Question: How are Bacteria good and bad for human health?

Freshman Year Conclusions:

Initial Thoughts:
It is estimated that within the human microbiome, there are 39 trillion microbial cells, including bacteria, more than the estimated 30 trillion human cells in a body. Though scientists have identified between 81-99% of the microbes in the body, their purpose and function are not all entirely known. Along with this problem, some bacteria can act good and bad. For example, *Staphylococcus aureus* is the most common microbe on human skin, and for most people, it will not harm them. But, when a person is infected with someone else's staph, it can cause skin infections and pneumonia. Because of this invariability, it cannot be pinpointed how bacteria, as a general term, are good and bad for health. And, many of the benefits of bacteria can lead to harmful results if not used correctly. However, general conclusions can be made for comparison between the benefits and issues that arise from the bacterial-human relationship.

Conclusions:
Beneficial

1. Symbiotic Relationship
Both the human body and bacteria have evolved together to help one another out. For example, *Bacteroides thetaiotetraiotamicron* lives in the human intestinal tract. It gets to live in a comfortable environment, and in exchange, it helps digest complex plant material that the human body can't do on its own. Both parties of the relationship continue to grow and live as a result of the other's assistance.

2. Product Creation
Because bacteria's DNA is easily accessible to scientists, it is easy to modify their genetics to produce a specific product. Then, these products can be harvested to mass produce materials that can help human health. For example, *Escherichia Coli* was modified to mass produce insulin for diabetics. Bacteria allow people to have access to life-saving treatments that weren't available beforehand.

3. Bioremediation
Specific bacteria can be used to bioremediate specific contaminents present in toxic wastes, such as oil and gasoline. They can decompose harmful substances in the environment, creating safer waters for the sea animals that humans consume and purer water to drink.

4. Infection Treatment
Antibiotics are used to treat people with bacterial infections. Bacteria naturally produce antibiotics to kill other bacteria that. threaten them. So, antibiotics can be harvested from these microbes to treat specific infections. 70-80% of all bacteria have come from the genus of bacteria *Streptomyces,* leading to many people being saved from deadly infections.

5. Energy Source

The health of the enviroment has deteriorated through the continuous use of fossil fuels. But, human society has developed a reliance on these fuels to live. Bacteria can be used to produce biogas and electricity without the use of these fossil fuels, allowing people to have their needs met without further ruining the environment. For example, *Enterococcus faecalis* is being studied for its usage of electron transfer to communicate, making it possible to use that energy to harvest electricity from them.

Harmful

1. Amensalism
Although generally, the bacteria in the human body are either helpful or harmless, they can change or move, resulting in deadly infections. For example, Clostridium difficle normally lives in the human intestines with no harmful or beneficial effects. But, sometimes it will begin producing toxins, leading to extreme inflammation of the intestines. These infections are extremely deadly to the person and hard to fight off since the body is use to the bacteria being present.

2. Antibiotic Resistance
As a benefit, bacteria produce antibiotics that humans can harvest to fight off other bacterial infections. The problem, though, is if a bacterium evolves to be resistant to the treatment, it can spread this evolution to other bacteria. The more antibiotics used, the more this spread will occur, making it even more difficult to fight off diseases in the future.

3. Resource Destruction
Not only will bacteria attack humans, but they can infect other living organisms, including plants and animals. These infections will hurt their health and development, leading to the limiting of resources for humans to consume. For example, Candidatus Liberibacter spp. causes Citrus Greening Disease, a pandemic spreading throughout the state of Florida. Many people there rely on these products to survive, and once their crops are infected, they lose their source of income. So not only do bacteria make the food dangerous to eat, it prevents people from living healthy lifestyles by ruining their production of crops.

4. Who knows?
One of the most dangerous aspects of bacteria is how fast they evolve. Parts of their DNA are located in circular loops called plasmids that are easily exchangeable between different bacterial cells. When a different plasmid is received, the bacteria can incorporate it into its DNA, thus giving it a new trait. So, no matter how fast humans work to combat bacteria, there will always be a new disease, new resistance, and a new strain arising from bacteria. Humans will always play a losing race, as they will be trying to catch up to the ever-evolving bacteria.

