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The Dangerous Rise of Antibiotic Resistance in Contemporary Spain

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The Misuse and Overuse of Antibiotics: The Cause of Antibiotic Resistant Bacteria

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Abstract

Antibiotic resistance is a global health threat that has jeopardized the worth of antibiotics, which have previously transformed medicine in the past decades by saving millions of lives. With thousands of people now dying yearly as a result of bacteria being resistant to antibiotics, we are in great need of new antibiotics. However, it is our careless overuse and misuse of the ones we already have that has resulted in this global health crisis. Thus, multidisciplinary approaches need to be made across the globe, in health care settings, and in agriculture to diminish our abuse of antibiotics so that when we *do* discover new ones, we are not presented with this problem once more.

Bacteria in the Human Body

Of all microorganisms and living creatures on earth, bacteria are the most abundant, inhabiting soils, oceans, and even human bodies. In ecosystems, these organisms play key roles in cycling essential nutrients such as carbon, hydrogen, oxygen, and nitrogen. In human bodies, they help metabolize food, provide essential nutrients, periodically fight off invading pathogens, and much more. For example, some bacteria in the intestinal wall play a vital role in fighting infection by producing bacteriocins, which are small proteins that prevent harmful microorganisms from growing (Gorbach 1996). Other bacteria in the human gastrointestinal tract are responsible for synthesizing vitamin K_2, an essential component of an enzyme necessary for blood clotting (Berkner 2000). Even more interesting, some studies have proven that changing the bacteria in the gastrointestinal tract has even been associated with cancer (Motevaseli et al. 2017). Thus, as you can see, not all bacteria are harmful and human bodies rely heavily on many

of them for survival. Unfortunately, however, some bacteria *are* toxic, these are known as pathogenic bacteria.

Pathogenic bacteria can give rise to an array of infections all over the body, ranging from skin and hair to blood and internal organs. These organisms typically cause infection through the release of harmful toxins and can spread it to others through direct contact, contaminated food and water, bodily fluids, and/or airborne transmission (Drexler 2010). What makes them all the more dangerous is their ability to rapidly reproduce and acquire new genetic material, such as genes that code for antibiotic resistance, from surrounding bacteria (Holmes 1996). Through these methods, bacteria are able to incorporate foreign DNA into their genome, creating recombinant DNA and allowing them to express those foreign genes permanently (Holmes 1996). As a result, bacteria are able to rapidly adapt to their environments and survive even in the presence of toxins such as antibiotics.

Antibiotics

Antibiotics are a type of drugs that fight *bacterial* infections through many different mechanisms (Table 1). Since bacteria (which are unicellular) and human cells share similarities in their structure, antibiotics are designed to be specific enough that human cells don't get harmed in the process of eradicating infections. For example, penicillins work by inhibiting the cross linking of bacterial cell walls, a structure that human cells lack, in order to cause disintegration (Strominger et al. 1971). In contrast, tetracyclines work by preventing the binding of an important RNA molecule (known as aminoacyl tRNA) to ribosomes, which are the organelles that synthesize proteins (Chopra and Roberts 2001). Even though protein synthesis is

also carried out by human cells, humans use different ribosomes than bacteria. While bacteria use ribosomes composed of 50s large subunits and 30s small subunits, humans use ribosomes composed of 60S large subunits and 40s small subunits (Berg et al. 2002). Thus, allowing tetracyclines to target *bacterial* protein synthesis specifically and not human protein synthesis.

Even though different classes of antibiotics target bacteria through distinct and specific approaches (Table 1), they all generally act as bacteriostatic agents to restrict cell growth/reproduction or as bactericidal agents to straightforwardly cause cell death (Ocampo et al. 2014). The range of side effects that patients experience as a result of these drugs perhaps is due to the drug mechanism of action. For example, accidentally targeting a human ribosome instead of a bacterial ribosome by tetracyclines might lead to unwanted symptoms. Other factors include the concentration of antibiotics used and the percent of healthy, pathogen-fighting bacteria that are accidentally killed in the process of fighting an infection. Consequently, the more that bacteria are exposed to antibiotics (and survive), the less sensitive they become to them, requiring higher concentrations of antibiotics to be prescribed (Zaman et al. 2017). This in turn results in unwanted effects, one of the biggest ones being antibiotic resistance.

