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The post-antibiotic era: An existential threat for humanity¹

by Dominik Koesling and Claudia Bozzaro

Currently, mankind is facing the risk of running out of working antibiotics. Such a post-antibiotic era bears tremendous risks such as globally spread or even pandemic bacterial infections. These infections become thus untreatable and possibly lethal, particularly endangering the health (care) of future generations. This paper discusses this acute concern for humanity in three main steps. After first elaborating on the role of antibiotics and the occurring resistance in modern medicine, the focus will be on the current scope of the problem of antibiotics and the prognosis of its future escalation. Then the possibility of a way out and its obstacles will be addressed, before finally assessing the existential threat of a post-antibiotic era.

Keywords: antibiotic crisis; post-antibiotic era; existential threat for humanity; global and intergenerational health (care); global and intergenerational (in)justice

Introduction: The lingering danger of a post-antibiotic era

Antibiotic resistance is on the rise and humanity is currently heading towards a post-antibiotic era. Although this scenario is unlikely to lead to the complete extinction of humanity, it poses an existential threat, as one of the most important means of fighting infections would then have become ineffective, resulting in the death of millions of people. Despite the fact that international bodies such as the World Health Organization have put this issue on the global political agenda, it continues to grow as problem. However, the actual danger posed by antibiotic resistance, which is essentially of anthropogenic origin (Mitchell et al. 2019: 1), does currently not correspond to its recognition as an immediate threat to humanity on a social, or more precisely on a societal level. Not even notorious catchwords like “superbugs” (Stolberg 1998) seem to be enough to bring the issue into public awareness. As of now, “warnings and crisis framings do not appear sufficient to prompt a response. Public attention and governmental action have lagged.” (Engström 2021: 19).

A post-antibiotic era is, simply put, “a new era in which bacteria have become resistant to existing antibiotics and the antibiotics no longer work.” (Hansson/Brenthel 2022: 381). Like some other current and anticipated future crises, such as the climate crisis, antibiotic resistance is developing day by day beyond our collective perception. This lack of awareness could make the current antibiotic crisis even more dangerous, as the absence of adequate threat perception is likely to reduce the willingness to tackle the problem. Picking up on these aspects, the guiding thesis of the paper at hand is, that, contrary to their widespread perception, *antibiotic resistance and the post-antibiotic age are an existential danger to humanity in form of a global and intergenerational threat.* The arguments to substantiate this claim are unfolded in three main steps: First, we will give an overview of the role of antibiotics and the occurring resistance in modern medicine. Building on this and taking a global perspective, we will highlight the current scope of the problem and elaborate on the prognosis of its future

escalation, revealing the intergenerational nature of the issue at hand. Afterwards, we will focus on potential attempts to tackle antibiotic resistance and prevent a post-antibiotic era by elaborating on the possibility of a way out and its obstacles, before concluding the proposed arguments.

Antibiotic resistance is on the rise and humanity is currently heading towards a post-antibiotic era. Although this scenario is unlikely to lead to the complete extinction of humanity, it poses an existential threat, as one of the most important means of fighting infections would then have become ineffective, resulting in the death of millions of people.

The role of antibiotics and the occurring resistance in modern medicine

Prior to humanity’s access to effective antibiotics in what can be called the pre-antibiotic era – most of human history – millions of people had to suffer and die from bacterial infections. This changed radically with the scientific discovery of antibiotics, and since then antibiotics have completely revolutionised medicine, not only being an effective means of treating infections, but also making medical procedures such as life-saving operations safe in the first place (Palmer 2022: ix; Friedman et al. 2016: 416, 420). Nowadays antibiotics are virtually omnipresent, especially in health care, and they have “extended the average human lifespan by 23 years.” (Hutchings et al. 2019: 1). As indicated by research, millions of doses of antibiotics are administered every day in hospitals alone. A German study, for example, showed that even in the adjusted, representative sample of all participating hospitals, 21.5% of patients were treated with antibiotics (cf. Nationales Referenzzentrum für die Surveillance von Nosokomialen Infektionen 2016: 2, 20-21). While patients receive antibiotics for various reasons, e.g. to treat acute infections, they are also regularly over- or misused. Hence, it is hardly surprising that Fleming-Dutra et al. (2016: 1872) conclude their study with the remark that “[i]n the United States in 2010-2011, there was an estimated annual antibiotic prescription rate per 1000 population of 506, but only an estimated 353 antibiotic prescriptions were likely appropriate.”

