Abstract

Currently, the face of the medical world is being transformed by a biological revolution. Physicians are being faced with increasing antibiotic resistance to common bacterial infections. At the beginning of the Antibiotic Era, physicians believed they were ensured cures to so-called bacterial infections, but the overuse of those "miracle drugs" led to a disastrous outcome.

Physicians throughout the world are being faced with resistant organisms that are either unrecognized or unfrequented by the medical community. Also, many common bacterial diseases such as Pneumonia, Lyme Disease, Tuberculosis, and Malaria have become resistant. Pharmaceutical firms reacted to the problem by chemically designing new miracle antibiotics at a rate of five to ten per year. At first, it seemed technology was winning, but now it appears that bacteria has caught up to man. The fear is that the evolution of resistant strains may soon outplace the development of new drugs, leaving the medical world powerless to treat what were once routine bacterial infections. Humans interfering with nature has been illustrated through the overkill of antibiotic use. Humans have indirectly created a pattern of multiple drug resistant strains. This is among one of the most serious problems facing the medical world.

Antibiotics

Antibiotics are chemical compounds used to kill or inhibit the growth of infectious organisms such as bacteria. Originally, antibiotics were organic compounds, but as a result of technology they encompass synthetic and semi-synthetic organic compounds. Usually, antibiotics are absorbed through one's intestine and circulate throughout one's body via the blood stream. Antibiotics are specific to the bacteria, and will enact only where there is an infection.

Antibiotics kill bacteria in one or more of the following ways: They inhibit cell wall formation to alter the function of cell membranes. When an antibiotic is successful in dissolving the cell walls, it wrecks the ability of the bacteria to produce life-sustaining proteins. Antibiotics also interfere with the genetic material (DNA or RNA) which prevents the reproduction of bacteria and impede the manufacture of certain proteins that are essential to sustain bacterial life.

The concern today with antibiotics are being used too frequently and often in inappropriate situation. Incorrectly prescribing antibiotics helps breed germs resistant to the bacteria. Any antibiotic can leave behind some bacteria which can then mutate and form a strain that will be resistant in the future.

Some important rules to follow when taking antibiotics: 1) Finish the bottle because bacteria can still be lurking, 2) Do not take left over prescriptions from previous illness because this sets the stage for resistance in the future, and 3) Do not skip doses because doing so gives the bacteria a "breather" in which more can reproduce.

Bacterial Resistance

Because bacterial cells contain a single chromosome, the bacteria usually needs more information than the amount provided on a single chromosome to ensure survival. So, in addition to the DNA contained in the chromosome, bacteria carry supplemental pieces of DNA separate from the chromosome called plasmids. These plasmids are self-duplicating genetic elements that depend on the bacteria.

A spontaneous DNA mutation can occur at a plasmid within a bacterial cell. This mutation could be one in which antibiotic-resistant genes arise from. The genetic information that the plasmids carry are not used to kill off the host, but instead carry vital information for survival. The plasmids replicate inside the host cell and then the replicated plasmid is transferred to another bacterium through the use of a pilus, which is a protein structure that reaches out and draws another bacteria near it. This type of transfer is called conjugation.

This exchange occurs between both bacteria of the same species as well as different species. In addition to the fact that plasmids may exchange genetic information between bacteria of different species, it is also capable of carrying resistant genes for more than one type of antibiotic which make it even more difficult for scientists or doctors to keep infections under control.

Transposition is a way genetic transfer using transposons, which are even smaller pieces of DNA that deliver genes, including those responsible for antibiotic resistance. The transposon can jump off of one plasmid and then integrate itself into a new host's DNA or into a resident plasmid after conjugation occurs. Consequently, the genetic information that is carried by the transposon is still alive even though the plasmid that transferred the information has died. Transposons do not need to rely on a particular host cell to multiply and survive since they simply integrate themselves into the bacteria's chromosome or into a residing plasmid.

Evolution

Charles Darwin's theory of Natural Selection is the key factor to understanding evolution amongst all species and organisms. Darwin's theory of evolution states that there are groups or individuals that are better suited to survive in their environment and therefor they survive longer and perpetuate the species. Selection is the consequence of events that act directly and indirectly on the reproductive abilities of individuals in the populations with a large amount of genetic variation (Lappe 32). Individuals of a species reproduce and in turn their genetic material is carried to the next generation. Because bacteria can reproduce so quickly, approximately every twenty minutes, and their generations are so short-lived, they can evolve quicker than any other organism. As a result of quick reproduction, bacteria acquire mutations that are beneficial to their survival. Consequently, these mutations or adaptations to their environments are passed onto future generations. In the end, more offspring with a resistant genetic make-up will survive and continue to reproduce with contributes to the evolutionary process of bacteria.