Table 1. Common Antibiotics and Their Modes of Action

Class of Antibiotic	Examples	Mechanism of Action
β-Lactams	Penicillins (penicillin G, methicillin, amoxicillin), Cephalosporins (cephalothin, cephalexin) Carbapenems (Imipenem, meropenem)	Enter the bacterial cell through porins and permanently acylate penicillin binding proteins (PBPs) which catalyze the formation of peptidoglycan in cell wall. Additionally, can bind to the active site of transpeptidase to inhibit the cross-linking of peptidoglycan, resulting in cell lysis.

Tetracyclines	Tetracycline, doxycycline, clomocycline	Inhibit protein synthesis by preventing the attachment of aminoacyl-tRNA to ribosomal acceptor (A) site.
Quinolones	Ciprofloxacin, temafloxacin	Harm DNA by increasing the concentration of enzyme-DNA cleavage complexes, such as topoisomerase IV and gyrase.
MLS Family	Macrolides (erythromycin, azithromycin) Lincosamides (lincomycin, clindamycin) Streptogramin (virginiamycin, pristinamycin)	Inhibit protein synthesis by binding to the large ribosomal subunit, near the peptidyl transferase center. Some inhibit the peptidyl transferase reaction, others block the exit of peptidyl tRNAs which results in premature dissociation.
Sulfonamides	Sulphanilamide, sulfathalidine	Act as competitive antagonists to *para*-aminobenzoic acid, a precursor to folic acid) and necessary for nucleic acid synthesis.
Glycopeptides	Vancomycin, telavancin	Form stable complexes, through hydrogen bonding, with clefts in bacterial cell walls which inhibit the formation of the glycan chain backbone.
Aminoglycosides	Streptomycin, kanamycin	Interfere with protein synthesis by either binding to the small 30s subunit or by incorporating incorrect amino acids into the growing chain.

Causes of Antibiotic Resistance on a Cellular Level

Due to natural selection and evolution, all living organisms develop mechanisms in order

to survive as the conditions of their environment change and become challenging. Just as humans

have developed antibiotics to fight bacterial infections, bacteria have developed mechanisms to

fight off those same toxins trying to kill them. The two major ways in which bacteria can

develop antibiotic resistance are intrinsically or with acquirance (Hawkey 1998). With intrinsic

resistance, the event is random and naturally occurring in an effort to adapt to environmental stressors and pressures. These mutations are often spontaneous and their origins tend to be obscure since they result from years of evolution (Hawkey 1998). With acquired resistance, the bacteria develop resistance after being sensitized to antibiotics or after obtaining new DNA. New DNA can be obtained through a process called *horizontal gene transfer* (HGT) in which genetic material is swapped between neighboring bacteria through transformation, transduction, or conjugation (Clark and Pazdernik 2013). With transformation, bacteria take up extracellular DNA from their surroundings. With transduction, bacteria are infected with bacteriophages (viruses) that carry donor DNA. With conjugation, donor bacteria transfer their DNA to recipient bacteria through mating. With either of these three methods, HGT allows bacteria to transfer DNA across all different types of bacteria, even with ones that are not of the same species. This is one of the factors that makes the spread of antibiotic resistance occur rapidly and easily.

The newly obtained DNA from HGT can code for one or more of **four** main mechanisms that bacteria use to avoid the effects of antibiotics. The **first** one consists of completely destroying the antibiotic molecule or modifying it through chemical alterations to render it inactive. For example, to modify aminoglycoside antibiotics, bacteria have developed an enzyme called aminoglycoside modifying enzyme (AME) that changes different chemical groups on that specific antibiotic (Munita and Arias 2016). To combat β-lactam antibiotics, bacteria have developed another enzyme called β-lactamase that destroys important chemical bonds in that antibiotic, ultimately diminishing its function (Munita and Arias 2016). The overarching goal of this mechanism is to alter the antibiotic but leave the bacteria unchanged. This is contrary to the **second mechanism**, in which bacteria *do* have to change something about themselves to fight