Prior to humanity’s access to effective antibiotics in what can be called the pre-antibiotic era, millions of people had to suffer and die from bacterial infections.

But as wide as the range of medically appropriate and inappropriate antibiotics use is nowadays, the “arguably [...] greatest medical breakthrough of the 20th century” (Gautam 2022: 225), are relatively new in historical retrospect. The discovery of the famous *penicillin* dates back to 1928 and from here on it took several years – until 1942 – before it was ready for widespread market use. Thus, humanity can only look back at round about 80 years

of effective antibacterial medical treatment and even today not all people around the globe have access to (proper) antibiotics. So while humanity as a whole has several generations of antibiotics at its disposal, not everyone benefits equally, if at all, raising questions about adequate supply and just global distribution of these goods.

In addition to creating broad access to antibacterial treatment options, however, one problem is particularly urgent, namely the loss of antibiotic efficacy. By now, it has become increasingly evident that the “[b]acteria are fighting back and are becoming resistant” (Davies et al. 2013: ix) to specific substances used against them. From an evolutionary point of view, this can be seen as an adaptation process of the bacteria to the selection pressure to ensure their own survival. Certainly, resistance should not be equated with the complete ineffectiveness of antibiotics, as any resistance that occurs is a specific response of bacteria to a particular antibiotic and not a general response to every antibiotic. Therefore, in some cases, it is possible to modify treatment with alternative antibiotics to provide or restore effective antibacterial treatment. However, this is highly unlikely in cases of so-called multi-resistant bacteria, which are characterised by simultaneous resistance to various antibiotics making their treatment extremely difficult or impossible. Some pathogens such as *Staphylococcus aureus* have shown a high adaptability and are “capable of becoming resistant to all classes of antibiotics clinically available” (Vestergaard et al. 2019: 1). For this reason, multi-resistant bacteria are a particular threat as medicine and mankind lack adequate treatment options in such cases. Causing “more than 100 000 deaths attributable to AMR (antimicrobial resistance, the authors) in 2019” (Antimicrobial Resistance Collaborators 2022: 629, cf. 638) the notorious strain of *Methicillin resistant Staphylococcus aureus* is evidence of the danger that antibiotic resistance poses to human life.

The current scope of the problem and its future trajectory

Surely, the prior considerations provide a sufficient basis for the implicit premise of the argument at hand that antibiotic resistance is indeed a serious problem. This is mainly due to the undesirable consequences, which range from increased resource consumption, e.g. in the form of treatment costs or duration, to treatment failure, leading to the death of the infected patients in the worst case. Despite these potentially serious consequences, antibiotic resistance is often not perceived as the problem it actually is, adding another dimension to the problem’s complexity, which Engström (2021) has recently addressed in detail. However, the issues outlined are by no means news to anyone familiar with the field, as knowledge of these facts dates back to the early days of the scientific discovery of antibiotics (Friedman et al. 2016: 417). Pioneer scholars on bacterial infections, such as Fleming, who discovered *penicillin*, observed antibiotic resistance and the associated loss of this particular antibiotic’s effectiveness. In his Nobel Prize speech in 1945, Fleming (1964 [1945]: 93) stressed the importance of understanding that it is the bacteria itself that become resistant when he stated:

“Here is a hypothetical illustration. Mr. X. has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs. X gets pneumonia and is treated with penicillin. As the streptococci are now resistant to penicillin the treatment fails. Mrs. X dies.”

Providing this example, Fleming reminds everyone of the basic yet commonly misconceived fact that “[b]acteria, not humans or animals, become antibiotic-resistant.” (World Health Organization 2020). By particularly zooming in on the micro-level of the family, he accounts for the potential extent of the problem at hand, which is both individual and social. In a nutshell: On the one hand, resistant bacteria can be lethal for the infected themselves, making them a matter of concern on an individual level. On the other hand, Mrs. X’s contagion reminds us of the social aspects and effects of bacterial resistance. Fleming even anticipates the societal problems, as pathogenic bacteria may not stay in the organism in which they have developed their specific resistance but can spread in and through human interaction. Such direct effects of antibiotic-resistant bacteria go hand in hand with indirect ones and therefore “[t]he negative impacts of antibiotic resistance on healthcare systems as a whole are substantial, as resistance adds to the number of infections that occur, to expense, to interrupted hospital activity and to limitation of treatment options.” (Friedman et al. 2016: 420).

