2015

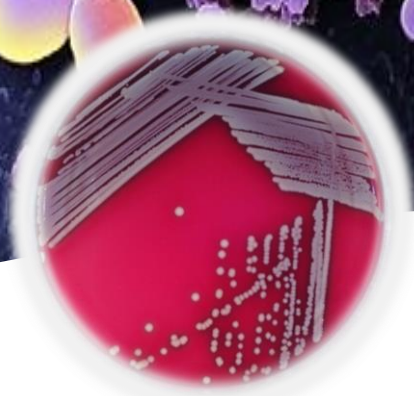
Antibiotic Resistance

Molly Kempa
Grand Valley State University

Antibiotic Resistance

By: Molly Kempa

“As a society we need to stand together and begin implementing solutions before antibiotic resistance becomes the next great pandemic our generation is forced to face.”



Antibiotic Resistance

Molly Kempa

Introduction

The Issue

Resistance

Overuse

Future Outlook

Prevention

For decades our society has been involved in a war against microorganisms, specifically bacteria. Over the years we have continued to design new products and technologies to fight off the bacteria in our world. Antimicrobials have been added to dish soaps, hand soaps, toothpaste, shampoo and even deodorant in hopes of stopping the threat of bacteria in our daily lives, but why are these microbes such a threat? "The calculated number of bacteria on Earth, above and below ground, is 5x10^30. To put into perspective, the number of bacteria on Earth is almost one billion times more than the total number of stars in the universe" (Schmidt, 15). It is true that some bacteria are harmful to humans, but some bacteria have the opposite effect. Throughout our body there are a variety of bacteria aiding in our daily bodily functions. For example, we have bacteria that live in our intestines that help break down certain foods and absorb nutrients that otherwise we could not, and are thus essential for our metabolism.

"To put into perspective, the number of bacteria on Earth is almost one billion times more than the total number of stars in the universe."

Antibiotic: a chemical substance that either kills or inhibits the growth of bacteria and other microorganisms.

These commensal bacteria are found in many other places, and in fact, the ratio of bacterial cells to human cells is 10:1. This means that bacteria account for around 90 percent of cells on and within the human body, which has prompted some scientists to now call us a "human-microbe hybrid" (Schmidt, 21). We can see that some bacteria are actually beneficial to our lives and killing all bacteria would not be advantageous. The true reason the war on microbes started was because some bacteria cause life-threatening illnesses if they are able to colonize in the body where bacteria are not normally found in that quantity. This threat of disease has led science to the discovery and use of antibiotics. According to Dr. Selman Waksman, an antibiotic is a "'chemical substance, of microbial origin, that…(inhibits) the growth or metabolic activity of bacteria and other microorganisms'" (Spellberg, 39). For quite some time we thought we had won the war on microbes due to antibiotics, but we were wrong. Bacteria have evolved and fought back against our medications and now the issue of antibiotic resistance is a serious one facing our population. Unfortunately, our society has not seemed to notice.

The Issue

Most people in the United States believe that infectious diseases are not a major problem in our nation, and that only third-world countries without advanced medical technology have a substantial number of people dying from infections. This public opinion on infectious diseases is somewhat false. While it is true that third-world countries statistically show a greater incidence of deaths due to infectious diseases, over 250,000 people in America die every year from influenza, pneumonia and sepsis (Spellberg, 35). Infectious diseases remain among the top ten causes of death in the United States and the world regardless of the variety of antibiotics we have available today. It would seem as though with the current antibiotics, vaccines, and public health, that infections would be no match for modern medicine. Since 1935, there have been more than 150 antibiotics produced and each has aided health professionals with curing patients of infectious diseases (Spellberg, 43). With this number of antibiotics, infectious diseases should not be an issue, and "in 1969 the US surgeon general, Dr. William Stewart, is said to have declared, 'It is time to close the book on Infectious Diseases and declare the war against pestilence won.'"(Spellberg, 22). This statement shows the arrogance that developed in the science community regarding antibiotics, and this arrogance has only diminished slightly since. Over 40 years later, we are still discussing antibiotics and it is clear the "war" has not been won. The World Health Organization (WHO) expressed concern five years ago that within the next decade there will be no effective therapies against infectious diseases such as malaria, tuberculosis and pneumonia (Schmidt, 6). These

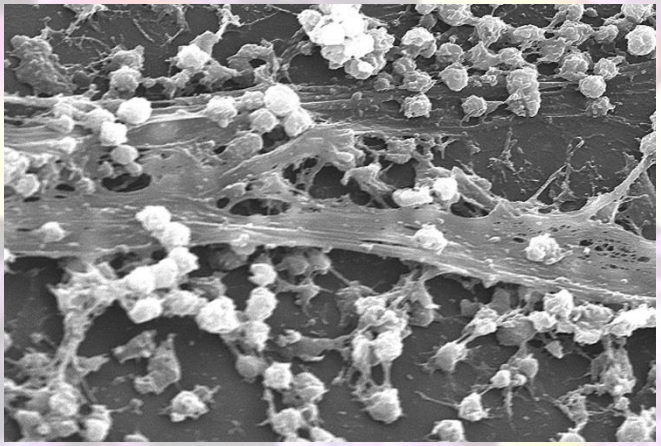


Figure 1. Bacteria forming a biofilm.

nosocomial infections have become progressively more common in countries with advanced medical technology, and are a consequence of the modern medical intensive care used in hospitals today. It is clear that, "this prevalent belief that infectious diseases had been overcome by modern medical technology should be remembered as one of the greatest blunders in the history of biomedical sciences" (Spellberg, 34).

Why are people still falling deathly ill due to bacteria? The answer is quite simple: resistance. Some bacteria have developed resistance to the antibiotics we currently use today and are therefore able to infect individuals more easily without being impacted by the use of medications as much as a non-resistant bacterium. The bacteria are quite intelligent and have a variety of mechanisms to endure harsh conditions: biofilms, cooperation, communication, gene swapping and spore formation (Schmidt, 7-8). We also see that the overuse of antibiotics in our daily lives creates an environment to train the bacteria to defend themselves against these antimicrobial agents and antibiotics. "Much as a musician or an athlete goes through endless hours of training to

"Soon there will be only resistant bacteria infecting patients with few to no treatment options unless a resolution against bacterial resistance can be developed."

hone his craft, antibiotics provide the training ground for microbes in our midst to accelerate their training in how to best handle…antibiotics" (Schmidt, xvii). This training will allow the proliferation of resistant bacteria, and infections by these bacteria will only trigger more infections to occur, which will increase the morbidity and mortality rates. Soon there will be only resistant bacteria infecting patients with few to no treatment options unless a resolution against bacterial resistance can be developed.