the antibiotics. This can be achieved by decreasing the antibiotic permeability into the cell and/or by incorporating efflux pumps on the cell walls of bacteria. To decrease their uptake of antibiotic molecules, bacteria can reduce their expression of specific porins, which are pores that molecules can use to diffuse through the cell membrane. This is what happens with the porin OprD gene in *P. aeruginosa*. Mutations in this gene allow *P. aeruginosa* to resist the up-take of carbapenem antibiotics (Munita and Arias 2016). Similarly, other mutations in the same OprD gene can also result in the incorporation of efflux pumps to remove carbapenems that do make it inside the cell (Munita and Arias 2016). In either case, the bacteria have to change something on themselves, instead of the antibiotic, to protect itself. This is similar to the **third** mechanism of antibiotic resistance, in which the bacteria alter the specific antibiotic target sites on themselves by protecting it or modifying it to ultimately cause a decrease in affinity. For example, chemical groups can be added to the 50S ribosomal subunits of the bacteria to inhibit the binding of macrolide antibiotics, thereby preventing them from disrupting protein synthesis (Munita and Arias 2016). If antibiotica like macrolides still manage to bind to the 50S ribosomal subunit or another enzyme, then bacteria can resort to a **fourth** mechanism where they can create an entirely new enzyme that does the same function but looks different enough that it can't be recognized by the antibiotic (Egorov et al. 2018).

Through these mechanisms, and perhaps many more that we're not yet aware of, bacteria have managed to survive. They've even managed to out-smart us by developing resistance at much faster rates than we are developing new antibiotics. In fact, the golden era of antibiotics, in which novel discoveries of these drugs took place, was between the 1950's and 1970's (Rustam 2010). Since then, we've only had variations *of* or modifications *to* those drugs, hence why

52.9% of the classes of antibiotics in *Table 1* all target protein synthesis and another 28.5% all target bacterial cell walls. Despite our remarkable advances in medicine, we simply have not had any ground-breaking discoveries, which wouldn't be an issue if the bacteria were also not having "ground-breaking discoveries" through these mechanisms. But what is causing bacteria to develop these mechanisms in the first place? What are we, as humans, doing to push them to develop these methods? The simple answer is: we're misusing and overusing antibiotics carelessly.

Causes of Antibiotic Resistance at a Social Level

The antibiotics discovered in the "golden era" perhaps could have lasted a longer time period, without the threat of resistant bacteria that we see today, if we weren't abusing them. Health care professionals are overprescribing antibiotics excessively, patients are misusing them, agriculture is overusing them, and health care facilities are simply lacking effective infection control and sanitation policies. All of these careless practices lead to bacteria developing resistance.

When antibiotics are prescribed or used by patients when they do not have a bacterial infection, the beneficial bacteria are attacked instead. This results in them either dying, which can cause an array of problems depending on what they're responsible for, *or* in promoting antibiotic resistance properties that they can share with harmful bacteria who were not exposed to those antibiotics. This "sharing" occurs through the HGT mechanisms mentioned in the previous section. This sharing also occurs in agriculture due to the increasing use of antibiotics in livestock. Farmers are constantly using antibiotics to promote growth and prevent disease in

otherwise healthy animals that don't need it. This overexposure to antibiotics, again, results in resistant bacteria that can spread to humans either by direct contact/consumption or through contaminated run-off water and manure (Martin et al. 2015). Harmful bacteria can also develop these resistant properties when patients don't finish their full course of antibiotics. This is because when a patient doesn't finish their full course, not all pathogenic bacteria are killed. These leftover bacteria have now been exposed to a chemical that didn't kill them but triggered them to develop a defense mechanism in case it comes back. In all of these cases, whether prescribed when not needed, used when not necessary, or used improperly, bacteria are exposed to new chemicals that they know can kill them. As most living organisms, of course they're going to want to protect themselves. That's exactly what we're trying to accomplish by using these antibiotics. The problem is, we are *too quick* to resort to them.

It can't be emphasized enough that health care professionals need to be more careful when prescribing antibiotics. They are sometimes quick to diagnose illnesses, often leading to misdiagnosis and therefore wrongful treatments. This is especially a problem with sore throats, which often get diagnosed with strep throat when in reality about 90% of sore throats are actually a result of viruses (Harvard 2017). A case study reported by Dr. Lisa Sanders in the Diagnosis sector of the *New York Times Magazine* shows just how true this is. According to her article titled "The Strep Throat That Wasn't," a little boy in St. Louis woke up one day with a sore throat and fever. He immediately saw his family doctor and was diagnosed with strep throat and prescribed azithromycin for five days. Upon the worsening of his condition a few days later, emergency department physicians prescribed him two more antibiotics after mistaking his illness for pneumonia. It turns out that the little boy had an infection caused by *fusobacterium*

necrophorum, an infection that almost killed him had Dr. Garrett not caught it in time (Sanders 2008). What is important from this case is that that specific strain of bacteria could have been detected from the very beginning had more laboratory tests been done prior to adhering to what seemed like other common infections. Instead, the boy's health care professionals jumped to diagnoses that were the most convenient. Patients also have the habit of doing this by assuming that antibiotics cure all infections, when in reality they can only occur bacterial infections. This pushes them to either use someone else's leftover antibiotic prescriptions or coerce physicians to prescribe them. As you can see from Dr. Sander's case study, some bacteria even require specific antibiotics, meaning that if they did have a bacterial infection, specific strains need to be identified before prescribing treatment.