Vancomycin

In order to effectively treat antibiotic resistant bacteria, the pharmaceutical and scientific industry have had to develop new antibiotics such as Vancomycin. Vancomycin was first developed in 1956 and became openly available in 1962. Phycians have since prescribed Vancomycin for bacterial infections that either do not respond to treatment or are resistant to other antibiotics. It is still today considered the most powerful antibiotic against antibiotic resistant bacteria. But, due to the misuse of Vancomycin, it has caused some bacteria to be resistant to it as well. It took thirty years of use for Vancomycin to become resistant.

Vancomycin works by interfering with the construction of the bacterial cell wall, but its action can be interrupted if bacteria modify the building blocks on their cell walls by substituting a molecule of lactic acid for one called alanine.

Vancomycin has a package of nine genes that when left in motion create a stratagem to fight bacteria. One gene enables the bacterium to make lactic acid while another codes for an enzyme that will cleave the alanine from the cell wall building blocks. The product of the building blocks pt lactic acid in the alanines place. Two more genes control the action of these three, insuring that they are active only when Vancomycin is present.

Now, Vancomycin has evolved to become resistant to enterrococci or VRE (Vancomycin Resistant Enterrococci). The fear is that enterrococci may transfer the resistant-causing plasmid to another, more virulent bacteria and resistance will spread further.

Like enterococci, many strains of staphylococcus have exhausted all but Vancomycin as their last line of defense. If one of these strains becomes resistant to Vancomycin, it could set off a major epidemic of infections that could be untreatable. The final conclusion would be that bacteria will have the selective advantage over organisms.

Lyme Disease

Certain diseases are spread to humans by insects or insect-like animals called arthropods - organisms that crawl with jointed legs. A mosquito transmits the deadly Malaria; a fly transmits Sleeping Sickness; a flea transmits the Bubonic Plaque; and a tick transmits Rocky Mountain Spotted Fever. More than two hundred diseases (Lappe 35) are transmitted to humans by arthropods. Through pest control, improved sanitation conditions, and antibiotics, most pest-born diseases have been brought under control in the developed nations of the world. One disease that has not been put under control is Lyme Disease, in which transmission requires forty eight hours or more of feeding. Between 1982 and 1993 (Zimmerman 90), more than fifty-three thousand cases (Zimmerman 90) have been reported nationwide.

When humans enter a previously undisturbed ecosystem, the ticks have an opportunity to parasitize to a new host (Lappe 23). When a tick born agent infects a human, it is often highly virulent because the new host has had little or no opportunity to evolve defenses against the invader. As a result, the Lyme Disease organism is being subjected to selective pressures where humans may then become a new intermediate host.

Many physicians prescribe antibiotics for everyone with a real or imagined tick bite to be on the "safe side". Often patients demand treatment with an antibiotic, but this is discouraged by public health officials unless a rash is present. The behavior of providing an antibiotic in every case encourages the emergence of antibiotics that are resistant to Lyme Disease. If Lyme Disease is not treated properly, it could become a threat to the human population.

Malaria

Any disease with a long history within the human population is likely to shape the genetic population that it occurs within. This is especially true for a disease that strikes a wide variety of people within a population. A disease such as this is Malaria. Malaria is a mosquito born parasitic disease that has played a large role in human evolution for as long as 40,000 - 50,000 years (Lappe 176). Ecological disturbances have given rise to this disease over the years and the number of people infected has risen.

Malaria is a devastating disease that is characterized by night sweats, weakness, and high fevers. It is caused by one of four species of the protozoan parasite known as plasmodium (Lappe 180). The disease is transmitted to humans through the bite of a female mosquito. The periodic resurgence of new parasites from one's red blood cells produce the characteristics of Malaria. If enough Red Blood Cells are filled with parasites, they can clog venules, which causes kidney failure and brain damage.