Solutions to this problem seem to be quite simple. In order to keep on top of the issue of antibiotic resistance we need to continue to research and develop new antibiotics to kill the bacteria who are resistance to every other antibiotic. In reality, many pharmaceutical companies have ceased research and production of new antibiotics, and bacteria are becoming more and more resistant as smaller quantities of antibiotics are being created. With fewer antibiotics being produced the future treatment of infectious diseases is narrowing. Another traditional response would be to limit the use of current antibiotics to only cases that require their use in order to slow the progression of resistance, but currently the medical community has not slowed down their use of these medications. What will medical professionals treat infections with when all the bacteria are resistant to antibiotics? These resistant bacteria, commonly referred to as super bugs, are not a work of fiction and should be taken seriously in every part of the world.

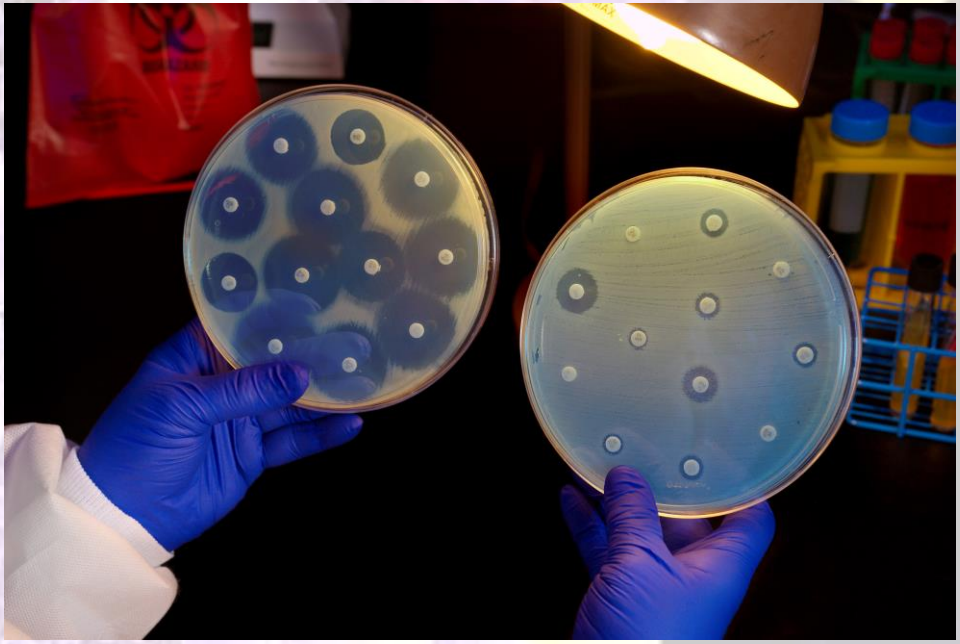


Figure 2. If a bacteria is sensitive to an antibiotic than it will not be able to grow in its presence (petri dish on the left). The petri dish on the right shows a bacterium that is resistant to each antibiotic disk on the plate.

Resistance

When examining the past use of antibiotics we can discover that our society recklessly prescribed antibiotics believing that they were the miracle drug needed to kill bacteria causing infectious diseases. Antibiotics have destroyed bacteria causing disease for decades, but their extended use has led to the natural selection of the bacteria that could survive through the harsh conditions brought upon by antibiotics. Charles Darwin's natural selection theory states that the genes that allow an organism the opportunity to procreate more than their genetically different peers will be selected for, meaning that they will survive longer due to their genetic advantages. Antibiotics have selected for bacteria that have the ability to gain resistance, and have wiped out the bacteria that were unable to gain resistance. This occurs because when an antibiotic is used there is a small population of resistant bacteria left behind after the use of the antibiotic that can continue to multiply. Also, we must recognize that in order for an antibiotic to kill a bacterium the bacteria must use the biochemical pathway that the drug is targeting, and the antibiotic must be able to infiltrate the bacterium in order to destroy it (Spellberg, 44). These two factors are a means by which bacteria can survive antibiotics due to inherent resistance[1].

Although bacteria are not considered complex organisms, there are multiple methods that a bacterium can implement in order to gain resistance. These resistance mechanisms vary and can involve factors ranging from the environment to genetics. The first method of gaining resistance involves the DNA of bacteria. A bacterium can get the genes for resistance from the DNA of bacteria in the surrounding area. Once

[1] Inherent resistance means that the bacterial is naturally resistant to an antibiotic.

these bacteria have these resistance genes they now have the ability to fight off certain antibiotics, and this process of gaining resistance genes occurs continuously in the microbial world. Gaining resistance genes occurs via conjugation, transduction or transformation which are all horizontal gene transfers. Conjugation is when there is cell to cell contact between the two bacteria and the genetic material is transferred in the form of a plasmid[2]. The process of transformation is when genetic material is taken up by the bacteria from its surrounding environment, and transduction occurs when the bacteria is infected with a virus specific to bacteria called a bacteriophage, which can transfer DNA between bacteria. Normally DNA transfers of this kind can only occur between organisms of the same species, which is the most specific of the classes of organisms. "In contrast, bacteria can reach out, grab, and mix and match DNA with bacteria of a different species, genera, family, order, class and all the way up through the phyla level" (Spellberg, 100).[3] This means that bacteria can share genetic information with organisms that are not closely related to them while most other organisms cannot do this.

[2] A plasmid is a small piece of DNA that can be transferred between cells.

[3] Scientists put organisms into groups. There are 7 levels of classifying living organisms: Kingdom, Phylum, Class, Order, Family, Genus and Species. Kingdoms are the most general categories and Species are the most specific.

"This process of gaining resistance genes occurs continuously in the microbial world."

