevent the spread of disease (Khachatourians 2). Antibiotics used non-therapeutically in livestock account for approximately 78.5 percent of total usage (Goldman 3). Antibiotics given to livestock amounted to 27.6 million pounds of antibiotics annually as of 2001. Humans used only 13 percent of these antibiotics, or approximately 4.5 million pounds (Goldman 4).

Table 1. Usage of antibiotics.

	Total pounds	% total use
Livestock uses		
Non-therapeutic (3 species)	24,600,000	70
Non-therapeutic (other)	3,000,000	8.5
Therapeutic (all species)	2,000,000	5.7
Pesticide uses	50,000	0.1
Companion animals	1,000,000	2.8
Total non-human uses	30,600,000	87
Human use	4,500,000	13
Total use	35,100,000	100

Source: Khachatourians, George G. "Agricultural use of antibiotics and the evolution and transfer of antibiotic-resistant bacteria." *CMAJ: Canadian Medical Association Journal* 159.9 (1998): 1129-1136. *Advanced Placement Source*. EBSCO. Web. 4 Nov. 2009: Table 1.

Farmers soon realized that animals also gained weight faster with the addition of the antibiotics. This weight gain, along with a heightened feed efficiency made giving antibiotics to animals an even more beneficial investment for meat producers (Khachatourians 2). In instances where antibiotics predominate, the selective pressure placed on the bacteria increases resistance. In response, farmers increased dosages of antibiotics, thus encouraging higher levels of resistance to develop. "In an examination of 3328 feeds in the US National Swine Survey, up to 25% of the feeds contained antibiotics at concentrations higher than the recommended levels" (Khachatourians 2). Still, many companies deny the role antibiotics fed to livestock play in the development of antibiotic resistance. In response to this scientists have studied various bacteria to attempt to prove a causal relationship. Five papers written on salmonella all concluded that resistant pathogens created in animals can remain in the food products consumed by humans (Goldman 8).

While factory farming facilitates a large portion of antibiotic resistance, human abuse of antibiotics in medicine plays a part as well. Through the over prescription of antibiotics, humans have undermined the ability to treat future generations. Misdiagnosis by a medical professional can often result in the prescription of an antibiotic for a viral infection. Antibiotics kill bacteria not viruses; therefore, in a viral infection, antibiotics provide no benefit to the patient. Needless exposure to antibiotics can create resistance among the body's natural bacteria and may pass resistance through horizontal gene transfer to other harmful bacteria. Human instinct and lack of knowledge play a role in the development of antibiotic resistance. This natural instinct commands us to survive at any cost and when impaired, we rush to fix ourselves. Even in minor infections, the patient's demand for treatment can result in the inappropriate prescribing of antibiotics. Furthermore, the failure to continue the use of antibiotics through the final dose by patients may result in a possibility of a recurring infection (Rao 2). Factory farming impedes our ability to fight bacteria and human recklessness when treating their own diseases has resulted in the building of resistance scientists face today.

Antibiotic resistance has developed from our use of antibiotics, but the application of other ideas can stop this reactive chain of events. Metaphorically "digging our way out" of this pit we have fallen into, will require the cooperation of all branches of society. With a large portion of resistance appearing on factory farms, an electrified debate rages on suggesting bans and regulations. Societies such as the American Medical Association and the American Public Health Association have supported bans on eight antibiotics currently used by farmers non-therapeutically that have functions in human medicine or similar properties to antibiotics in human medicine. The antibiotics suggested by this ban include penicillins, tetracyclines, macrolides, lincomycin, bacitracin, virginiamycin, aminoglycosides, and sulfonamides. Also supported is a ban on the non-therapeutic use of any newly developed antibiotic that could prove effective in humans. These banned drugs used in humans would prove more effective because of decreased development of resistance. (Goldman 11).