Senior Year Conclusions:

Beneficial

Point 1: Symbiosis

Bacteria play in many symbiotic relationships that are beneficial to humans. One such relationship is the microbiome within a human's gut. The gut microbiome is a collection of microorganisms that has co-evolved to live symbiotically with people (Thursby & Juge, 2017). They often feed off food ingested by humans, and in turn, their metabolic products are useful to the human body. One example of this symbiosis is the *Bacteroidetes* phyla (Jae & MacKenzie, 2019). *Bacteroidetes* make up 30% of our gut bacteria microbiota. They primarily function by breaking down carbohydrates into fatty acids that serve as energy for the human (Aleksandr Birg et al., 2019). It has been revealed recently that in obese individuals, they have a lower proportion of *Bacteroidetes* within their microbiota (Clarke et al., 2012). The population of *Bacteroidetes* is linked to our ability to use carbohydrates for energy, and the lack of population makes it difficult to use carbohydrates before they are stored in adipose tissue, leading to obesity development. *Bacteroidetes* are a classic example of how bacteria can be beneficial to human gut health.

Another symbiosis that bacteria have with humans is their regulation of harmful bacteria. The microbiome of the human body keeps a balance between each other based on the availability of nutrients and space (Maldonado-Contreras, 2021). This balance prevents the growth of one bacterial population into a harmful overgrowth. An example of this balance is regarding *Clostridium difficle. C. difficle* is a part of the normal intestinal flora and normally causes no harm to the human host (Wisconsin Department of Health Services, 2019). However, if *C. difficle* overgrows, it will cause pseudomembranous colitis and antibiotic-associated diarrhea that is often antibiotic resistant (Wisconsin Department of Health Services, 2019). To treat these *C. difficle* infections, one option is fecal microbiota transplantation (FMT). To perform an FMT, a collection of stool from a healthy donor is introduced into a patient's colon to reintroduce healthy bacteria. The healthy bacteria will then control and limit the *C. difficle* infection (Johns Hopkins Medicine, 2022). FMT shows that bacteria are helpful in preventing bacterial overgrowth and can even function as effective treatments.

Point 2: Production

Because bacteria are sustainable, easy to alter, and readily available, they are often used for different productions beneficial to people. One of the most impactful products made with bacteria is insulin. Initially, insulin for diabetic patients was isolated from bovine or porcine pancreas (Baeshen et al., 2014). However, the process of isolating insulin from these animals was expensive and prolonged. In the 1970s, scientists Stanley Cohen and Herbert Boyer invented DNA cloning, where recombinant DNA can be entered into a bacterial genome to change what proteins they produce. By using this technique, genes for human insulin were placed into *Escherichia coli*'s genome, and the bacteria began mass producing insulin (Baeshen et al., 2014). This insulin was isolated from the bacteria and made into a licensed drug, where it is the main source of insulin production to this day. Bacteria are incredibly useful in the mass production of medicine that is needed for people to remain alive and healthy.

Bacteria are also used to produce materials other than medicines. Many bacteria in the genus *Acetobacter* are used to produce vinegar (Acetobacter: An Overview | ScienceDirect Topics, n.d.). *Lactobacillus helveticus* makes the byproduct propionic acid that leads to the development of holes within Swiss cheese (Condon et al., 2017). Even *Staphylococcus* species, which are related to the infections of methicillin-resistant *Staphylococcus areus* (MRSA*),* are used in the production of main dairy and meat products (Podkowik et al., 2013). Bacteria are vital to produce everyday items we need, and they contribute to human health through providing our needed resources.

Point 3: Bioremediation

Similarly to the second point, since bacteria are easily reproducible and maintainable, they can be used to break down harmful components within the environment. Bioremediation can be used to undo the harm that humans have created within nature. The best bacterial species for bioremediation potential include *Bacillus subtilis, Bacillus cereus, and Bacillus thuringiensis*. Interestingly, *B. cereus* causes food poisoning in humans, yet it can be used to improve human health as well. The *Bacillus* genus can reduce the amounts of metals, including lead, mercury, arsenic, and nickel, within the environment (Wróbel et al., 2023). There are many other bacteria that can be useful in bioremediation, including *Pseudomonas sp.* and *Acinetobacter sp.,* which are used to remove harmful chemicals from marine environments (Dell' Anno et al., 2021). Bacteria are continually used to undo the harm that humans have created to the environment so that we can continue to live on this earth.

Point 4: Research

Bacteria have been a main source for the development of new research techniques used to understand different diseases or even how the world works. One major innovation based on bacteria is CRISPR. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats, meaning they have repetitive DNA sequences. These were first observed in *E. coli* with spacer DNA sequences in between each repeat that match bacteriophage sequences (Ishino et al., 2018). The bacteria with CRISPR transcribe the DNA elements into RNA when infected and then use a nuclease called Cas to cut up the viral DNA, thus killing the virus. In 2019, this unique mechanism was adjusted to where a scientist can guide the Cas to a specific DNA sequence to cut it, allowing them to insert new nucleotides (The Jackson Laboratory, 2021). The CRISPR/Cas system has been used to adjust the mutation that causes sickle cell disease and cure a patient of it (FDA, 2023). The discovery of CRISPR as a genetic altering mechanism has expanded the capabilities of genetic research. The unique mechanisms within bacteria are extremely useful in the field of research.