Many individuals are under the impression that our lack of antibiotic discoveries/development since the golden era is the cause of our antibiotic resistance problem today. However, as you can see, it's our careless use of the ones we have already discovered that has put us in this predicament today. Not to mention, if we had better control of the spread of infections and better sanitation in hospitals, especially in infection-prone rooms like intensive care units, then there would be no need for this drastic use of antibiotics in the first place. We have become way too reliant on them, to the point where we're using them when they're not needed. If we were to have novel discoveries of new antibiotics *today*, but still continued to abuse them the way that we currently are, we'll eventually be presented with the same problem once again. It's time for us to change our habits.

Antibiotic Resistance: Spain Case Study

To better explore how the misuse and overuse of antibiotics affect the rates of antibiotic resistance that we see today, take into consideration Spain. Spain has a gross domestic product (GDP) of $34,526, a human development index (HDI) of 0.87, a long life expectancy, a low infant mortality rate, and quality health care and higher education, all of which render it a developed country (Investopedia 2019). To put it into perspective, the United States has an HDI of 0.92 and Sierra Leone of 0.28. Though some people might be inclined to believe that developed countries have good health outcomes, Spain proves this to be otherwise true as a result of its dangerously high levels of antibiotic resistant strains of bacteria. In 2016, the European Centre for Disease Prevention and Control (ECDC) visited Spain to discuss the country's antimicrobial resistance. They concluded that Spain posed a major public health threat to the country as a result of the levels of threatening bacteria such as meticillin-resistant Staphylococcus aureus (MRSA), extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and Acinetobacter baumannii, all of which were higher than the European Union average (ECDC 2018). Though the level of carbapenemaseproducing Enterobacteriaceae (CPE) were not as high as those three, there was evidence pointing to a rapid increase of CPE over the previous five years (ECDC 2018). The ECDC therefore suspected that this strain could be making its way up to urgent surveillance, which is troubling because CPE's are exceptionally dangerous due to their resistance to almost *all* classes of antibiotics. The ECDC also found that Spain not only had high levels of antibiotic resistant bacterial strains, but also high rates of antimicrobial consumption, once again higher than the European Union average (ECDC 2018).

Other studies outside of the ECDC have been successful in providing evidence to prove why that is the case.