On the one hand, resistant bacteria can be lethal for the infected themselves, making them a matter of concern on an individual level. On the other hand, pathogenic bacteria may not stay in the organism in which they have developed their specific resistance but can spread in and through human interaction.

Already, these negative effects have taken their toll on humanity’s potential to provide antibacterial medical treatment. As such “[o]ur ability to cure infections that were once considered benign is already damaged.” (O’Neill 2016: 10). The danger of this becomes particularly clear when considering not only the possibility and impact of a global spread of bacterial infections, but also the speed with which this can happen in a globalised world connected by fast and almost non-stop traffic by land, sea, and air. Of course, bacterial spread depends on various factors, such as the respective specificity, overall survivability, and potency of transmission, but despite this, in the worst case such a spread could become devastating for humankind, as e.g., the plague pandemics demonstrate throughout history. Even without any major hotspots of bacterial outbursts, it is estimated that there are currently more than 670,000 infections with antibiotic-resistant bacteria per year in the European Union alone, resulting in roughly 33,000 deaths. Globally, untreatable bacterial infections account for not 700,000 deaths (not: infections) annually (cf. WHO Regional Office for Europe/European Centre for Disease Prevention and Control 2022: xiv; Antão/Wagner-Ahlf 2018: 501, Davies et al. 2013: xii). According to recent findings by the Antimicrobial Resistance Collaborators (2022: 629, 639), the problem is even bigger, with 4.95 million deaths worldwide associated with antibiotic resistance, of which 1.27 million are directly caused by antibiotic-resistant bacteria. So although there are some significant geographical differences, with sub-Saharan Africa and South Asia currently most threatened by antibiotic-resistant bacteria, antibiotic resistance is a health problem of global proportions.

Against this background, it becomes evident that cautionary or alarming statements according to which “AMR is a looming threat to the health of millions of people worldwide” (WHO Regional Office for Europe/European Centre for Disease Prevention and Control 2022: xii) do not describe an apocalyptic scenario of a distant future. After all, humanity is already in midst of an antibiotic crisis. As Friedman et al. (2016: 421) remind us,

“resistance and MDR (multiple drug resistance, the authors) bacteria have spread and the negative impacts of antibiotic resistance have become more apparent” for decades. Despite the fact that the problem continues to grow, however, the danger of antibiotic is still commonly underestimated. As problematic as current developments may be, they are “only the tip of the iceberg” (Davies et al. 2013: 36), as the dangers of antibiotic resistance that lie ahead are even bigger. The way we try to counteract, reduce, or prevent already existing antibiotic resistance today has enormous impacts both on current use of antibiotics but also on the future. This is the case for those alive today as well as the generations yet to be born. This is because antibiotic resistance and its effects are somewhat comparable “to a slow-motion car crash: sadly, it is one that has already started” (O’Neill 2016: 71) and that cannot be prevented anymore. In particular, this is due to the irreversible failures and omissions that have occurred to date. Historical and current overuse, misuse, and abuse of antibiotics, as well as negligence of investment, research, and development of new antibiotics or adequate alternatives have put future generations at risk of losing effective means to treat bacterial infections.

Like the climate crisis, antibiotic resistance is developing day by day beyond our collective perception. (...) Its effects are somewhat comparable to a slow-motion car crash: sadly, it is one that has already started.

On its current path, humanity is heading for a future escalation of the problems described, which will not only lead to poorer health care and an increase in the number of deaths, but also to severe economic consequences, as “[t]he impact of AMR on economic growth will result in a pronounced increase in extreme poverty.” (World Bank 2017: 22) One of the commonly cited prognoses “estimate[s] that by 2050, 10 million lives a year and a cumulative 100 trillion USD of economic output are at risk due to the rise of drug-resistant infections” (O’Neill 2016: 4 and 12). This very prominent projection must be taken with caution, especially because of its rather speculative nature due to the opaque methodology (Kraker et al. 2016; Foreman et al. 2018: 2085; O’Neill 2014). However, it cannot be dismissed entirely. One may reasonably disagree about the extent of the problem, but its current trajectory is crystal clear: Humanity is not putting enough effort into addressing the problem of antibiotic resistance and averting the scenario of a post-antibiotic era (Engström 2021: 21). Since our current handling of antibiotics and antibiotic resistance have a very significant impact on the future, this becomes not only a long-term issue, but also a question of intergenerational justice. For as medically and morally defensible as some of our current antibiotic use may be, it (re)imposes the extreme vulnerability to bacterial infections that has plagued humanity for most of its existence on future generations. The danger is imminent, because „if we allow resistance to increase, in a few decades we may start dying from the most commonplace of ailments that can today be treated easily.” (Davies et al. 2013: x)

