Love in the Time of Antibiotic Resistance: How Altruism Might Be Our Best Hope

Dien Ho

The emergence of antibiotic-resistant bacteria is nothing new. In 1921, Alexander Fleming discovered the antibacterial property of lysozyme. Merely 2 weeks later, Fleming et al. identified strains of bacteria in their culture that had been exposed to lysozyme and survived the lytic action. The cultures grown using these strains retained their lysozyme resistance 9 months after their initial discovery (Fleming and Allison 1927). Fleming, of course, went on to discover penicillin in 1928. Penicillin transformed modern medicine: it not only cured previously fatal infectious diseases, but it also made possible invasive surgical procedures that would have otherwise exposed patients to dangerous risks of infections. Clive Butler recounts his experience on the staff at London Hospital before and after the introduction of penicillin in his treatment of more than 500 cases of acute osteomyelitis between 1919 and 1937. He writes,

> The overall mortality rate [before penicillin] was 25%—due, in almost every case, to staphylococcal bacteraemia…[S]urgical treatment consisted in early relief of tension by drilling the affected bone and then prolonged immobilisation…I particularly recall one youth who used to pass the time by killing the maggots when they emerged from his plaster by squirting them from an ethyl chloride spray…Towards the end of the war penicillin became available in Britain and I had the opportunity of treating 21 patients—none died…What a transformation from killing maggots, and all this achieved in under 10 years: it seemed miraculous to me and others of my generation. (Butler 1979: 482)

In his Nobel Lecture of 1945, Fleming highlighted the danger of antibiotic-resistant microbes. "The time may come," he warned, "when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant" (Fleming 1945: 93). Yet, 70 years after his warning, we find

D. Ho (✉)
School of Arts and Sciences, MCPHS University, Boston, MA, USA
e-mail: dien.ho@mcphs.edu

D. Ho (ed.), *Philosophical Issues in Pharmaceutics*, Philosophy and Medicine 122,
DOI 10.1007/978-94-024-0979-6_15

our arsenal of antimicrobials becoming less effective in the face of growing resistance. In this essay, I wish to explore the causes of antibiotic resistance. The solution will require not merely a change in the development, distribution, and usage of antibiotics but a willingness to put aside our rational self-interest. If one is pessimistic of our chances to place other's interests before our own, then one should be pessimistic of our chances of winning the war against microbes.

The Dreaded Reality

Antibiotic-resistant pathogens have been identified in virtually every corner of the world. Nevertheless, the exact scope of the problem remains unclear. The World Health Organization (WHO) estimates that of the 6.1 million cases of tuberculosis diagnosed worldwide in 2013, approximately 300,000 of them are multidrug-resistant tuberculosis (MDR-TB) defined as being not responsive to two of the standard treatments (isoniazid and rifampicin) (WHO 2014a). MDR-TB has been identified in all six WHO global regions: Africa, the Americas, Eastern Mediterranean, Europe, Southeast Asia, and the Western Pacific. Although treatment success rate for TB is about 86%, it drops to 48% with MDR-TB. More worrisome is the emergence of extensively drug-resistant TB (XDR-TB): TB that is resistant to standard treatments including the most effective second-line treatments. Nine percent of all patients with MDR-TB were also diagnosed with XDR-TB, and more than 100 countries reported cases of XDR-TB in 2013 (WHO 2014b). The data collected by WHO, however, do not paint a complete picture. Although the number of reported cases of MDR-TB in Southeast Asia, for instance, has grown from 68 in 2005 to 28,618 in 2013, it is not entirely clear if the dramatic change was a result of significant increase of antibiotic resistance or better diagnostic and reporting efforts. Indeed, data collection has remained a major hurdle in our attempt to gain a full understanding of the scope of the problem. Zumla et al. report that among 27 countries with a high burden of MDR-TB, "only 1% of new tuberculosis cases and 3% of previously treated cases are screened for [drug-resistant] tuberculosis by a laboratory" (Zumla et al. 2012: S229). The actual number of individuals who suffer from MDR-TB is likely significantly higher.

In addition to a lower treatment success rate, patients who suffer from antibiotic-resistant infections are also more costly to treat. On average, treatment for MDR-TB cost 3–100 times more (Koenig 2008: 894), and they last three to four times longer than drug-susceptible TB (leading to a greater chance of the TB spreading). A broad study commissioned by the Prime Minister of the United Kingdom and conducted by Jim O'Neill and the Wellcome Trust warns that unless drastic measures are taken, by 2050, antimicrobial-resistant diseases will claim ten million lives per year (O'Neill and Wellcome Trust 2014).

What Stokes the Fire?