In 2014, a study was conducted in which a woman went to 220 pharmacies in Spain displaying fictitious symptoms of strep throat, urinary tract infection and acute bronchitis (varying per pharmacy) and found that 54.1% of the pharmacies sold her antibiotics without a medical prescription (Guinovart et al. 2015). The rates of prescription found by Guinovart et al. (2015) were much higher than those found in a previous study by Llor and Cots (2009) five years earlier, proving that the misuse of antibiotics in Spain has been increasing over the years. When using the *Center for Disease Dynamics, Economics, & Policy* (CDDEP)'s chart to compare the rates of antibiotic use in Spain to other European countries in 2015, there's further evidence showing that Spain has much higher rates of consumption than neighboring countries (Fig. 2) (CDDEP 2019). The abuse even extends to agriculture, with Spain having one of the highest rates of antibiotic use in animals (Fig. 3) (Vergely 2019).
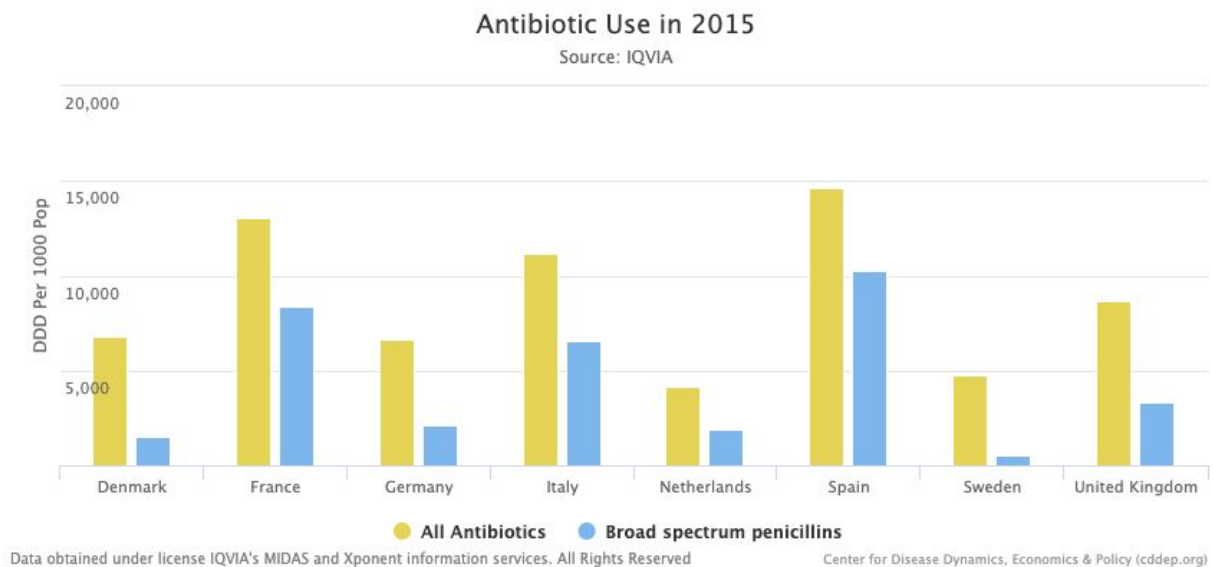
Figure 2. Rates of antibiotic use in Spain in 2015, retrieved from the *Center for Disease Dynamics, Economics, & Policy* (2019). Graph shows defined daily doses (DDD) per 1,000 individuals of all antibiotics and broad spectrum penicillins amongst different countries in Europe.
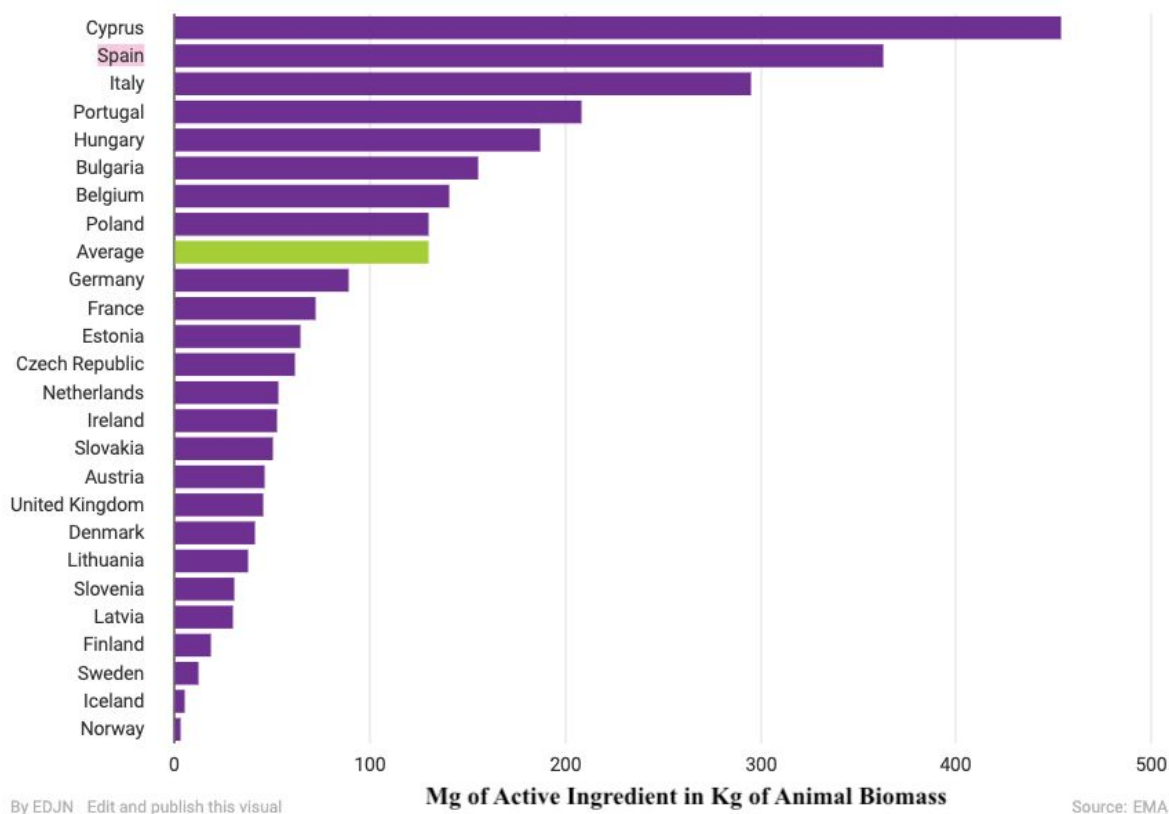
Figure 3. Veterinary use of antibiotics European countries between 2011 and 2016, retrieved from the European Data Journalism Network (2019).

