Antibiotic Resistance: WHO cares?

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Imagine going to the doctor for a bacterial infection. Maybe strep throat or a UTI. The doctor scribbles down a common antibiotic and sends you on your way to the pharmacy within 10 minutes. You get your antibiotics and feel better almost immediately. Life is finally good again.

But what happens if the antibiotic the doctor prescribed isn't for the bacteria that is causing discomfort? Then, you basically messed up the microbiomes in your gut and possibly caused some other bacteria to grow stronger and resistance to the antibiotics you took. Yikes! Many people disregard how problematic this simple doctor-patient interaction can be. I mean, why would you? Antibiotic resistance isn't something the average person thinks about after they finish their pill bottle. However, over 40 million antibiotics are prescribed each year unnecessarily (CDC).

The World Health Organization (WHO), declared the evolution of antimicrobial resistance to be one of the top threats for humans. Just in the United States, 23 thousand deaths are a result of evolution of antibiotic resistance in 2013. During this year, there was an additional 2 million hospitalizations and 50 billion dollars in medical costs. These statistics are quickly approaching car accidents and gun violence (Antonovics 2016).

People think this resistance is something that shouldn't be worrisome for many more years. However, an epidemiological study concluded that the evolution of just one pathogen to one antibiotic caused 18,650 deaths in one year (Baym 2016). How is this something not conversed more in society?! To the general public, many people do not care about antibiotic resistance. But in the scientific community, there is a fundamental disconnect between the conceptual foundation of evolutionary biology and the conceptual foundation of medicine. Today in medicine, the utmost priority is given to individual patients whereas the theoretical foundation of evolutionary biology is based on the population. This can be harmful in the long run to the health of individuals. So why aren't we trying to solve this inevitable crisis? When it comes to funding research, there isn't a lack of money or shortage of expertise. Don't fret just yet! We will discuss why there's a disconnect in science and public knowledge and what can be done to overcome this crisis! There are many alternative approaches to this public health crisis which includes probiotics, antibodies, and vaccines (Aslam et al. 2018).

Before we dive in, let's do a brief history about antibiotics. The turning point of antibiotics started with the discovery of penicillin in 1928 by Alexander Fleming. During World War II, penicillin was frequently used for bacterial infections where it saved many lives. However, by the 1950s, penicillin resistance became a clinical issue. Scientists then discovered various beta-lactam antibiotics to combat the penicillin resistance. Unfortunately by 1968, the first case of methicillin-resistance *Staphylococcus aureus* (MRSA) was identified in the United States. Since then, resistance for most antibiotics have developed all over the world. In 1972, vancomycin was discovered to treat methicillin resistance and researchers thought that this would be the most difficult antibiotic to become resistant to. To

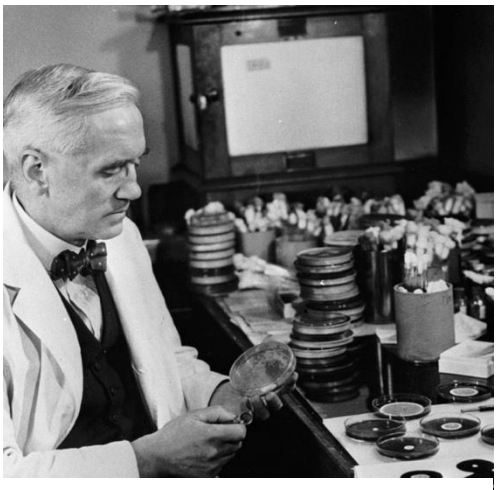

Figure 1: Alexander Fleming's discovery of penicillin

their dismay, cases of vancomycin resistance was reported in the 1980s. Since the beginning, pharmaceutical companies have played an integral role to developing and distributing antibiotics. But as more antibiotic resistance developed in the country, fewer drugs have been developed. Bacterial infections have now become a threat again ever since 2015 (Ventola 2016).

So why the disconnect between evolutionary biology and medicine? This disconnect first starts at the regulatory level. In the United States, the FDA (Food and Drug Administration) approves all drugs. When manufacturing companies come forward with their proposal of an antibiotic, there is no regulatory requirement for an evolutionary assessment on the drug, such as the assessment of risks and rates of resistance evolution. This evidence can be easily provided from lab experiments and clinical trials. It may seem like a long process because of the word "evolution", but that is not the case for pathogenic resistance. A simple solution would be to require a "Evolutionary Assessment Statement", or an EAS, prior to a medication release to the general public. This documentation would include protocols that have been used to measure whether and at what rate resistances are likely to evolve and provide the protocol to detect them. The document wouldn't necessarily do anything for the present day, but in the long run, it can increase options, promote research and achieve compromises for the drug manufacturing industry. Many companies are worried that this may slow the development of antibiotics, but predicting the "evolutionary shelf-life" can provide better economic forecasts, provide realistic pricing and prolong antibiotic use. The whole point of this document is to raise sensitivity and increase research to achieve the proper regulatory goals. As of right now, the only regulatory requirement is biomedical research that focuses on the mechanism of antibiotic resistance but not the dynamic of its evolution. It seems silly that these pharmaceutical companies are ignoring the evolutionary response in antimicrobial drugs, which is the main reason for ineffective antibiotics. Pharmaceutical companies should know they are on thin ice when it comes to class action suits as the general public becomes more aware of antibiotic resistance. Patients can die because on an ineffective antibiotic that does not have adequate warnings for ineffectiveness (Antonovics 2016).