One commonly cited cause of the growth of antibiotic resistance is the unnecessary use of antibiotics at the clinical level. In a 2014 study, Schultz et al. identify redundant antimicrobial usage in 394 of the 505 hospitals examined in the United States, amounting to 32,507 cases (Schultz et al. 2014: 1231). Physicians, even those who are familiar with the danger of overprescribing antibiotics, often do not consider the broader public health implication in their prescription habits. Of the 400 generalists and 429 infectious disease specialists they surveyed, Metlay et al. note that "risk of the drug contributing to the problem of antibiotic resistance" ranked last among a list of seven considerations in determining what antibiotic to prescribe, well behind ease of use and cost to patients (Metlay et al. 2002).[1]

Similar failures to prescribe properly have been noted in other developed nations and often at community healthcare access points such as pharmacies. Marković-Peković et al. report that of the 131 pharmacies their "secret shoppers" visited in the Republic of Srpska in Bosnia and Herzegovina, 58% sold antibiotics to clients without prescriptions. Among these pharmacies, 25% did not offer any symptomatic therapies and only sold the antibiotics to the clients (Marković-Peković and Grubiša 2012). Without proper diagnostic indications for antibiotics and emphasis on the importance of correct usage (e.g., the completion of a treatment), pharmacists risk under- and overuse of antibiotics that contribute to the proliferation of antibiotic-resistant pathogens.

The dispensing and usage of antibiotics in developing nations often involve even less rigor and monitoring. Indira et al. examined the prescribing behaviors of clinicians in health centers in four Indian cities, and they report that 70% of antibiotics were given for viral conditions (e.g., diarrhea and upper respiratory infections) that are nonresponsive to antibiotics (Indira et al. 2004). In a 2010 study in Abu Dhabi, 68.4% of clients were able to obtain antibiotics in community pharmacies without prescriptions (Dameh et al. 2010). Not only is dispensing antibiotics over-the-counter illegal in UAE, 63% of them obtained antibiotics after complaining of respiratory problems, which are often viral in origin. Similar inappropriate dispensing of antibiotics has been identified in China as well. One study reports up to 79% of patients suffering from the common cold were given antibiotics in hospitals (Yip and Hsiao 2008: 462). A study by Means et al. shows that 40% of the 45,591 patients

[1] It is important to note that a number of factors contribute to well-informed physicians' failure to prescribe antibiotics properly. Often, physicians succumb to pressure from patients who explicitly seek antibiotics. These requests can be a result of misunderstanding of the therapeutic use of antibiotics (e.g., they do not work on common colds). They can also be a product of intense marketing campaigns by pharmaceutical manufacturers. Pfizer's marketing campaign for Zithromax (Z-Pak) geared heavily toward parents who wished to seek short-term antibiotics for their children's ear infections (Petersen 2000). The campaign included a donation of a zebra to the San Francisco Zoo, sponsoring of Sesame Street episodes, and large-scale distribution of Max the Zebra to various clinics. Max proved so popular that patients reported that they thought it was the mascot for Boston Children's Hospital.

in Uganda with malaria received antibiotic treatments, even though they lacked documented clinical indications (Means et al. 2014).

The cause of inappropriate antibiotic prescription is a complex phenomenon. In the case of China and India, often pharmacies and clinics profit from selling antibiotics, thus creating a perverse incentive to overprescribe. There is also the lack of oversight of healthcare providers' prescribing habits. Of the 47 member states constituting WHO's African Region, only eight countries had the means to report antimicrobial resistance data, and only one has a funded national action plan to combat antimicrobial resistance. In China, the rampant counterfeit drug market also increases the difficulties in controlling antibiotic distribution and usage. *Wired* magazine reported that in 2001, 192,000 Chinese patients died from fake drugs, and the Chinese authorities closed 1,300 factories and pursued 480,000 cases of counterfeit drugs (McKenna 2011).

Although questionable motives certainly led to the failure to prescribe antibiotics appropriately, often the reasons are far less nefarious. Consider the decision as to whether one should prescribe a broad-spectrum or narrow-spectrum antibiotic when a patient has a bacterial infection. Given that standard diagnostic cultures can take days to grow (and weeks for some bacteria), the use of a broad-spectrum antibiotic prior to securing an accurate diagnosis allows care providers to begin treatment for the patient.[2] Of course, broad-spectrum antibiotics also render more likely the development of antibiotic-resistant pathogens since they kill more than they need to. Ignoring for the moment the health risks a patient undertakes by using a broad-spectrum antibiotic (e.g., the destruction of possibly helpful bacteria), we can see a potential conflict of interest. To wit, it is in the best health interest of a patient to receive speedy and effective treatment including broad-spectrum antibiotics. At the same time, the treatment involves a cost (an externality) that is shouldered by everyone else in the form of an increased risk of an antibiotic-resistant pathogen emerging. By killing a wide gamut of bacteria (many of which pose no health risks to the patient), a broad-spectrum antibiotic leaves a bacterial vacuum in which the remaining resistant bacteria have ample opportunities to repopulate. A widespread use of broad-spectrum antibiotics thus exerts selection pressure against antibiotic-susceptible bacteria tilting the reproductive landscape in favor of antibiotic-resistant ones. In addition to vertical transmission of antibiotic resistance (via reproduction), antibiotic resistance can also transmit horizontally. Segments of a bacterium DNA that confer antibiotic resistance can break off and attach themselves to other bacteria including those not in the same species. Thus, a broad-spectrum antibiotic may select antibiotic resistance in a banal bacterium, but the resistance can be passed on to pathogens creating a new lethal antibiotic-resistant strain.[3]

Nevertheless, there are many immediate benefits to using broad-spectrum antibiotics. In addition to being able to start treatment before diagnostics are completed,

[2] To be sure, there are newer and faster diagnostic methods. But these methods often require resources including sophisticated laboratories that many health centers simply do not possess.