In addition to the overconsumption of antibiotics, Spain also lacks a consistent implementation of policies and procedures for infection control. In that same visit in 2016, the ECDC "saw evidence that infection prevention and control (hand hygiene, contact precautions, isolation, environmental cleaning) and environmental cleaning measures [varied] significantly among hospitals and units" (ECDC 2018). In the late 1980's, Spain suffered from its first hospital outbreak by MRSA and while some hospitals implemented control programs, there was still an increase from 1.5% of MRSA in 1986 to 17.9% in 1996 (Rodriguez-Baño and Pascual 2001). In 2006, that number increased to 29.2% (Vindel et al. 2009). It was also discovered that

there was a higher prevalence of MRSA in smaller hospitals, potentially reflecting "a higher level of control in larger hospitals" (Rodiriguez-Baño and Pascual 2001). Given that Spain is comprised of an array of different regions, some small and rural, others large and urban, there needs to be better policies and implementation of those policies in order to suppress the growth and transmission of these strains.

As you can see, there is a positive correlation between the misuse and overuse of antibiotics and the rates of antibiotic resistance. Spain has levels of MRSA, ESBL-producing Enterobacteriaceae, Acinetobacter baumannii, and soon CPE too, that are higher than the average of the European Union. It also has higher rates of antibiotic use than the rest of the European Union, making that no coincidence. These high rates of antibiotic use are a result of both the overprescription of antibiotics when they're not needed (as demonstrated by Guinovart et al. [2015]) *and* the overprescription of antibiotics in hospital outbreaks when they are needed, likely due to a lack of infection control (as demonstrated by ECDC [2018]). Spain has been careless in its use of antibiotics and as a result, is now suffering a major public health threat with approximately 2,500 deaths a year and 150 million euros in extra hospital costs (Belmonte 2016).

Spain was simply used in this context to provide evidence of how specific social factors and practices influence the biology of our bodies and our environment. However, these scary truths are not only specific to Spain, they pertain to everyone. In fact, a study done by the CDDEP, Princeton University and the Princeton Environmental Institute (PEI), ETH Zurich and the University of Antwerp, found that the global antibiotic consumption rate has increased by 65% from 2000 to 2015 (Princeton University 2018). Some of the strains discussed before, such as MRSA, are already present in other countries and quickly growing and spreading across the

globe. Spain is not the only country abusing antibiotics with high levels of overconsumption and/or poor sanitation control. These are practices that are tangible across all continents and the reason why in the U.S. *alone*, each year approximately 2.8 million people get infected with an antibiotic resistant strain of bacteria and as a result at least 35,000 die (CDC 2019).

Preventive Measures

In order for us to successfully combat antibiotic resistance, we need to start working together. We are in great need of implementing new policies and innovative strategies, in addition to better educating patients, health care professionals, and agriculturers on the use of antibiotics. The following plan of action is by no means an exhaustive list of what can be done but rather mere suggestions on what shows great promise.

 I. International Measures

It's difficult for organizations such as the World Health Organization (WHO), the Center for Disease Control and Prevention (CDC), the ECDC, and the CDDEP to monitor and analyze all the different levels of antibiotic resistance globally since every country collects data differently. Different regions have distinct thresholds for what they consider alarming or safe. Some regions don't even have the means or resources to collect and report all of their data. There may even be patients who are falling in between the cracks. Similar to the study done by Guinovart et al., some patients could be obtaining antibiotics from pharmacies without prescriptions and never even make it to the hospital and thereby onto these reports as data points.