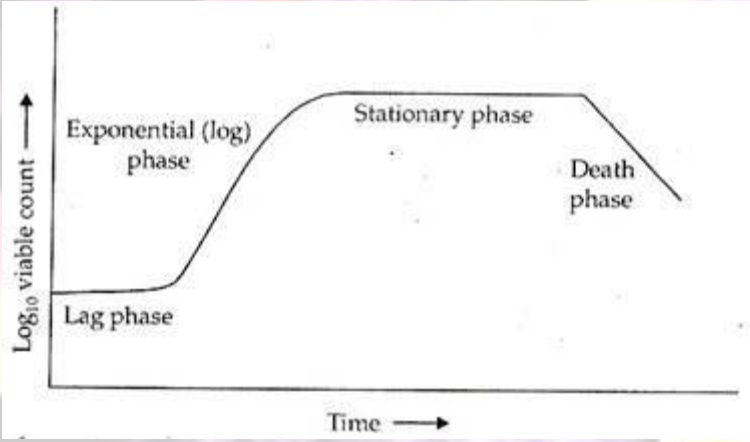
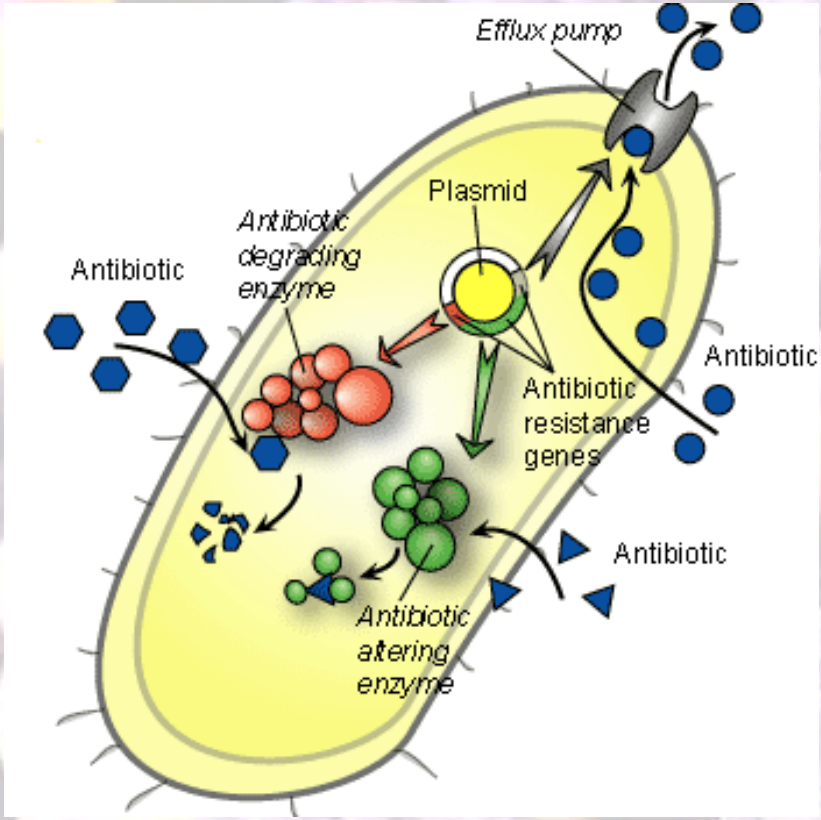


Figure 3. This graph represents the growth cycle of a bacterium.

Another way for bacteria to gain resistance is through mutations. Mutations in a bacteria's DNA occur during reproduction which is a process that is ridiculously fast in bacteria. The time it takes some bacteria to reproduce is somewhere between twenty to thirty minutes (Spellberg, 98). Each time a bacteria reproduces there is an opportunity for small changes in the DNA to occur while replicating, and these changes are passed on to the offspring of the bacteria via a vertical gene transfer. Due to the accelerated rate of reproduction in bacteria the odds are very high that mutations can occur, and this translates into an increased chance of bacteria gaining mutations that code for resistance genes. Once the mutation coding for the resistance gene is transferred to the progeny of the bacteria, the gene is within that bacterium's DNA unless another mutation occurs. "Of every million progeny produced by a single dividing bacterium, up to 30,000 may have unique, random DNA mutations. These mutations may specifically enhance their ability to survive despite hostile environmental conditions, such as the presence of antibiotics" (Spellberg, 99). Due to their ability to replicate swiftly it is easy to see that bacteria are the most diverse and numerous organisms on our planet.

Bacteria are also able to gain resistance through the environment in which they reside, and bacteria are found in almost every climate and environment on the planet. One of the many ways the environment can impact the resistance of a bacteria is whether or not the bacteria is living around plants. "Most plants have developed a formidable arsenal of chemical agents to ward off all manner of pests. Bacteria that live around these plants and their anti-pest arsenal must develop their own defenses against the plant defenses" (Schmidt, 215). These defenses the bacteria develop for protection are similar to the antibiotics used today, and thus the bacterium develops resistance against antibiotics. If the bacteria are in an environment where the plants are being sprayed with a fungiocide or a bacteriocide[4], than resistance can also increase due to the survival of the resistant bacteria. These bacteria will then reproduce and make offspring that possess their resistance genes as discussed previously. The surrounding environment also proves vital if there are heavy metals near the bacteria. Heavy metals such as mercury, copper, lead, cadmium or arsenic can contaminate the environment around bacteria, and in response to this contamination the bacteria use efflux pumps to get rid of the heavy metals (Schmidt, 215).[5] The bacteria have learned to adapt these efflux pumps for use against antibiotics by pumping out the antibiotic if it enters the bacterial cell.

Resistance can also occur from the environment due to the incomplete digestion of antibiotics in the human body. When a patient takes an antibiotic for an illness their body's digestive system is unable to absorb most of the antibiotic. Due to this lack of absorption, most



[4] Words ending in –cide refer to "the killing of", thus bacteriocide refers to agents that kill bacteria.

[5] An efflux pump is comparable to a water pump that would pump water out of a basement during a heavy flood (Schmidt, 215).

"Due to this lack of absorption, most antibiotics just pass on through the intestinal tract and are excreted into the environment."

antibiotics just pass on through the intestinal tract and are excreted into the environment. "It has been estimated that 85-95 percent of antibiotics used remain in their basic molecular form once they hit the environment" (Schmidt, 210). Thus, these antibiotics that make it out into the environment provide the bacteria with the opportunity to "train" their resistance mechanisms against that antibiotic.