[3] See Morley et al. (2005) for an explication of the mechanisms that give rise to bacterial resistance.

the use of broad-spectrum antibiotics can also lower the cost of care for the patients and the clinics. Even if we assume that a liberal use of broad-spectrum antibiotics will shorten the effective lifespan of these drugs, it is not an obvious conclusion that we ought not to be aggressive with our use of broad-spectrum antibiotics. Diagnostics cost money and time. Given how cheap broad-spectrum antibiotics are, hospitals and clinics might be able to save money by prescribing them and using the savings to meet other healthcare needs. Such a practice would likely impact future patients by lowering the effectiveness of antibiotics, but it may provide better care for current patients.

In order to conclude that limiting broad-spectrum antibiotic usage allows us to provide optimal care for the long run, we need to answer two questions: (1) how long is the long run and (2) what is the cost to the patients who suffer, either because of the denial of broad-spectrum antibiotics or because of the decline in available medical resources due to the burden of more expensive diagnostic techniques? The first question is obviously a philosophical one that requires difficult trade-offs between the well-being of people in the future and those in the present. Although a number of scholars have attempted to balance the two, justifying a particular tipping point where the interests of nonexistent future people outweigh those of real sick people is hardly an easy task (Leibovici et al. 2012: 4).

Indeed, the very idea that a physician might provide less than optimal care (from a patient's point of view) for the interests of future individuals might erode the trust between patients and physicians.[4] Physicians are advocates for patients' healthcare interests. If patients believe that their physicians are actively limiting care in order to benefit others, patients would rightly question whether their healthcare needs are in fact the determinants of the treatments recommended.

One way we can avoid this problem is to enact regulations that restrict and guide physicians' clinical practices when patients' interests need to be compromised. Physicians sometimes make clinical decisions that place their patients' interests below the welfare of someone else. Quarantine orders, reporting of gunshot wounds, therapists' breaking confidentiality to report the abusing of minors, and emergency triage all can place the interests of a third party over that of the immediate patient. Clear and enforceable regulatory restrictions—be they from professional organizations or governmental agencies—allow physicians to remain full advocates of patients' healthcare interests while taking into consideration public health concerns. By "tying the hands" of clinicians, we preserve the trust essential for the proper working of a physician-patient relationship.

Strong regulatory guidelines for the prescribing of antibiotics can also limit unnecessary prescriptions of antibiotics that stem from liability worries on behalf of healthcare providers. In a 2009 study, Sakoulas et al. note that among 17 European countries and 41 states in the United States, there is a statistical correlation between the density of attorneys and cases of methicillin-resistant *Staphylococcus aureus* (MRSA). Sakoulas et al. hypothesize that the fear of malpractice lawsuits (e.g.,

[4] For a discussion of why trust is necessary for the proper functioning of medicine, see Ho (2008: 81).

undertreatment) causes physicians to overprescribe antibiotics, thus leading to a higher rate of MRSA (Sakoulas et al. 2009). Strong regulatory guidelines can alleviate some of the fear of litigation by providing institutional support for the proper usage of antibiotics.

National regulations that limit access to antibiotics can help eliminate a number of factors that contribute to the emergence of antibiotic resistance; for example:

1. Limit antibiotic usage for clinically indicated conditions (e.g., prohibiting prescription of antibiotics for viral infections).
2. Decrease antibiotic prescriptions for marginally indicated conditions such as ear infections.
3. Rigorous monitoring of antibiotic prescriptions by clinicians.
4. Reserve broad-spectrum antibiotics as second-line treatments.

Clear national policies restrict clinical decisions while preserving the trust between physicians and patients. In addition, they also lessen that pressure physicians feel when prescribing antibiotics out of fear of litigation.[5]

When Local Meets Global

Professional and governmental guidelines, however, run up against the fact that the emergence of antibiotic-resistant pathogens is a global problem that requires transnational-coordinated solutions. However, effective intranational agencies are at monitoring and regulating antibiotic resistance; the porous nature of international borders renders these efforts futile unless other nations also undertake similar efforts. Pathogens can spread easily and become endemic to their new environment. A recent genetic study of samples of typhoid in two dozen countries has revealed that in the past 30 years, a drug-resistant strain—H58—has spread from India to African and Pacific island nations. H58 is becoming the dominant strain of typhoid displacing those that are susceptible to traditional drug treatments in their new homes (Wong et al. 2015). Here the lack of any strong regulatory bodies renders controlling antibiotic resistance a far more daunting task. The United States, for

[5] It is important that we should retain a healthy dose of skepticism with regard to the political wisdom and will necessary to draft and implement rational antibiotic policies. When it comes to public health concerns, the United States has a troubling history. In 2014, for instance, Congress appropriated $5.2 billion to an emergency bill for combating the Ebola virus. The White House requested in the 2016 budget $1.2 billion for all antibiotic research. Although Ebola is a formidable infectious foe, its threat pales in comparison to antibiotic-resistant bacteria. Ebola killed approximately 11,000 individuals by 2015 (The Data Team 2015). Antibiotic-resistant bacteria kill about 700,000 people/year (O'Neill and Wellcome Trust 2014). Media attention on Ebola probably helped shift awareness and the subsequent funding to Ebola research. The creation of effective regulatory guidelines concerning antibiotic usage would depend heavily on an objective evaluation of public health independent of political biases. The fact that the United States' political system is designed to be influenced by political action committees and lobbying groups suggests that competing private interests might not make for ideal public policies.