The disease Sickle Cell Anemia has developed in populations where Malaria is present. Sickle Cell is a natural defense of the human body against Malaria. While Sickle Cell has been successful in controlling the present Malaria epidemics, not much success has been made with antibiotics. The malarial parasites have developed a resistance to the traditional and newest antimalarial diseases with an alarmingly high frequency. Because of dependency on the antibiotic such as chloroquine, selective pressures continue to create new strains of Malaria. In addition to the overuse of certain antibiotics, sub-optimal doses and sporadic treatments have contributed to the problem of resistance.

Tuberculosis

Tuberculosis is not a new disease, it dates back at least seven thousand years (Zimmerman 63). Tuberculosis is the most common serious infectious diseases in the world. About seven million new cases (Brown 1), and slightly more than two million deaths (Brown 1) occur each year. In the 1930's when Penicillin was discovered, many thought the disease would be eradicated, but it is now coming back with resistance to multiple drugs.

Mycobacterium Tuberculosis is the bacterium which causes tuberculosis usually infects the lungs which allows for TB to be transmitted through the air, especially in crowded or enclosed environments. The microbe breathes oxygen and has a very way cell wall that gives it particular staining properties called, acid fast, and makes it resistant to destruction by drying and be chemical agents. Consequently. TB germs that are coughed out into the air can remain alive and viable for weeks or months - much longer than most other bacteria.

About one and ten new cases of Tuberculosis is resistant to at least one of the common drugs used to treat the disease (Brown 1). Resistance to multiple drugs is a problem that renders the disease untreatable in most parts of the world. Drug-resistant strains of the bacterium almost always arise from strains that are initially drug susceptible, but survive inadequate causes of therapy. The new antibiotic resistant TB bacteria develop by mutation when patients discontinue antibiotic treatment early. Public health officials are trying to prevent this from occurring by ensuring that TB is correctly treated when first diagnosed and encouraging patients to finish their antibiotic treatment even if they are feeling better.

Decreasing the spread of antibiotic resistance requires that the selective pressures placed in using antibiotics also be decreased. Both physicians and consumers play a large role in the misuse of antibiotics and at the same time can play a large role in using antibiotics correctly and decreasing resistant strains. Physicians must change their prescribing habits and practices and patients must reduce the demands they place on physicians to prescribe antibiotics when they are not necessary.

In order to see if the doctors in the Tri-Valley area are contributing to the problem of antibiotic resistance, we developed a survey consisting of ten objective questions. The survey was handed out to doctors at the local hospital.

Experiment

Hypothesis: Doctors in the Tri-Valley community are contributing to the current problem of antibiotic resistant bacteria by the method in which they prescribe antibiotics and the frequency they prescribe antibiotics.

Prediction: If doctors in the Tri-Valley community do not vary the antibiotics they prescribe for bacterial infections, then they will contribute to the current problem of antibiotic resistant bacteria.

In order to put together an objective, unbiased survey, we first researched our topic through books, the internet, and talking with the Microbiology Department at the local hospital. We learned how bacteria and antibiotics worked and how resistance occurred. We also read about how doctors and patients are contributing to the problem of antibiotic resistance.

Background Questions

1. What type of doctor are you?

It is important in a survey to know who your population consists of and what type of patient the doctor deals with on a day to day basis. For example, the patients a Cardiologist would see would differ greatly than what a Pediatrician would see daily. Therefore, the antibiotics prescribed would be different and at different frequencies.

2. How long have you been practicing?

This question gave important insight as to when the doctor attended medical school. This is beneficial information to have because it is only in the last five years that antibiotic resistance has become a very hot topic in the medical field and we thought there might be a pattern found in antibiotics prescribed and the frequency they were prescribed at relating to how long the doctor has been practicing. The number of years in practice also reflects how much experience a doctor has had.

3. Since you have been practicing medicine, have you changed your criteria for prescribing antibiotics?

We included this in the survey simply to see if the doctor was staying current within the medical field and if they are willing to change the way they practice medicine as the times change.

Common Misuses

4. Would you prescribe an antibiotic for a viral infection?

Prescribing an antibiotic for a viral infection is one of the major contributions to the problem of resistance. If an antibiotic is prescribed for a virus, then the resistant bacteria is allowed to emerge or evolve and may not be effective when needed for a bacterial infection. It is better to let viruses run their course. We felt that it was important to our hypothesis to find out if doctors in the Tri-Valley area are contributing to resistance in this form.