There are many important factors that also need to be addressed regarding how antibiotics gain resistance. In today's world our ability to travel is dramatically increased since the beginning of the human race. Anytime you want to travel you could take a car, bus, train or an airplane to any part of the world you desire to go. The increase in transportation mechanisms for humans has also increased the transportation abilities of bacteria. Bacteria can now travel to any place in the world, and this is no different for resistant bacteria. Outbreaks of resistant bacteria in one part of the world can travel to any part of the world and cause an outbreak there. This is an alarming notion to fathom because we have no way to kill these resistant bacteria and prevent them from spreading across the globe if an outbreak were to occur. This provides an important reason why our society needs to pay attention to this issue.

Overuse

Just as antibiotics were introduced to the world, incidents of resistance began to occur. It took only ten years since the introduction of penicillin for *Staphylococcus aureus* to become completely resistant to penicillin and have this resistance spread across the United States (Spellberg, 54). Ten years is a short time, considering it takes more than ten years for an antibiotic to be approved for use in patients since its discovery. This makes it easier to understand why our society has extended the use of antibiotics outside of treating patients with infections because they want to kill off these potentially harmful bacteria before they invade and cause an infection. Although this extended use of antibiotics and antimicrobial agents may have helped with the incidence of infectious diseases over the years, the extended use has also caused people to use these agents where they are not necessary. A common antibacterial agent used in many products is Triclosan, and its wide use was estimated to be around one million

Figure 4. Products containing antimicrobial properties.

pounds each year (Schmidt, 211). These agents, such as Triclosan, are found in a variety of products: soaps, shampoos, conditioners, toothpaste, cosmetics, deodorant, shaving cream, cutting boards, plastic toys, towels, mops and pesticides. Many companies have developed a mindset that marketing their products as antimicrobial or antibacterial will help them sell more products thus gaining more of a profit. This mindset is a significant concern to our issue of antibiotic resistance. "A tragic irony is that recognition of the issue of emerging infections is driving well-meaning people to use antibacterial products where they are not needed-furthering the problem of antibiotic resistance" (Schmidt, 211). The use of these agents in products where they are not needed exposes the bacteria that are around these products to a small amount of an antimicrobial agent. This small dose will kill most of the unwanted bacteria that are susceptible, but there are still a slight percentage of bacteria that develop resistance to the agent. As we discussed earlier, the resistant bacteria are then able to reproduce and more resistant offspring are created. The resistant genes are then fixed into the population of bacteria and will be effective against the antibacterial agents used against it.

This issue of the overuse of antibacterial compounds has been seen in the medical field as well. It is quite common for people to get infections, and it is well-known that these infections will most likely be treated with an antibiotic. As patients we often desire to be treated with an antibiotic, but strong caution needs to be used when determining what to treat infections with. Antibiotics are ineffective against infections that are not a result of bacteria. Viral infections, for example, should not be treated with antibiotics because the antibiotics will not help the infection, they may kill the beneficial bacteria in

the body, or they may help the bacteria in the body gain resistance to the antibiotic. This resistance could then be transmitted to harmful invading bacteria in a future infection eliminating the use of that particular antibiotic in that patient experiencing the infection.

Another issue involving the use of antibiotics to fight a patient's infection is the actual duration and dosage of the antibiotic taken. Some patients will stop the use of the antibiotic they are taking for their infection at the first signs of returning health because they feel they do not need the remainder of their prescribed dose of medication. Most patients would argue that this would be a beneficial practice to aid in the fight against antibiotic resistance due to less exposure of the bacteria to the antibiotic, which would result in a lower probability the bacteria could develop resistance. This statement is false, the duration the antibiotic is prescribed for is carefully

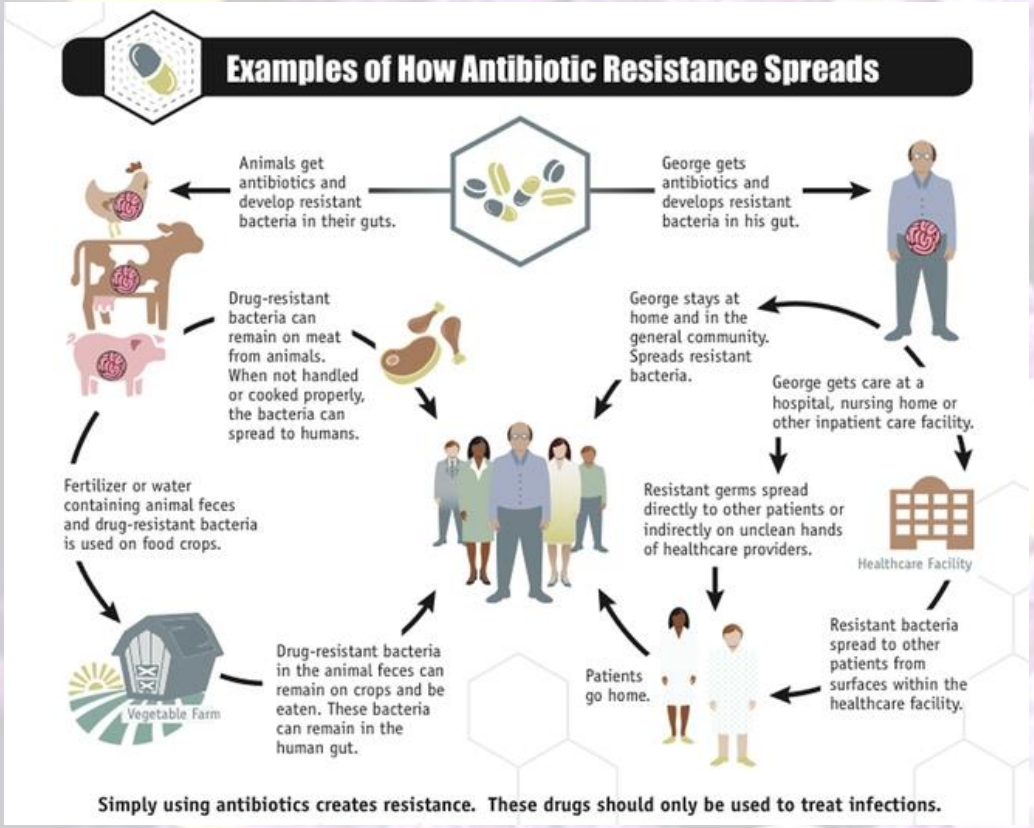
"Self-administration of medication has led to the selection of resistant bacteria, and has also led to bacteria that develop resistance to multiple medications."