instance, constitute only 5% of the world's population. Even with the most effective domestic policies guiding the use of antibiotics, its contribution to the curbing of antibiotic-resistant pathogens globally is minimal, especially if the consumption of antibiotics in the rest of the world increases.[6]

Good antibiotic stewardship requires supportive services that permit rational infectious control. Antibiotic usage is but one arm of a holistic approach to limiting infections. Indeed, if there were no infections, there would be no need for antibiotics. Access to clean water and nutrition, adequate sanitation, properly trained healthcare providers, patients who are educated about their treatment, affordable methods of traveling to and from clinics, concerted efforts to control comorbidities that exacerbate infections (e.g., HIV), and other public health efforts that limit the spread of infections (e.g., cheap or free condoms to combat STIs) are but parts of a coherent effort to combat infection and to lower the use of antibiotics. To institute a global policy on antibiotic usage without addressing these related issues could end up depriving those who need them most of antibiotics.

Prisoner's Dilemma

Ignoring for a moment obviously inappropriate antibiotic usage (e.g., using them to treat viral conditions) and putting aside logistical challenges intra- and international organizations confront in monitoring antibiotics usage in clinics and pharmacies, a global effort to slow the growth of antibiotic-resistant pathogens faces the classic problem of multi-person prisoner's dilemma or n-person prisoner's dilemma (NPD). An NPD arises when more than two parties have the choice of either cooperating or not with other parties. Moreover, a dominant strategy has to be present for each party; that is, no matter what the other party does, a given party is always better off not cooperating. Finally, if all parties fail to cooperate, the outcome is worse than if they cooperate. Voluntary recycling is a good example of NPD. Suppose I value a clean environment and I believe that a community with a high percentage of

[6] One area of antibiotic usage that we will not discuss is the sub-therapeutic use of antibiotic in raising animals for meat. In the Unites States, 80% of all antibiotic used for the raising of farm animals for meat consumption is given at a sub-therapeutic level in order to promote animal growth (Levy 2002: 152). In a 2007 survey, "the estimated annual antibiotics production in China was 210 million kg, and 46.1% were used in livestock industries"—four times higher than in the United States (Zhu et al. 2013: 3435). The sub-therapeutic use of antibiotics for growth promotion has been banned in European countries. Although the volume of antibiotics used for growth promotion is alarming, it is not entirely clear what the health consequences are to humans and animals in banning their use. A 2003 study shows that the banning of antibiotics for growth promotion in Europe has led to an increased use of antibiotics in animals for therapeutic purposes because of greater incidents of infections (Casewell et al. 2003). However, what is clearly worrisome is the lack of close monitoring of sub-therapeutic use of antibiotics for livestock farming in both United States and China. Given the potential enormous impact their usage has on animals' and humans' welfare, a careful collection of data on antibiotic uses in farming is a minimal first step we need to take to ensure good antibiotic stewardship.

recycling provides the best chance of a clean environment. Suppose further that I believe my contribution to the improvement of the environment via recycling makes a negligible difference. If everyone else recycles, I am better off not recycling since I can reap the environmental benefit without undertaking the hassle of recycling. If no one else recycles, I am better off not recycling since my effort would not make any difference. The dominant strategy is not to recycle because I would be better off no matter what other people do. Thus, the rational self-interested strategy is not to recycle.[7] Of course, if everyone else does the same thing, we would lose out on the environmental benefits of recycling (something most of us value).

There are various ways to encourage cooperation in a game of NPD. The most obvious way is to identify those who are not cooperating and punish them. This strategy essentially changes the cost-benefits of the player by moving the cost of noncooperation high enough such that it is no longer in the player's self-interest not to cooperate. A fine levied against those who do not recycle is a good way of realigning the self-interest of the non-recycler with the collective interest of a clean environment. Likewise, mandatory contribution in the form of taxation also provides us with the funds necessary for public goods like paved roads, sewer system, and clean water. From a rational self-interest point of view, although each citizen might desire to have these goods, their individual contributions make negligible differences. A tax to fund public goods essentially removes the choice a citizen has in terms of whether or not to cooperate; thus, it eliminates one of the prerequisites of an NPD.

Antibiotics as Global Climate: Kyoto vs. Montreal

Suppose we think of antibiotics like clean air. We all want to have access to them and we think future generations ought to have access as well. However, suppose a sustainable usage of antibiotics requires all nations to make minor sacrifices (from more expensive meat to not having quick access to broad-spectrum antibiotics). How do we motivate nations to cooperate (for instance, signing a treaty and being monitored for compliance)? One natural place to look for a possible solution to NPD at a global level is to adopt lessons learned from international treaties on pollution control. Looking to the Montreal and Kyoto Protocols as models of successful and unsuccessful international efforts, respectively, Jonny Anomaly outlines a number of features that make a treaty more likely to succeed (Anomaly 2010). They are:

1. Flexibility: goals must be adjustable on the fly and nations must be able to meet goals in a variety of ways (e.g., cap and trade, taxes, etc.).