5. If a patient demands that an antibiotic be prescribed, do you comply?

This is once again another misuse of antibiotics. By giving an antibiotic unnecessarily, the doctor is once again allowing for the bacteria to evolve and become resistant in the future. This question is important to our hypothesis and prediction also.

6. Please circle the following antibiotic you most often prescribe:

We added this question to the survey to see if the doctors within the population are prescribing the same antibiotic and whether they are varying what they prescribe. Variation in antibiotics is important so that one's immune system does not become resistant to a specific antibiotic. If every doctor were to prescribe the same antibiotic, then resistance would occur at a much higher frequency. This question was also important to the rejection r fail to reject of our hypothesis.

Scenarios

7. If your patient is allergic to penicillin and has a respiratory infection, what would be your alternate antibiotic?

We felt it was important to include free response scenarios in the survey to see how the doctors responded and if a variety of antibiotics were prescribes to the patient population. Once again, variation in prescribing antibiotics is very important to stop the problem of resistance.

8. If a patient returns with the same type of infection, which of the following is your common course of action?

We gave the doctor three different responses for them to chose from. The first response stated: prescribe the same antibiotic with an increased dosage. An answer to this choice would indicate that the doctor is contributing to the evolution of resistance. The second response was: Prescribe the same antibiotic with the previous dosage. This also indicates that the doctor is contributing to the problem of resistance, but not as severely as the first response. By continuing to prescribe the same antibiotic, the patient becomes immune to it and eventually not be able to fight it off. The third response was: Prescribe and alternate antibiotic. This is the idea response and shows that the doctor is correctly prescribing antibiotics. By varying antibiotics, the doctor ensures that all strains of bacteria are killed. The first two responses would support our hypothesis that doctors are contributing to the problem of resistance.

9. If a patient has an upper respiratory infection, what do you normally prescribe?

We were once again trying to see if the doctor was varying the antibiotics they prescribe.

Opinion

10. Do you perceive bacterial resistance to antibiotics as a problem in the future.

This was simply to get the doctors feeling on our research topic.

Results

Question: What type of doctor are you?

Responses: Gastrointestinal Specialist - 1

Emergency Room - 2

Neurosurgeon - 1

Pediatrician - 6

Internal Medicine - 4

Cardiologist - 1

Family Practice - 3

OBGYN - 1

Oral Surgeon - 1

Nephrologist - 2

Orthopedic Surgeon - 1

Oral Surgeon - 1

Urologist - 1

Pulmonologist - 1

Explanation: A wide variety of doctors was obtained at the local hospital. This was beneficial because it allowed us to see how different types of doctors practice medicine. This prevented having only one population of doctors that deal with all the same type of patients. For example, if only pediatricians were surveyed would only indicate what was occurring and being prescribed for children in the community.

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Question: How long have you been practicing?

Responses: 1-10 Years 11-20 Years 21-30 Years

12 13 5

Explanation: From the above results, we were able to obtain data on doctors that were practicing anywhere from three to thirty years. Two surveys obtained, one form a doctor practicing three years and one from a doctor practicing thirty years answered each question the same which was interesting because one would assume that the way in which medicine is practiced would be different for the newer doctors. That is the reason we chose to put this question in the survey.

Question: Since you began practicing medicine, have you changed your criteria used for prescribing antibiotics?

Responses: Yes No

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Explanation: Our data indicated that a majority of the doctors are trying to stay current with the increasing problem of resistance. There were still some doctors that are not changing their ways, but no pattern was found between the number of years in practice and whether or not they have changed their habits.

Question: Would you prescribe an antibiotic for a viral infection?

Responses: Yes No

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Explanation: We found that all but one doctor answered "No" indicating that doctors in the community are not intentionally contributing to the resistance problem and that the doctors are following guidelines for prescribing antibiotics.

Question: If a patient demands that an antibiotic be prescribed, do you comply?

Responses: Yes No

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Explanation: Although a majority of the data reflected that doctors are not following patient orders, five doctors wrote in "sometimes" which indicates that some doctors are giving into their patients and consequently adding to the problem of resistance. Those doctors that answered "yes" or "sometimes", support our hypothesis. Some doctors may feel it is necessary to prescribe antibiotics when their patients want them, but they need to educate their patients on the resistance factor and in some cases maybe the doctor needs to be further educated on the subject.