calculated to fight off the infection, and stopping the medication early can be detrimental to the recovery of the patient as some can relapse and require further treatment. The dosage of the antibiotic used in patients is also shown to be dramatically increased from that of bacteria. "Secretion into the environment of a trillionth of a gram of antibiotic may well be enough to protect a single, tiny bacterium from its neighbors. But a trillionth of a gram of antibiotic would do nothing for a patient. Rather, every day of antibiotic therapy requires that a billion or trillion times more antibiotic be administered to cure infections in patients" (Spellberg, 107). Due to the amplified amount of antibiotics that need to be used in a patient it is crucial that patients keep taking their medication in order to recover from their bacterial infection. Self-administration of medication has led to the selection of resistant bacteria, and has also led to bacteria that develop resistance to multiple medications.

It is also important to realize that the use of antibiotics does not cause bacteria to gain resistance, but does affect the rate at which resistance spreads amongst the population of bacteria.

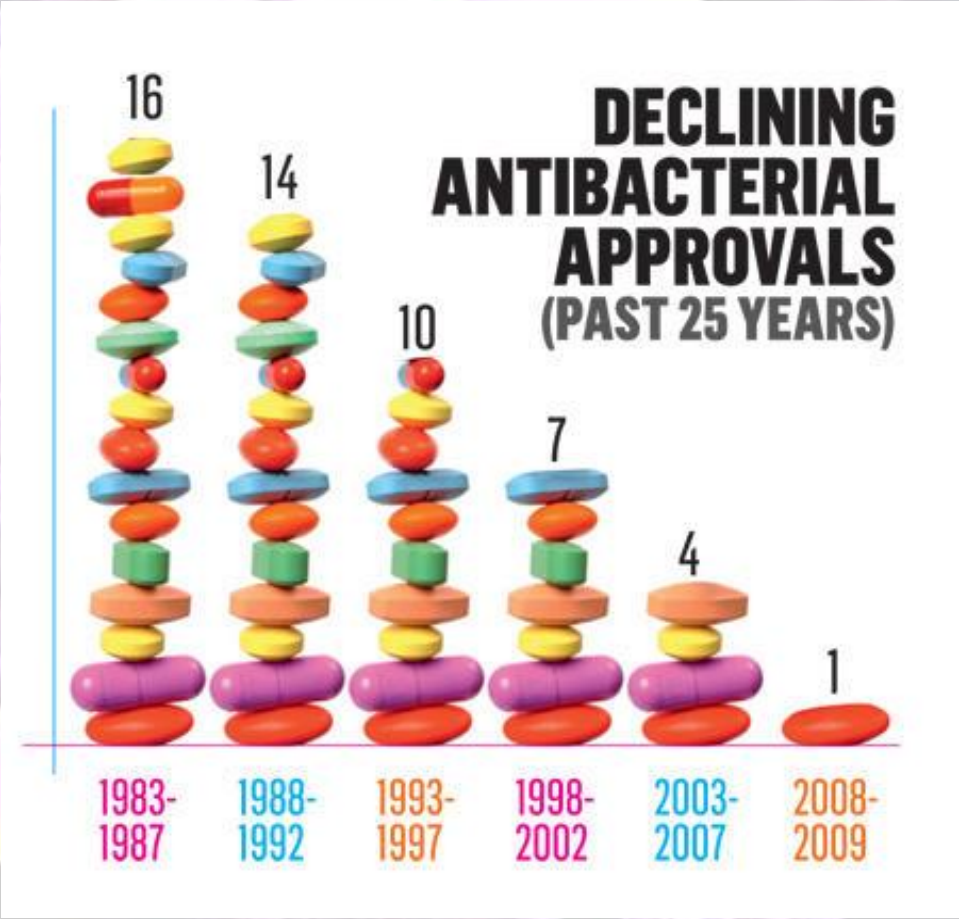
Another component affecting the issue of antibiotic resistance involves the overuse of antibiotics in countries that do not have the technology to effectively diagnosis bacterial infections. "Suboptimal use of antimicrobials is a particular problem in low-income countries, where there is often a lack of laboratory data to guide prescribing, and where antimicrobials are often 'prescribed' by non-medical practitioners or are freely available in markets. In such situations, sub-therapeutic doses are often taken…" (Wax, 370). In these low-income countries, the availability of antibiotics to any and every one dramatically increases the use of the drugs which results in a greater selection of resistant bacteria due to the inadequate amount of antibiotics taken. Although there is a great incidence of selection of resistance in these low-income countries, this is still an issue for the entire globe due to travelling and migration.

The overuse of antibiotics is not just within the human population. In fact, around 70 percent of antibiotics produced in the United States are used on farms. The use of antibiotics on farm animals, such as livestock and chickens, accounts for most of the antibiotics produced in America ("The Trouble with Antibiotics"). Why are antibiotics being used in farm animals? Farmers who raise animals for slaughter to supply food for the nation are using antibiotics as a means to promote growth in the animals, fight infections, and prophylaxis. The antibiotics are mixed in the water supply or the feed given to the animals, and farmers have found that with the use of antibiotics the animals gain as much weight with less feed and faster than if no antibiotics were used. Because of this finding the farmers have continued their use of antibiotics as a means to cut



costs while raising the animals. "Most of the growth promotion actions of the growth promoting antibiotics are due to prevention of illness…It involves giving antimicrobials to a large number of animals, over a long period of time, at lower than therapeutic doses, a usage pattern that is favorable for development of antimicrobial resistance" (Lawrence, 189). Just as low doses of antibiotics create an ideal environment for the training of bacteria to become resistant in humans, the same effect occurs in animals. These resistant bacteria found in animals very well may be transmitted and cause incidents of resistant bacterial infections in hospitals. This could be possible through the consumption of the meat from these animals containing resistant bacteria, or the fecal matter used to fertilize fields of plants harvested for our food supply. Remember that most antibiotics are not digested by the body and are excreted into the environment through waste. Manure that is used to fertilize fields from animals that are treated with antibiotics will contain antibiotics. These antibiotics can cause bacteria around the plants to become resistant, can go airborne via dust particles if experiencing a period with no rain, or can wash off the field while experiencing a rain storm and run off onto neighboring lawns. Although it has yet to be proven that the use of antibiotics in animals is causing infections of superbugs in the human population, there is currently promising research being conducted that provides evidence that resistance is spreading between the two populations (animal to human) ("The Trouble with Antibiotics").