[7] The most self-serving action would be to appear as if one recycles and convinces other people to recycle. One enjoys the benefit of a clean environment without putting any work into it while getting other people to do the hard work.

2. Signatories must perceive the burdens as being distributed in a fair way and beneficial to all participants by effective use of carrots and sticks.

The Kyoto Protocol places a significant burden on industrialized nations to cut emissions of greenhouse gases while allowing nations with smaller per capita GDP (including China) exemptions. The result was the creation of free-rider states and the withdrawal of large industrialized nations who felt they were shouldering most of the burden of cutting emissions. The Kyoto Protocol also lacked the necessary flexibility. As Asian countries began to absorb migration of heavy industries from developed nations, the Kyoto Protocol could not adjust and restrict new emitters (e.g., China and India) of greenhouse gases who had been exempted from the treaty. The cuts by industrialized nations that remained parties to the protocols have been dwarfed by emissions from China and other parts of Asia, South America, and Africa. Worldwide emissions of greenhouse gases have gone up by 50% since 1990 even though US contribution has decreased from 66% to 50% (Schiermeier 2012).

Contrast the failure of the Kyoto Protocol with the success of the Montreal Protocol—a treaty strongly advocated by conservative political leaders like Ronald Reagan and Margaret Thatcher. The Montreal Protocol aimed to limit production of ozone-depleting gases and does so by first creating incentives for small nations to sign on (Gillis 2013). When a non-developed country becomes a signatory, it immediately receives subsidies to help it create non-ozone-depleting alternatives. The treaty also imposes trade restrictions between those countries that have signed on and those that have not. However, the restriction does not kick in until a critical mass of nations has signed on to the treaty. The result was that after the initial surge of small nations signing on (motivated by subsidies), larger nations had a disincentive to remain on the sidelines. The Montreal Protocol has been held up as a model of an international treaty that provides flexible carrots and sticks to all nations to sign on while minimizing free riders in a game of NPD.

As Anomaly rightly points out, however, controlling ozone-depleting gases presents a set of challenges different from instituting a sustainable antibiotic global policy. For starters, there are currently no effective alternatives to antibiotics that are of similar costs. In addition, unlike the elimination of ozone-depleting gases, restricting access to, say, broad-spectrum antibiotics can have immediate and serious implications to individuals' welfare. Internal political pressure would be of a different magnitude: trade restrictions might not be sufficient to motivate a citizen to forgo beneficial antibiotics. Monitoring antibiotic usage (i.e., compliance with a treaty) might also present far more logistical problems. Unlike a blanket prohibition of ozone-depleting gases like chlorofluorocarbon (CFC), for example, detecting inappropriate use of antibiotics would require close monitoring at the clinical level to determine if a particular prescription of antibiotic is appropriate. Given the fact that even nations that have robust healthcare monitoring systems like the United Kingdom and the United States have had an exceedingly difficult time gathering data on antibiotic usage domestically, the mechanism necessary for a global monitoring of antibiotic usage would be tremendously complex and resource intensive.

Free Market Fails to Rescue

One might be tempted to appeal to the invisible hand of the free market to align national and individual's interests with the public health interest of having a global policy of sustainable antibiotics. The problem, as Michael Selgelid has argued, is that we have no reason to believe that a free market distribution of antibiotics would actually deliver the desired outcomes (Selgelid 2007). A major obstacle to the proper distribution of antibiotics is the lack of access to affordable antibiotics in developing nations. The slim profit margins undercut the financial incentive for pharmaceutical companies to develop antibiotics for poor nations. What we need is a coordinated effort to fund research that looks to create affordable and effective antibiotics and ensure that they are distributed and used properly. The solution "will require governmental intervention/funding. The fact that the problem of drug resistance is global in scope, while there is no global government, however, is troubling" (Selgelid 2007: 229).

Here lies, I believe, the most serious problem with a global solution to the antibiotic-resistant threat. In order for us to solve an NPD problem, we need to be able to identify, monitor, and punish those who do not cooperate (or provide incentive for those who do). The absence of any robust international organization that can undertake these arduous tasks means that a traditional solution to this NPD is unlikely to materialize. We cannot simply change the cost-benefit calculus of the parties involved hoping that we can steer them to do the right thing by appealing to their rational self-interests.[8]

Spreading Altruism as a Public Health Effort

The core conflict in a game of NPD is that if the participants decide to act on the basis of their rational self-interest, they would all be worse off than if they had not followed their rational self-interest. Real life examples of individuals not acting out of rational self-interest are plentiful. For instance, individuals often vote in general elections even if their self-interest dictates that they are better off not voting. For US presidential elections, an individual's vote would make minimal difference to the eventual outcome and casting votes often entail long waits. Yet, 59% of registered voters voted in 2012 presidential election (FairVote). Turnout in the 2005 Iraqi

[8]There are a lot of reasons why we would want to control the emergence of antibiotic-resistant pathogens. The most obvious is self-preservation. We care about ourselves, the people we love, and their offspring. But there are also moral reasons as well. The severe inequality of wealth in the world means that many individuals, in virtue of being born in the poorer parts of the world, will not have access to adequate healthcare. Healthcare, as Norman Daniels (1995) has argued, is special in that it is strategically important to one's ability to pursue the normal range of life's opportunities. Our failure to ensure that poor nations have adequate access to antibiotics not only runs contrary to our self-interests, it is also unjust.

parliamentary election—the first in the history of Iraq—was estimated at 70% even though insurgent groups threatened violence. From the point of view of rational self-interest, individuals should not be voting voluntarily. The same altruistic behavior occurs with regard to voluntary recycling. In 2012, 34.5% of all US households recycled. The majority of these households are in municipalities that do not mandate recycling (EPA). Rational self-interest does not always dictate our choices. We often pursue a course of action that is not in our best interests guided by considerations such as the well-being of others.