Question: Please circle the following type of Penicillin you most commonly prescribe

Responses: Penicillin G 1

Penicillin V 3

Ampicillin 6

Amoxicillin 24

Pivampicillin 0

Cloxacillin 0

Explanation: Amoxycillin was overwhelmingly prescribed over all the other types of Penicillins listed. This supports our hypothesis in that doctors are contributing to the problem by not varying the antibiotics they prescribe. Penicillin is one of the most commonly prescribed antibiotics and it is alarming that the type of Penicillin is not being varied.

Question: If your patient is allergic to penicillin and has a respiratory infection, what would be your alternate antibiotic?

Responses: Bioxcin 3

Erythromycin 20

Depends 3

Ceplialexis 1

Doxycyeline 1

Ciproploxocin 1

Zithromax 1

Keflex 1

Septra 2

Pediazole 1

Explanation: Erythromycin was the number one response antibiotic by the doctors. This was a free response question which gave doctors the option to write in many different types of antibiotics and a majority of them still wrote Erythromycin. Even if the doctor chose another antibiotic, they still wrote in Erythromycin. Our results reflect that doctors need to vary the antibiotics they are prescribing, which again, supports our hypothesis. Though there was some variation in antibiotics, there is still a high frequency of Erythromycin, and antibiotics should be further varied to avoid resistance.

Question: If a patient returns with the same type of infection, which of the following is your common course of action? (Please circle a letter)

Responses: a) Prescribe the same antibiotic with an increased dosage 0

b) Prescribe the same antibiotic with the same dosage 4

c) Prescribe an alternate antibiotic 26

Explanation: Not one of the doctors in the population chose response "a" which is positive for the medical community because that would most likely contribute to the resistance problem. By prescribing a higher dose, doctors would simply help the bacteria evolve to resist the stronger antibiotic. A majority of the doctors said they would prescribe an alternate antibiotic which is positive because it shows variation which is one of the leading ways to fight resistance.

Question: If a patient has an upper respiratory infection, what do you normally prescribe?

Responses: Varied. Many doctors wrote comments.

Explanation: We decided to throw this question out of our survey because it was highly subjective and open to interpretation. Some of the doctors did provide us with an antibiotic they would prescribe, but followed it with a comment or an explanation of why they would prescribe that particular antibiotic. Many of the doctors simply left it blank or asked their own questions such as: "Is it viral?", "What are the symptoms?", and "What kind of infection is it?"

Question: Do you perceive bacterial resistance to antibiotics as a problem in the future?

Responses: Yes Somewhat Not At All

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Explanation: This question illustrates that doctors are aware of the current problem of resistance and in order to be a part of the solution, they should continue to inform their patients on the importance of taking antibiotics correctly and they should be educated on prescribing antibiotics.

Conclusion

At this point in time, there are no real solutions, that will help to completely eradicate the problem of resistance. However, it is possible to slow their rate of evolution and weaken their resistance factors. To keep bacteria from evolving so quickly, antibiotics must be prescribed correctly by the medical community and used correctly by patients. Some patients fail to take antibiotics when they have an infection, and therefore, the infection does not get completely eradicated. Those few bacteria that are left have the highest resistance, so they multiply and kill the weaker strains. Consequently, this speeds up the process of bacterial evolution and the development of resistance. Also, as mentioned, antibiotics should never be given for viral infections. First off, they do nothing for viruses and second, they help to give rise to stronger bacteria within the patients. Overall, behavior by patients and the medical community must be altered to keep resistance under control.

Another way to fight resistance is to take certain antibiotics out of circulation for a period of time so that the bacteria no longer can build up a resistance to that specific antibiotic. The bacteria will evolve to a point where they are no longer resistant to this drug, and once it is put back in circulation, it will be effective for the time being.

There is currently a lot of medical research being done on the effects of acidity on bacteria. As a bacterial environment becomes more acidic, bacteria have a harder time of surviving. Perhaps, in the future, new drugs will be developed to raise the acidity of the area of infection in order to cure the patient. This way, no drugs would have to be used.

Another area of research being conducted is to find a way to keep bacteria form passing on their resistance traits to non-resistant bacteria. This would hypothetically be done by blocking the path of the information transfer so that bacteria would be unable to evolve, and could be treated with normal antibiotics. The problem that bacteria could evolve to fight this drug is still a possibility.

It is likely that no real solution will be found. Humans will continue to run a race to outwit bacteria, but so far bacteria is continuing to win the race against mankind.