"There is currently promising research being conducted that provides evidence that resistance is spreading between the two populations (animal to human)"



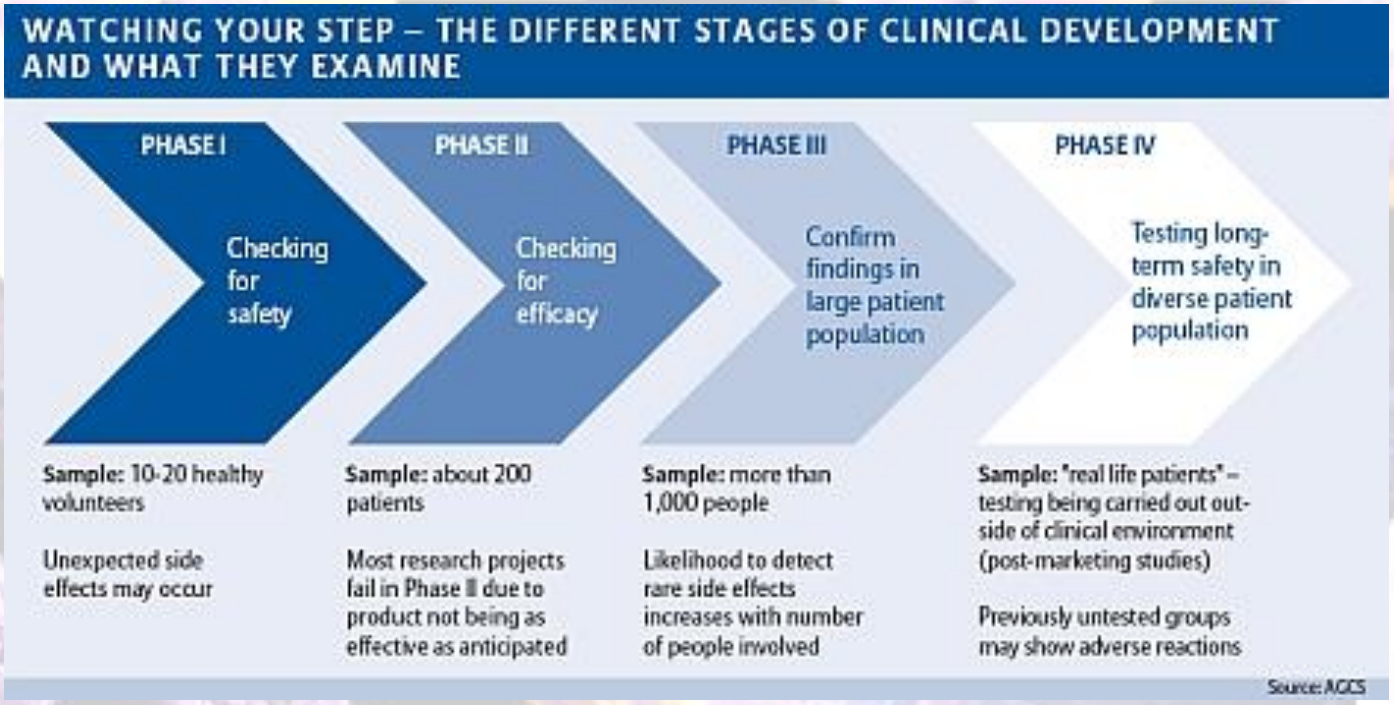
Future Outlook

It appears that antibiotics are one of the only technologies on Earth that actually become less effective the more it is used (Spellberg, 122). Members of the science community are sensing that the technology of antibiotics will soon be obsolete. According to a CDC representative interviewed about antibiotic resistance and the use of antibiotics on farms, "Anywhere you use antibiotics you will have resistance." ("The Trouble with Antibiotics"). It is estimated by Dr. Walter Gilbert, a Harvard professor, that "there may be a time down the road when 80 percent to 90 percent of infections will be resistant to all known antibiotics" (Schmidt, 4). The devastation that would occur if the previous statement were to become true is unfathomable. This issue is not one to be taken lightly by the science community and the public, but should be given a substantial amount of attention in the coming years.

The obvious solution to this issue of bacteria gaining resistance to antibiotics is to discover and produce new antibiotics that the bacteria do not have a resistance to, but most pharmaceutical companies have stopped researching new antibiotics. This reduction is not suggestive that all research is being decreased because the area with the most significantly decreased research is antibiotics (Spellberg, 90). This reduction seen in antibiotic research is occurring for a multitude of reasons, but what it all comes down to is money. A pharmaceutical company, above all else, is a business that is looking to make a return on their investments. The cost of researching and developing a new drug is extensive, and companies are simply not making enough of a return on their production and sales of antibiotics to compensate for such a large amount of money spent on researching new antibiotics.

Another factor that weighs against the research of new antibiotics to fight against these superbugs is time. The process involved in the discovery and production of a new drug is lengthy. First, researchers need to discover a new way to stop the bacteria from causing a harmful infection in its host, and most mechanisms of action have already been discovered over the last century. Thus, the research stage of development of a new antibiotic would be extensive because we have used all of our current knowledge to make the antibiotics of today. Next, the development of the new antibiotic is a long process. This process entails ensuring that the new antibiotic is drug-able, which means "the compound used in the medication has to be active at concentrations that are feasible for administration to people" (Spellberg, 114). The new medication must also be safe and effective in animals first and then humans. Researchers would first have to test the new antibiotic in animals to make sure there are no harmful side effects, and that the drug performs as intended. After the trials involving animals are completed with favorable results, the researchers will then get approval to run a clinical trial involving four phases. Phase 1 of a clinical trial involves testing the drug on healthy human volunteers to see if there are any adverse effects. Phase 2 and 3 of a clinical trial tests the new drug on actual patients, and Phase 4 involves the surveillance of the new medication after it is approved for public use to make sure no other side effects occur once the public begins using the medication. As you can see this process would take a long period of time to complete, which is a great deterrent for pharmaceutical companies.