The global monitoring approach to solving the problem of antibiotic resistance depends on extensive surveillance of appropriate drug use at the clinical and pharmacy level, a combination of proper carrots and sticks to incentivize nations to participate, and a sufficiently objective and resourceful organization to implement the consequences of cooperation and defection by signatories. Given the slim chance that such a system can exist, it is wise for us to explore a possibility that has been largely ignored: that is, encouraging individuals to act not just in their rational self-interest but also the interests of other individuals including future and distant people. Dan Ariely has done extensive research into the psychological mechanisms at work when one decides whether or not to cheat (Ariely 2012). What he has uncovered is that most subjects in his studies do not base their actions on a simple cost-benefit analysis in the face of an opportunity to cheat. In one study, Ariely et al. provide their subjects with a matrix of simple mathematical questions. After a short period of time, the subjects report how many questions they have solved and they are paid accordingly. In one variation, the subjects' answer sheets are shredded by the subjects after they have had a chance to check their answers. There is no way the experimenters can tell if the subjects were lying about the number of correct answers they had on their sheets. In experiment after experiment, Ariely et al. observe that the majority of subjects lie about how many answers they get right by only a small margin when they could easily have lied to a greater degree and receive more money. (They determine the subjects regularly lie by comparing the subjects' reported number of right answers with their control group whose answers are checked by the experimenters.) One of the key conclusions that Ariely et al. draw is that the degree of cheating and propensity to cheat is determined by our perception of ourselves as morally decent people. Cheating a little allows us to benefit from our transgressions while letting us retain the sense that we are still good people. In other words, for most of us, the sense of moral self-worth trumps simple rational self-interest.

Indeed, moral decency plays a significant role in one's decision to cheat. Ariely et al. discovered that if subjects were exposed to a "moral reminder" prior to reporting their answers, their propensity to cheat decreases. Ariely et al., for instance, ask one group of subjects prior to an opportunity to cheat to try to list the Ten Commandments and another group to list ten books they read in high school. The Ten Commandments group cheated less while the other group did not behave differently.

Ariel's insights into the psychology of cheating can perhaps help us craft a global public health effort to encourage individuals to think about the well-being of future and distant people when it comes to the use of antibiotics. Such an effort might

include an emphasis on the impact antibiotic usage has on other people. Perhaps we can use moral reminders in the form of signing an education form that highlights the externalities of antibiotics prior to receiving care (on a par with consent forms). Likewise, a public health campaign to educate the public on the virtues of good antibiotic stewardship can help create a culture of viewing the cavalier use of antibiotics as morally dubious. Such a campaign can model itself on other attempts to encourage altruistic behaviors. In the United States, for instance, we value and celebrate the virtues of democratic elections, and there are subtle and not so subtle efforts to instill in citizens a sense that voting is important and morally admirable. We teach elementary school children about the electoral process and the importance of voting. States and municipalities ensure that voting in an election is relatively easy, recent efforts by some states to limit participation in the form of voter ID laws notwithstanding. Voters get little "I Voted" stickers to show off their participation. The swearing in ceremonies for many immigrants often take place in historically significant places emphasizing the value of a liberal democracy. These subtle efforts all contribute to a climate in which individuals feel a sense of duty to participate in a democratic political system even when it is not in their rational self-interest to do so. Our value for voting is so ingrained that we hardly notice the mechanisms that went into its cultivation in our political and cultural psyche.

Antibiotic-resistant pathogens represent a serious threat to our well-being. The typical solutions take for granted that individuals will always act as rational self-interested agents. As such, like any NPD, cooperation can only come about by aligning individuals' interests with public health interests with the use of incentive and punishment. Nonetheless, given the scope of the problem and the level of logistical challenges involved, such a solution is unlikely to materialize. Perhaps a more promising approach is to encourage individuals to act not on the basis of rational self-interest via a broad educational campaign that stresses and celebrates the importance of altruism. Parents, for instance, might feel the moral nudge not to demand antibiotics for their children's ear infections (that would likely clear up on their own). This nudge might be on a par with our attitude toward littering: even though one can likely get away with doing so, there is a sense of internal shame that often leads one not to litter.[9] This internal policing is a product of successful public service campaigns that fosters the communal values. It is certainly a challenge to create a culture where thinking of our collective interests comes naturally but our success in urging one another to cooperate (from voting to recycling) gives us some hope that teaching altruism might not be entirely a pipe dream. Adding moral education as a component of public health effort has not been seriously explored.[10]

[9] One of the most startling experiences a traveler might encounter in a foreign country is the realization that our disdain toward littering is not universally shared. It is a stark reminder that our own attitude toward littering is the result of carefully crafted public campaigns.