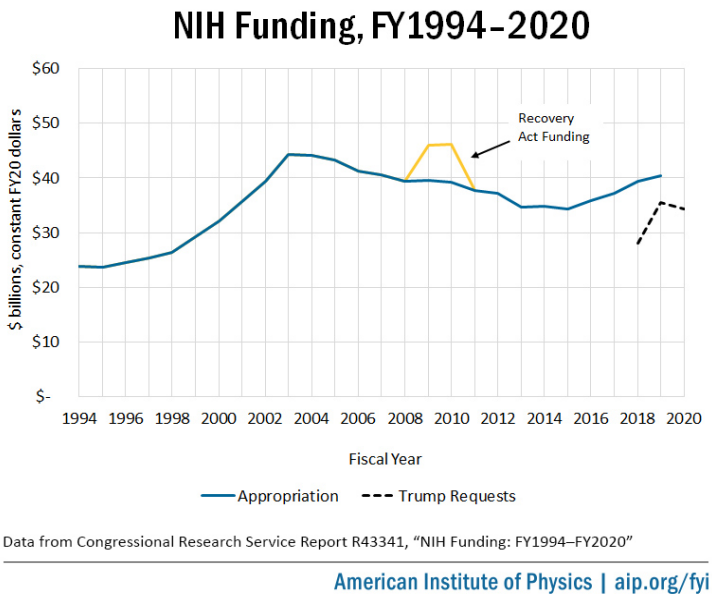

Figure 2: Funding for NIH in the past 25 years

There also seems to be a disconnect at the funding and research level for the evolution of antibiotic resistance in the scientific community. The NIH is the main investor for research in the United States. They fund a whooping 31.1 billion dollars per year for medical research. In Figure 2, there is an increase in funding for research in the past couple of years. However, antibiotic resistance research is only mentioned 1.5% of the approved abstracts, and when searched with the term evolution, the number drops to less than 0.4%. There is a serious discrepancy between research for the evolution of antibiotic resistance and the threat it can

cause to public health. This issue seems to come back to how researcher and pharmaceutical companies are more interested in short-term goals and not long-term problems.

There is also a level of disconnect with evolutionary biologists: they do not seem interested or excited about the topic of antibiotic resistance. Even though this mechanism seems very fascinating, evolutionary biologists want to pursue other areas of research and leave this issue up to the medical community, but that is very much not the case. To clearly understand the evolutionary processes in antibiotics, there has to be a sustained research effort, not just casual conclusions. One of the drawbacks to these studies is that population level processes are not easily replicable, especially in the lab. Many observation studies and experiments have to undergo predictive modeling to obtain accurate results about population level processes. Many evolutionary biologists are not attracted to these research conditions and practices, but clear arguments for sustained evolutionary investigation of antibiotic resistance should be made from the biomedical community to prevent this public health crisis from going too far.

Obviously, the scientific community and hopefully, the world, want long-term solutions to this problem. It isn't something that can happen overnight, but with the effort of the general public and the scientific community, it can be done with slow, short steps. One simple fix that can start at the prescriber level is lowering dosage of antibiotics to possibly slow the evolution and spread of antibiotic resistant strains. There needs to be a lot more testing done for this, but these tests need to be done in real clinical and community settings which hasn't been done yet (Antonovics 2016).

Another short-term solution is educating the general public about antibiotic resistance and its threat to public health. In the United States, there's a particular heavy focus on individual medicine instead of general public health. Maybe after the COVID-19 pandemic people will be more mindful of public health, but I know after a couple of years, people will slip back into their old ways. Personally, I wish I had some knowledge on this topic a couple a months ago! Recently, I went to the doctor for the second time because my sinus headaches were getting so bad and I didn't know what to do. Sinus infections are usually caused by viruses, but my doctor prescribed me a very strong antibiotic for "precaution". This antibiotic had many side effects, so many that when I picked it up from the pharmacy, the pharmacist sat me down and reminded me not to go in direct sunlight, not to lie down 2 hours after I take this medication, and not to drink milk with the medication. I remember feeling panicked after I left, but I finished the 10 day course because of my doctor's orders even though I didn't feel better from it. Months later, I went to an allergist who informed me that I have a couple of environmental allergies which is the reason for my sinus headaches. After a couple of Zyrtecs, I finally felt relief, but now some of the bacteria in my body has probably built up resistance to the antibiotic I was taking months prior for no reason. After experiencing this, I wish I knew what I know now; otherwise, I wouldn't have taken that strong antibiotic for 10 days knowing that it may not work.

For long-term solutions to this issue, many scientists are still looking answers. Since this field isn't something explored or researched as much as it should be, there must be a global effort to defeat this public health crisis where it starts by looking at the evolution of antibiotics. There are a few alternatives to antibiotics, such as probiotics and lytic bacteriophages, but these practices aren't used nearly as much as antibiotics. Antibiotic resistance could be contained

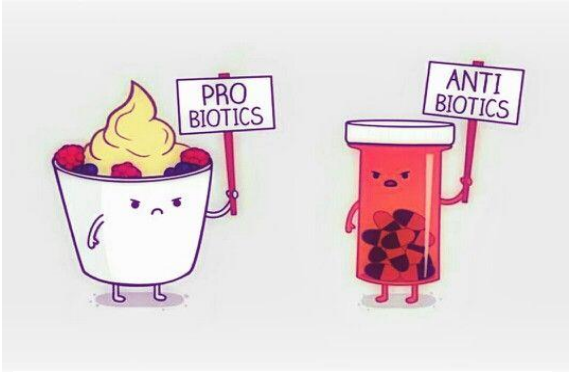

Figure 3: The battle between probiotics and antibiotics

with the rational use of antibiotics, infection control, immunization, awareness and education, but these changes must happen on a global scale (Aslam 2016). It all starts with us. It's important to inform others of this crisis so everyone takes their health into their own hands. What will you be thinking about the next time you are prescribed an antibiotic?

References

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Images

Figure 1:
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Figure 2:
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Figure 3:
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