The lack of federal funding for new antibiotics is also a factor in the reduction of research and development of new antibiotics. Diseases such as HIV/AIDS, have substantial federal funding available to pay for the cost of developing anti-HIV medications because the government and the public believe that



HIV is a huge issue needing a resolution. This was not always the case of HIV/AIDS. Before this disease was a serious issue in our country and throughout the world, few people paid any attention to its threat. It was only after a noteworthy portion of the homosexual population began contracting this disease that the public began to respond to the issue. Resistance to antibiotics is another issue of similar magnitude that needs attention, but we should not wait until it is a major issue to act. Now is the time for the public to realize that antibiotics are beginning to fail as a treatment method and that precautions need to be taken against this threat. It is only when the public believes antibiotic resistance is an issue that our elected officials in the government will act against the issue.

There are a variety of steps that need to be taken in order to reduce the implications of antibiotic resistance. One of the first steps to be taken is to compile a list of the most problematic bacterial infections our society is facing today and ones that we will face in the near future (Spellberg, 181). This list will allow researchers to focus on the infections we are experiencing the most hardships with first, and thus hopefully develop new antibiotics for those infections before moving on to others. The next step would be for the government to provide incentives to pharmaceutical companies in order to get them to start researching new antibiotics again. An incentive to pharmaceutical companies that could cut cost of researching new antibiotics in some way, such as a tax break, could promote increases in research in this area. Another step that should be taken involves the development of vaccines. "Since defects in host immune systems predispose patients to developing drug-resistant infections, finding a way to boost the immune system

"It is only when the public believes antibiotic resistance is an issue that our elected officials in the government will act against the issue."

should be an effective way to prevent or treat such infections…Vaccines and antibiotics complement one another, and both are needed" (Spellberg, 194). The current method of treating a bacterial infection is to prescribe a patient an antibiotic and send them on their way to the pharmacy. We can see that this method is a short term fix to a long term problem. Not only does the science community need to develop new antibiotics for infections, they also need to broaden their method to how to kill off the bacteria. The use of vaccines that can provide extra immune support to the patient while experiencing an infection could prove to be quite beneficial to the recovery of the patient. It is essential that the medical community develop combination therapies to help fight off the bacteria causing the infections in order to help with the never ending issue of antibiotic resistant. Bacteria will always possess their resistance mechanisms against antibiotics, and humans need to realize that just using antibiotics may not always be the answer to treating bacterial infections.

Another solution to the problem of antibiotic resistance would be to monitor the amount of antibiotics used on farms. Currently farmers are not required by law to provide any data regarding their use of antibiotics while raising animals, and this should be changed immediately. About 40 years ago, the FDA tried to reduce the amount of tetracycline and penicillin used on farms, but everyone opposed the reduction due to the lack of evidence between the use of antibiotics on farms and infections in humans. "Relatively few studies have been done to evaluate the distribution of antibiotic resistance patterns in environmental bacteria, especially bacteria in sites outside of farms or areas of human settlement" (Wax, 18). The more antibiotics we use to raise animals the more selective pressure we put on the environment to kill off susceptible bacteria leaving behind resistant bacteria. One way to decrease the amount of resistant bacteria in the environment is to decrease the use of antibiotics. The use of a surveillance system that monitors the use of antibiotics on farms will help control the amount of antibiotics used, and this will decrease the production of superbugs. Last year there were proposals made to Congress that required farmers to report information regarding their use of antibiotics, but the proposals did not pass. Today, the FDA is working on another approach that involves the pharmaceutical companies to cease production of the antibiotics that are commonly used for growth promotion on farms ("The Trouble with Antibiotics").

Food and safety regulations should also be implemented in regards to the amount of antibiotics that are safe to use in raising farm animals to help control the rate at which antibiotic resistance is spreading, and help keep the public safe from antibiotic-resistant bacteria that are found to be contaminating meats. Scientists should also conduct more research to link the use of antibiotics on farms to the prevalence of superbugs in humans in order to provide the public with more evidence which would fuel this issue's prominence.

"The more antibiotics we use to raise animals the more selective pressure we put on the environment to kill off susceptible bacteria leaving behind resistant bacteria."

Figure 5. Hand washing is still the most important factor in prevention of illness.

Prevention

As a society we must all realize that bacteria are essential to our lives, and they are critical for the survival of the planet. "For example, bacteria are the only organisms on the planet that are capable of fixing nitrogen from the atmosphere into the food chain. This process is essential to the creation of macromolecules, such as proteins, that are the basis of life. Bacteria also produce a variety of vitamins and cofactors essential to our diet, such as vitamin K" (Spellberg, 103). The human population must learn to coexist with these organisms that have managed to develop a bad reputation since the beginning of life on Earth. Yes, some bacteria are harmful and should be killed, but many we come in contact with are not harmful and exposure to these bacteria is a normal part of life. The most important way to protect your body from an infection is to keep yourself healthy. This consists of many factors: healthy diet, adequate amount of rest, exercise and hand washing. Eating a healthy diet will make sure your body is getting the essential nutrition it requires, and this in turn will keep your immune system running more effectively. "Sleep is one of the most fundamentally essential components needed to maintain strong immune defenses, efficient energy production and appropriate recovery and repair functions" (Schmidt, 192). Health professionals suggest that you get 8 to 9 hours of sleep each night. It has also been shown that moderate exercise may increase your immune response by increasing your white blood cell count. The last factor, hand washing, is still the most powerful action to prevent infections. All of these factors will lead to an increase in your immune system, and this will help you fight off any kind of bacteria that is trying to invade your body.