[10] The evolutionary biologist Richard Dawkins first introduced the concept of a meme in his 1976 book *The Selfish Gene* (2016). Dawkins notes that natural selection can occur in an infosphere as well as a biosphere. The unit of transmission would be a meme (which is the information analogy to a gene). "Releasing" an altruism meme that combats antibiotic-resistant pathogens via the prop-

Given the gravity of antibiotic resistance and our limited options, perhaps it is time to explore altruism as a solution to our shared woes.

Conclusion

The emergence of antibiotic-resistant pathogens represents a steady and accelerating global existential threat. Unless we collectively develop a global strategy, piecemeal efforts will be of marginal benefits. To be sure, the development of new antibacterial might buy us more time. Nevertheless, the fact that vast populations of bacteria constantly mutate in ever-growing sites of severe selection pressure (e.g., dense factory farms that utilize sub-therapeutic antibiotics as growth promoters) means that we are confronting a relentless and strengthening foe. Past attempts to identify solutions to global crises have assumed that nations and individuals will always behave as rational self-interested agents. The lack of any viable means to shift the costs and benefits of using antibiotics to generate analogous global cooperation suggests that we ought to look for a different type of solution. Spreading altruism might not save humanity, but it might be the best hope we have to coexist with hostile pathogens.

References

Anomaly, J. 2010. Combating Resistance: The Case for a Global Antibiotics Treaty. *Public Health Ethics* 3(1): 13–22.

Ariely, D. 2012. *The (Honest) Truth about Dishonesty*. New York: HarperCollins.

Butler, C. 1979. Surgery – Before and After Penicillin. *British Medical Journal* 2(6188): 482–483.

Casewell, M., C. Friis, E. Marco, P. McMullin, and I. Phillips. 2003. The European Ban on Growth-promoting Antibiotics and Emerging Consequences for Human and Animal Health. *The Journal of Antimicrobial Chemotherapy* 52(2): 159–161.

Dameh, M., J. Green, and P. Norris. 2010. Over-the-counter Sales of Antibiotics from Community Pharmacies in Abu Dhabi. *Pharmacy World & Science* 32(5): 643–650.

Daniels, N. 1995. *Just Health Care*. Cambridge: Cambridge University Press.

Dawkins, R. 2016. *The Selfish Gene: 40th Anniversary Edition*. New York: Oxford University Press.

EPA. *Municipal Solid Waste*. Retrieved May 15, 2015, http://www.epa.gov/epawaste/nonhaz/municipal/.

Fair Vote. *Voter Turnout*. Retrieved May 15, 2015, http://www.fairvote.org/research-and-analysis/voter-turnout/.

Fleming, A. 1945. *Penicillin*. Nobel Lecture. http://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-lecture.pdf.

agation of responsible antibiotic usage might present a promising line of research for public health advocates.

Fleming, A., and V. Allison. 1927. On the Development of Strains of Bacteria Resistant to Lysozyme Action and the Relation of Lysozyme Action to Intracellular Digestion. *British Journal of Experimental Pathology* 8(3): 214–218.

Gillis, J. 2013, December 9. The Montreal Protocol, a Little Treaty That Could. *New York Times*.

Ho, D. 2008. When Good Organs Go to Bad People. *Bioethics* 22(2): 77–83.

Indira, K., R. Devi, R. Pillai, L. Jeyaseelan, S. Chandy, Rashmi Kumar, S. Suresh, S. Kumar. 2004. Antibiotic Prescribing Pattern (APP) and Related Factors in Primary and Secondary Health Care Facilities of Government and Private Settings. http://www.inclentrust.org/inclen/uploadedbyfck/file/publication/theinclen/USAIDIIDI-finalversion.pdf. Accessed 11 May 2015.

Koenig, R. 2008. In South Africa, XDR TB and HIV Prove a Deadly Combination. *Science* 319(5865): 894–895, 897.

Leibovici, L., M. Paul, and O. Ezra. 2012. Ethical Dilemmas in Antibiotic Treatment. *The Journal of Antimicrobial Chemotherapy* 67(1): 12–16.

Levy, S. 2002. *The Antibiotic Paradox: How the Misuse of Antibiotics Destroys Their Curative Powers*. Cambridge, MA: Perseus Publishing.

Marković-Peković, V., and N. Grubiša. 2012. Self-Medication with Antibiotics in the Republic of Srpska Community Pharmacies: Pharmacy Staff Behavior. *Pharmacoepidemiology and Drug Safety* 21(10): 1130–1133.

McKenna, M. 2011, August 1. Are Counterfeit Drugs Driving Antibiotic Resistance? *Wired*. http://www.wired.com/2011/08/counterfeit-driving-resistance/. Accessed 11 May 2015.

Means, A.R., M.R. Weaver, S.M. Burnett, M.K. Mbonye, S. Naikoba, and R.S. McClelland. 2014. Correlates of Inappropriate Prescribing of Antibiotics to Patients with Malaria in Uganda. *PloS One* 9(2): e90179.