That is why there's a great push for us to work together, globally, with a surveillance network such as the WHO's Global Antimicrobial Resistance Surveillance System (GLASS).

GLASS shows a great promise to strengthen the evidence base on antimicrobial resistance (resistance to antibiotics, antifungals, antivirals, etc.) by promoting a standardized approach for data collection, analysis and sharing of antimicrobial resistance data between different countries (WHO 2019). In addition to laboratory data, this system contains epidemiological, clinical, and population-level data. For example, upon getting lab results, GLASS also provides supplementary clinical information such as morbidity, mortality, cost, intervention outcomes, and even potential causes of antibiotic resistance (Sirijatuphat et al. 2018). Some studies have analyzed the effectiveness of GLASS and found it to be useful. One in particular concluded that "the data derived from GLASS was more useful for developing antibiotic guidelines for patients suspected of having bacteremia" (Sirijatuphat et al. 2018). They also concluded that the additional data collected from GLASS "was important to understand the epidemiology of bacteremia at [their] center, to enhance [their] ability to develop more appropriate local antibiotic guidelines, and to estimate health and economic burden of bacteremia caused by antimicrobial resistance bacteria" (Sirijatuphat et al. 2018).

In summary, GLASS offers a platform in which levels of antibiotic resistance across the globe can be tracked and monitored to assess the spread of resistance, possible causes, and solutions that may have already worked in some regions and can be implemented in others. As promising as this program may seem, not all countries are participating in this initiative, in fact only 37% are (WHO 2019). Interestingly, Spain is not one of them. If Spain had been participating in GLASS, then perhaps it could have noticed its rise of antibiotic resistance, and

how it compares to other countries across the globe, much earlier. GLASS can potentially provide Spain with the guidelines and supporting information that it needs to tackle this crisis. Similarly, it can do this with any country. GLASS can be a critical tool used by public health systems to identify emerging and re-emerging outbreaks and how to properly assess them.

II.   Health Care Settings

According to the CDC, "one of the biggest risks for getting an antibiotic-resistance infection is staying in a healthcare facility, such as a hospital" (CDC 2019). Health care facilities serve as petri dishes for bacteria to grow and spread, where patients can come in with one infection, spread it to others, and acquire more. This is why health care facilities should be one of the first places to target when combating antibiotic resistance.

Referring back to Dr. Sander's case study, one of the biggest issues that medicine is facing today is misdiagnosis. Studies have found that each year in the U.S., approximately 12 million adults in outpatient medical care are misdiagnosed (Firger 2014). Some of the common reasons for these misdiagnosis range from problems ordering diagnostic tests to errors interpreting test results (Finger 2014). One of the factors contributing to these errors could be physicians rushing during examinations. Some studies have found that "shorter visits, especially those less than 15 minutes, were a risk factor for inappropriate prescribing" (Dugdale et al. 1999). This is why there needs to be stronger policies reinforcing that patients get the appropriate time they need during visits. One of the ways this could be implemented is by cutting state funding from health care facilities that do not have a minimum of 15 minutes per patient visit. Something needs to be done to train physicians, and other health care providers, to be meticulous

in their examinations and stop rushing. This careless behavior is what results in antibiotics being prescribed for anything that mimics the symptoms of bacterial infections, thereby unnecessarily exposing patients to antibiotics and triggering resistance mechanisms.

Another contributing factor to the spread of antibiotic resistance infections we see today, especially in health care facilities, is inadequacy is hand hygiene practices (CDC 2017). Health care facilities need to implement stronger policies that enforce more frequent, and longer, hand washing. If everyone exercised cleaner practices, then there would be no need to mass prescribe antibiotics. Other policies that could be beneficial is the implementation of personale, such as a committee or team, in health care facilities that solely monitor and assess infections. This team could be composed of physicians, nurses, infection control practitioners, public health specialists, environmental services, and microbiologists. This group of people with diverse expertise could work together to monitor how many patients physicians are prescribing with antibiotics, assess if their prescription is appropriate, investigate if the right diagnostic tests were done, establish hospital hygiene policies, etc. Overall, they'd be responsible for monitoring and assessing infections and prescriptions. Additionally, they can (and should) be the ones responsible for reporting corresponding data related to antimicrobial resistance to GLASS and implementing the guidelines provided by GLASS.