Harmful

<u>Point 1: Disease</u>

In 2019, around 13.6% of all global deaths were attributed to bacterial infections (GBD 2019 Antimicrobial Resistance Collaborators, 2022). More than half of these deaths were caused by five bacterial species: *S. aureus, E. coli, Streptococcus pneumoniae, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa* (Nuffield Department of Medicine, 2022). Sadly, most of these deaths were preventable with antibiotics, but the lack of availability for these medicines has kept bacterial infections as a leading cause of death.

One of the five bacterial species listed above, *P. aeruginosa,* only infects as an opportunistic pathogen. An opportunistic pathogen is one that can only infect a person when their immune system is compromised. This compromise could come from another infection weakening the human, the lack of protection from the microbiome, or immunosuppressant medications (NIH, 2021). These infections are particularly dangerous because they do not happen as often, so the treatment of these infections is not well understood.

Recently, the gut microbiota has been linked to mental health as well, and an imbalance can lead to the development of mental disorders, including anxiety and depression. It has been shown that *Firmicutes* and *Bacteroidetes* species effect mental health through the gut-brain axis based on the by-products they produce. These bacteria impact neuroendocrine function, production of neuroactive compounds, regulation of neurotransmitters, and controlling neuro-immune signaling (Xiong et al., 2023). The impact of bacteria upon our bodies is still not fully known and could have more implications on our overall health than what has been discovered so far.

Some bacterial infections have also been linked to the development of cancer later in a patient's life. Stomach cancer is one of the more common types of cancer worldwide. *Helicobacter pylori* causes stomach ulcers within the stomach, and repeated damage to the inner layer makes it prone to cancer (ACS, n.d.). *Chlamydia trachomatis* has not been shown to cause cancer, but women with infection are shown to be at greater risk for cervical cancer (ACS, n.d.). It was also recently found that tumors have their own microbial communities that produce secondary metabolites that encourage tumor development and progression (*How Bacteria Give Cancer a Helping Hand*, 2022). Bacterial infections can encourage other deadly conditions that are extremely harmful to human life.

<u>Point 2: Evolution</u>

For every antibiotic created, there has been bacteria that developed antibiotic resistance against it (World Health Organization, 2023). Bacteria develop resistance by developing small mutations that make them stronger against antibiotics. As they are exposed to more antibiotics, the stronger bacteria are selected for survival, so they are the only bacteria that proliferate. By doctors overprescribing antibiotics and patients not completing their dosage, these bacteria are exposed more often and given the opportunity to develop resistance.

Bacteria also have the capability of sharing their antibiotic resistance. Bacteria have small, circular DNA called plasmids that encode for secondary functions, including antibiotic resistance mechanisms. Bacteria will exchange their plasmids through a process called conjugation to perform horizontal gene transfer (Virolle et al., 2020). So if a certain bacteria has never been exposed to an antibiotic, it could achieve resistance by receiving a resistant plasmid from another bacteria. This evolutionary advantage of bacteria has led to the rapid development of antibiotic resistance.

Point 3: Resource Destruction

Bacterial diseases have a major impact on the agricultural resources needed to maintain human life. In many food animals, a bacterial disease can easily wipe out a population and destroy an entire harvest. One example is Columnaris disease, caused by *Flavobacterium columnare*, in fish. It causes loss of scales, necrotic lesions on the gills, and eventual death (Declercq et al., 2013). Columnaris disease can kill a fish in 24 hours, and it can live in the water without a host for 32 days (Lafrentz et al., n.d.). The best prevention of further outbreak in a catfish farm is to kill all of the fish in a holding tank, as the infection rate is incredibly high.

Similarly, there are many bacterial diseases in plants that can destroy an entire crop quickly and are difficult to treat. Bacterial blight is caused by the *Pseudomonas syringae* that naturally live in the soil. Infection occurs when the bacterium enters wounds of the plant and causes death to the leaves (*Bacterial Blight*, n.d.). Bacteria blight infects many plants, including barley, wheat, soybeans, and oats (Province of Manitoba, n.d.). Bacteria not only affect human health directly, but they also hurt the supplies needed to maintain the human population.

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