In regards to the use of antibiotics there are two rules that patients can follow to help the issue of antibiotic resistance. First, do not ask your physician to prescribe you an antibiotic. Let your doctor determine whether your infection is a result of a bacterial infection, and if it is, then they will prescribe you the proper antibiotic for the infection. The pressure that a patient can put on a doctor to prescribe unnecessary medication is a continuous issue in the health profession, and one way to eliminate this issue is for you, the patient, to stop asking for unneeded medications. The second way to help prevent antibiotic resistance is to take the full dosage of antibiotic prescribed. "If a drug concentration drops below the MIC before infection is cleared, residual pathogens may regrow and cause disease relapse. During regrowth, spontaneous errors in DNA replication generate new resistant mutants and the resulting mutant populations will be enriched when antibiotic therapy is restarted" (Drlica, 82). [6] In order for the antibiotic to be effective in killing the bacteria the MIC must be met, and this is why it is essential that a full dose of the antibiotic is taken as directed. If for some reason a patient stops their treatment of the antibiotic before prescribed to do so, than some bacteria causing the infection may still be living. These bacteria can then reproduce and possibly develop resistance via mutations in their DNA or a horizontal gene transfer from a neighboring resistant bacterium.

[6] MIC is the minimum inhibitory concentration, or the minimum amount of a drug necessary to inhibit growth of the bacteria. If a drug concentration falls below this level than it not effective, and the bacteria can continue to grow.

There are a few more preventative measures that each person can begin today that can aid in the prevention of infections, which will ultimately decrease the use of antibiotics. The first preventative measure is actually the reduction of the germ free home movement that our society has grown to desire. There are two major issues regarding this movement, and the first is the negative impact it may have on people, especially children. As a child you were involved in anything and everything that interested you, and not all of these things were germ free. For example, a young child puts objects in their mouth. Any new object a child comes in contact with they put in their mouth as a means to learn and discover all about the new object. This practice is not a germ free one, and is actually quite beneficial to that child. Your child's body needs to be exposed to the world around it in order to build his/her immune system, and cleaning your home so it is completely germ free would be a disservice to your child's development of his/her immune system. The second issue with the movement

"Cleaning your home so it is completely germ free would be a disservice to your child's development of his/her immune system."

Figure 6. Examples of products consisting of probiotics.

toward a germ free home is the development of resistance against the disinfectants and antiseptics used to clean the home. "Resistance to antiseptics and disinfectants may remove our last line of defense against pathogens on our skin and on environmental surfaces; it could seriously compromise surgical procedures" (Drlica, 84). In order to keep disinfectants and antiseptics effective we must not overuse them.

Probiotics are another means by which you can strengthen your immune system which will in turn strengthen your body's response to an infection. Probiotics are "selective, nonpathogenic, living microorganisms, including some commensal bacterial flora, which have beneficial effects on host health and disease prevention and/or treatment" (Lawrence, 213-214). The sources of probiotics in the diet are dairy products, products that have been fermented, and probiotic supplements. The mechanisms by which probiotics can help your immune system fight off an infection are the production of acids resulting in an acidic environment, and this causes a decrease in the number

of microorganisms. The other mechanism consists of the production of bacteriocins which inhibit the growth of the microorganisms infecting the host.[7] Some of the major health effects of probiotics are: control overgrowth of intestinal bacteria, antioxidant activity, suppression of pathogenic microorganisms found in the intestines, immune potentiating activity, aid in breakdown of nutrients properly, reduction of the production of toxins and prevent cardiovascular disease (Lawrence, 213-214). The consumption of probiotics is an indirect method to help people in their fight against antibiotic resistance by supporting the immune system in fighting off harmful bacteria when they first invade and attempt to colonize the body.

Health education and spreading the word are the two key methods of prevention. Gaining the knowledge about this issue will enlighten the world about how serious an issue antibiotic resistance is, and what preventative measures need to be taken. "Not only has the general public not known about the lack of antibiotic development, or the extent of the problem, it turns out that many physicians do not know either. Nor do general medical journals appear to be particularly interested in the problem" (Spellberg, 196). Spreading the information you learn about this topic is the only way that people will begin to notice and start to care. Throughout history there is a general trend that the issues that get the most attention are the ones that affect the greatest number of people, but antibiotic resistance is not getting the attention it deserves. This issue does affect a large number of people, and will eventually affect the entire world population if a resolution plan is not developed soon. As a society we need to stand together and begin implementing solutions before antibiotic resistance becomes the next great pandemic our generation is forced to face.

"Throughout history there is a general trend that issues that get the most attention are the ones that affect the greatest number of people, but antibiotic resistance is not getting the attention it deserves."

[7] Bacteriocins are toxins made of proteins that will inhibit the growth of microorganisms.

References

Amabile-Cuevas, Carlos F., Maura Cardenas-Garcia, and Mauricio Ludgar. "Antibiotic Resistance." *American Scientist* 83.4 (1995): 320-29. *JSTOR*. Web. 17 Sept. 2014.

Bush, Karen, Patrice Courvalin, Gautam Dantas, Julian Davies, and Barry Eisenstein. "Tackling Antibiotic Resistance." *Nature Reviews Microbiology* 9 (2011): 894-96. Web. 17 Sept. 2014.

Drlica, Karl, and David S. Perlin. *Antibiotic Resistance, Understanding and Responding to an Emerging Crisis*. Upper Saddle River: Pearson Education Inc., 2011. Print.

Lawrence, Rubina, ed. *Antimicrobial Resistance, From Emerging Threat to Reality*. N.p.: Narosa Publishing House Pvt. Ltd., 2009. Print.

Lawrence, Rubina, and Ebenezer Jeyakumar, eds. *Antimicrobial Resistance, A Cause for Global Concern*. N.p.: Narosa Publishing House Pvt. Ltd., 2014. Print.

Martinez, Jose L., Fernando Baquero, and Dan I. Andersson. "Predicting Antibiotic Resistance." *Nature Reviews Microbiology* 5 (2007): 958-64. Web. 17 Sept. 2014.

Schmidt, Michael A. *Beyond Antibiotics*. 3rd ed. Berkeley: North Atlantic Books, 2009. Print.

Spellberg MD, Brad. *Rising Plague*. Amherst: Prometheus Books, 2009. Print.

"The Trouble with Antibiotics." *Frontline.* PBS. WGVU, Grand Rapids. 14 Oct. 2014. Television.

Wax, Richard G., Kim Lewis, Abigail A. Salyers, and Harry Taber, eds. *Bacterial Resistance to Antimicrobials*. 2nd ed. Boca Raton: Taylor & Francis Group, LLC, 2008. Print.