Even with better physician awareness, better hygiene, an entire infection control team, and the incorporation of a global surveillance system like GLASS, hospitals may still be prone to infections. After all, that's where everyone goes when they are sick. This is why healthcare facilities should also consider implementing innovative strategies to prevent infections from spreading. For example, Infection Prevention Technologies (iPT) is working on a

UV-Disinfection robot that uses UV light to disinfect hospital rooms (Baker 2018). Studies performed by iPT have shown evidence of its robot's success in reducing populations of microbes in under five minutes (Baker 2018). This is a great innovation because the UV light is powerful enough to kill the microorganisms' DNA while not harming humans. Many other studies have shown that UV light is a promising agent for a disinfectant system (Katara et al. 2008). Copper alloy touch surfaces in healthcare facilities also demonstrate to be promising agents for a disinfectant system (Colin et al. 2018). It has been proven that copper surfaces on doorknobs and handrails can lower the contamination levels of MRSA in health care facilities, indicating just how powerful this innovation can be in controlling the spread of threatening infections (Colin et al. 2018).

In summary, there are a multitude of approaches that health care facilities, which are highly prone to transmitting antibiotic resistant infections, can take. These approaches include (but are not limited to) enforcing that physicians spend more time with patients in order to make more reasonable diagnosis, implementing stronger policies with hand hygiene, incorporating an infection control team, and using innovative strategies (such as UV light) to diminish germs. The most effective way to treat antibiotic resistant bacteria is by preventing them from spreading to humans in the first place. If hospitals were able to diminish their spread of infection, then we wouldn't be in a rush to develop new antibiotics.

III.   Educating Patients

It's inevitable for people to become sick. Even if hospitals are able to significantly lower the spread of infections, some patients are still going to come in with one. In this case, of course

it's appropriate to prescribe antibiotics to patients suffering from bacterial infections. However, health care professionals should educate their patients on how to properly take them. I suggest that physicians provide pamphlets to patients informing them on the horrors that can arise when you don't finish your full course of antibiotics or when you share prescriptions with others. Further emphasis can be made by pharmacists, who can also warn patients either verbally or with a written notice on prescription bottles. I also suggest the mass distribution of posters and/or videos teaching patients to stop insisting on antibiotic prescriptions. As previously mentioned, one of the main factors influencing antibiotic prescription (sometimes when they're not necessary) is patient pressure (Strumilo et al. 2016). Not all infections (viral, fungal, protozoa, etc.) can be cured by antibiotics and many people do not recognize this. Physicians sometimes cater to patients because they fear they'll obtain the prescription elsewhere. When patients coerce physicians to prescribe antibiotics when they're not needed, the only ones that ultimately end up getting hurt are the patients themselves.

IV.   Agriculture

The overuse of antibiotics is not only a problem in humans but also animals. As the WHO recommends, I also insist that farmers only administer antibiotics to healthy animals *if* other animals in the herd, flock, or fish population have been diagnosed with a disease (WHO 2017). In other words, *antibiotics should stop being used as a preventive measure*. Just as the bacteria in humans can acquire resistance from exposure to antibiotics, so can the bacteria in animals, making it of vital importance that antibiotic use be kept to a minimum. That being said, the transmission of infection amongst animals should also be tightly monitored and kept to a

minimum. Farmers need to implement better sanitation procedures, instead of administering drugs, to prevent infections. Policies should be in place to ban the use of antibiotics for non-medical or treatment purposes. Some countries in Europe have already done this and have seen a drastic decrease in antibiotic resistance bacteria (Ganzler 2018). Other countries, like the United States and Spain, should do the same. The WHO also recommends that the food industry stop using antibiotics listed as critically important for human medicine in livestock (Chan 2016). If common antibiotics used to treat humans are constantly being used in animals, and the bacteria in animals develop resistance, once those bacteria spread to humans they will be incurable because our antibiotics will no longer work on them.

Conclusion

Antibiotic resistance is a global health crisis affecting millions of people everywhere. Though the lack of new antibiotics is contributing to this threat, it is the careless use of antibiotics that has put us all in this predicament in the first place. In order to successfully combat antibiotic resistance, we need to manage our use of antibiotics and spread of infection. Global surveillance systems such as the World Health Organization (WHO)'s Global Antimicrobial Resistance Surveillance System (GLASS) is a promising platform for monitoring and assessing threatening infections. Other strategies such as better educating patients, implementing innovations in health care, and banning antibiotic as a preventive measure in agriculture, are some of the key aims that we can start working towards now.

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