Regulations among Third-world countries have proven minimally effective for antibiotics. The lack of monitoring of antibiotics in these areas has caused multiple epidemics among both humans and animals. Transcending species, the prevention of antibiotic resistance must apply to human medicine as well. Much like factory farming, loose monitoring of antibiotics has shown itself to encourage the use of antibiotics (Rao 6). Humans naturally have resistance to bacteria that we develop from childhood. Often times we ignore this fact, demanding sometimes unnecessary antibiotics. Letting our natural immune system defend itself will not only increase our resistance to bacteria but also prevent the development of antibiotic resistance.

To lower our consumption of antibiotics, better physician and public education as well as the application of natural remedies to bacterial infections has been suggested. With increased education, people will have the ability to help slow the development of resistance. Using natural remedies offers another option. For example honey, when placed on a cut, can prevent the growth of microorganisms and heal skin faster (Jones 168).

These plans, however, all have one flaw, the need for humans to work together to prevent antibiotic resistance. By creating new treatments for bacteria, antibiotics could lose their application in medicine. One of the most promising concepts, the bacterial genome, could allow us to construct molecules inhibiting the growth and function of bacteria through exploring which enzymes help bacteria operate (Walsh). Another prospect turns viruses against bacteria. Special viruses called bacteriophages kill bacteria. These bacteriophages have already treated ear infections with surprising success. Bacteriophage treatment requires only one dose preventing the need for a daily regimen. The concept of one dose has researchers excited because forgetting to complete an antibiotic treatment can cause antibiotic resistance (de Lange). Introducing our own bacteria has shown itself as a potential asset to fighting bacteria.

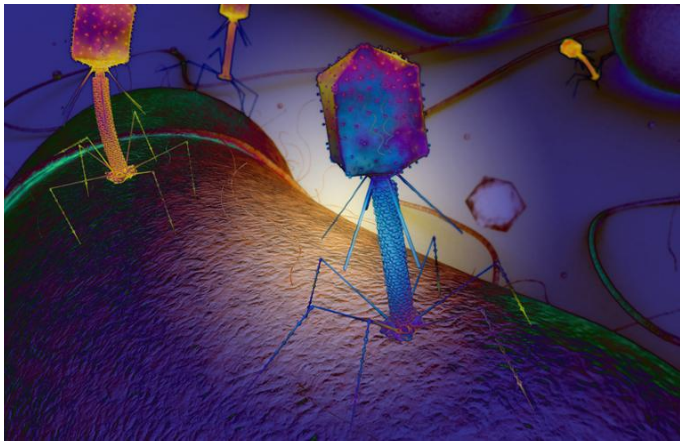

Figure 3. Bacteriophage. A depiction of what scientists believe a bacteriophage looks like.

In the 1960s, scientists discovered quorum sensing, a message system between bacteria. If we create bacteria with the ability to only send or receive messages, and introduce them into the population, reproduction occurs more rapidly in these bacteria. As a result more “half-blind” bacteria prevail over the usual strain and a quorum can not form. The loss of a quorum then lowers the virulence of the infection. Creating bacteria with altered genes and letting those genes spread through the population could allow us to take advantage of those genes to destroy a large portion of a bacterial population (Wenner).

Antibiotics have not lost all potency, however, and with narrow spectrum antibiotics resistance develops far less often. "We have been using the penicillin-tobramycin regimen for neonatal sepsis in all our NICUs for 2 years since the end of the study. There have been no further or new problems with resistance or treatment failures in this period" (de Man 6). By altering our current views of bacterial infections, we can reclaim our advantage over bacteria.

The discovery of antibiotics to battle bacteria proved a great achievement for mankind. Broadened applications for antibiotics and overutilization have led to increased bacterial resistance. Each exposure provides bacteria a new opportunity to thwart our attack. Research into the mechanisms of resistance could lead to new options for bacterial eradication or control. Education and judicious prescription of antibiotics will extend the effective life of our current antibiotic regimens. Before we enact any new policies, we must think of all possible consequences that could occur, or the events contributing to antibiotic resistance could parallel in these policies. In replacing old practices with contemporary ones, tentativeness will prove imperative to prevent the failure of newly developed techniques. The ongoing battle for bacterial supremacy will challenge scientists for years to come.

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Extra images

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