Metlay, J.P., J.A. Shea, L.B. Crossette, and D.A. Asch. 2002. Tensions in Antibiotic Prescribing: Pitting Social Concerns Against the Interests of Individual Patients. *Journal of General Internal Medicine* 17(2): 87–94.

Morley, P.S., M.D. Apley, T.E. Besser, D.P. Burney, P.J. Fedorka-Cray, M.G. Papich, J.L. Traub-Dargatz, and J.S. Weese. 2005. Antimicrobial Drug Use in Veterinary Medicine. *Journal of Veterinary Internal Medicine* 19(4): 617–629.

O'Neill, J., and Wellcome Trust. 2014. *Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations.*

Petersen, M. 2000, August 27. What's Black and White and Sells Medicine? *New York Times*. Retrieved from http://www.nytimes.com/2000/08/27/business/what-s-black-and-white-and-sells-medicine.html?pagewanted=1.

Sakoulas, G., G.P. Wormser, P. Visintainer, W.S. Aronow, and R.B. Nadelman. 2009. Relationship Between Population Density of Attorneys and Prevalence of Methicillin-Resistant *Staphylococcus aureus*: Is Medical-Legal Pressure on Physicians a Driving Force Behind the Development of Antibiotic Resistance? *American Journal of Therapeutics* 16(5): e1–e6.

Schiermeier, Q. 2012. The Kyoto Protocol: Hot Air. *Nature* 491(7426): 656–658.

Schultz, L., T.J. Lowe, A. Srinivasan, D. Neilson, and G. Pugliese. 2014. Economic Impact of Redundant Antimicrobial Therapy in US Hospitals. *Infection Control and Hospital Epidemiology* 35(10): 1229–1235.

Selgelid, M.J. 2007. Ethics and Drug Resistance. *Bioethics* 21(4): 218–229.

The Data Team. 2015, May 10. The Toll of a Tragedy. *The Economist*. Accessed 20 May 2015.

WHO. 2014a. *Global Tuberculosis Report 2014*. http://apps.who.int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf?ua=1. Accessed 11 May 2015.

———. 2014b. *Multidrug-Resistant Tuberculosis (MDR-TB) 2014 Update*. http://www.who.int/tb/challenges/mdr/mdr_tb_factsheet.pdf?ua=1. Accessed 11 May 2015.

Wong, V.K., S. Baker, D.J. Pickard, J. Parkhill, A.J. Page, N.A. Feasey, R.A. Kingsley, N.R. Thomson, J.A. Keane, F.-X. Weill, D.J. Edwards, J. Hawkey, S.R. Harris, A.E. Mather, A.K. Cain, J. Hadfield, P.J. Hart, N.T.V. Thieu, E.J. Klemm, D.A. Glinos, R.F. Breiman, C.H. Watson, S. Kariuki, M.A. Gordon, R.S. Heyderman, C. Okoro, J. Jacobs, O. Lunguya, W.J. Edmunds, C. Msefula, J.A. Chabalgoity, M. Kama, K. Jenkins, S. Dutta, F. Marks,

J. Campos, C. Thompson, S. Obaro, C.A. MacLennan, C. Dolecek, K.H. Keddy, A.M. Smith, C.M. Parry, A. Karkey, E.K. Mulholland, J.I. Campbell, S. Dongol, B. Basnyat, M. Dufour, D. Bandaranayake, T.T. Naseri, S.P. Singh, M. Hatta, P. Newton, R.S. Onsare, L. Isaia, D. Dance, V. Davong, G. Thwaites, L. Wijedoru, J.A. Crump, E. De Pinna, S. Nair, E.J. Nilles, D.P. Thanh, P. Turner, S. Soeng, M. Valcanis, J. Powling, K. Dimovski, G. Hogg, J. Farrar, K.E. Holt, and G. Dougan. 2015. Phylogeographical Analysis of the Dominant Multidrug-Resistant H58 Clade of Salmonella Typhi Identifies Inter- and Intracontinental Transmission Events. *Nature Genetics* 47(6): 632–639.

Yip, W., and W.C. Hsiao. 2008. The Chinese Health System at a Crossroads. *Health Affairs (Millwood)* 27(2): 460–468.

Zhu, Y.-G., T.A. Johnson, J.-Q. Su, M. Qiao, G.-X. Guo, R.D. Stedtfeld, S.A. Hashsham, and J.M. Tiedje. 2013. Diverse and Abundant Antibiotic Resistance Genes in Chinese Swine Farms. *Proceedings of the National Academy of Sciences of the United States of America* 110(9): 3435–3440.

Zumla, A., I. Abubakar, M. Raviglione, M. Hoelscher, L. Ditiu, T.D. Mchugh, S.B. Squire, H. Cox, N. Ford, R. McNerney, B. Marais, M. Grobusch, S.D. Lawn, G.-B. Migliori, P. Mwaba, J. O'Grady, M. Pletschette, A. Ramsay, J. Chakaya, M. Schito, S. Swaminathan, Z. Memish, M. Maeurer, and R. Atun. 2012. Drug-Resistant Tuberculosis—Current Dilemmas, Unanswered Questions, Challenges, and Priority Needs. *Journal of Infectious Diseases* 205(Suppl 2): S228–S240.