This forecast underpins the World Health Organization’s (2020) urgent and point-blank reminder that “[w]ithout urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.” Notwithstanding the limitations that humanity already faces, if this post-antibiotic scenario becomes a reality, humankind will no longer be able to treat bacterial infections as it can today. As a result, future generations may no longer be able to benefit from the medical-

pharmaceutical achievements we have come to know, and indeed face an existential threat. With this in mind, the task ahead seems to be quite clear: Possible solutions for tackling antibiotic resistance are needed.

The possibility of a way out and its obstacles

Although the rampant antibiotic crisis is a serious problem, it does not necessarily have to reach catastrophic proportions. A closer examination reveals a whole spectrum of possible ways that humanity could try tackle antibiotic resistance. Those include (a) novel drugs, (b) alternative treatments, (c) improvements in diagnostics, (d) a reduction in irrational use, (e) a reduction in general use, (f) education on antibiotic resistance, and (g) preventive measures to prevent bacterial infection. Subsequently, all of these possibilities need to be discussed in order to assess to what extent they could be key factors – individually and in combination – to prevent the worst-case scenario of a post-antibiotic era.

(a) The first possible response to the antibiotic crisis is to research, develop, and disseminate new drugs. However, there have been no significant innovations in this area in recent decades. Ever since the so-called ‘golden age’ of antibiotics, roughly dating to the middle of the last century, there is a serious slowdown in research and development and “[s]ince the 1980s, newly marketed antibiotics were either modifications or improvements of known molecules.” (Iskandar et al. 2022: 1; cf. Kwon/Powderly 2021: 471. Friedman et al. 2016: 421). Whatever the reasons for this decline – scientific challenges on the matter itself, a lack of economic stimuli, or something completely different – may ultimately be, “[w]orldwide, the antibiotic development pipeline has all but dried up” (Dutescu/Hillier 2021: 416) and such omissions cannot simply be made up for. This is mainly due to long development periods as “[i]t typically takes 10 to 15 years to develop an antibiotic through regulatory approval.” (Kwon/Powderly 2021: 471). Of course, antibiotic development must not take that long necessarily and it might well be that, analogous to the development of vaccines during the SARS-CoV-2-pandemic, the combination of a societal need and an enormous economic and time investment could accelerate this process. Despite this possibility, one must always bear in mind that new antibiotics are ultimately only an interim solution, as the development of new resistances is very likely and “[t]he race between AMR and antibiotic discovery shall continue” (Iskandar et al. 2022: 28).

(b) In the face of this constant chase, it is worth exploring alternative therapies. Vaccines or bacteriophages are amongst the better-known options that might prove effective in offering protection against dangerous or even lethal bacterial infections (cf. Hutchings et al 2019: 78; Dyar et al. 2017: 795). Furthermore, there may be supplementary drugs or therapies making use of experimental evolution (Jansen 2013). Here, it might be possible to actively exploit the evolutionary process of the bacteria for a more refined, future treatment. However, as innovative as such approaches may be, their practical applicability is still uncertain at present and requires further research.

(c) Another and already foreseeable way in which scientific-technological progress could contribute to solving the problem outlined is an improvement in diagnostics of bacterial infection as “it is likely that in the near future the immediate identification of pathogens through rapid whole-genome sequencing and other technologies will cut the time it takes to diagnose a microbial infection.” (Davies et al. 2013: 53). Improvements in diagnostic procedures will help in choosing the most suitable therapy as fast

as possible. Especially in life-and-death situations, current methods often take too long, forcing doctors to treat bacterial infections as broadly as possible or rely solely on their best guess (cf. e.g., Davies et al. 2013: 51). However, for an optimally tailored therapy, knowledge of the exact pathogen is required. Otherwise, the right medication as well as the assessment of the optimal treatment duration, the possible change and specification of therapy or the administration of the drugs cannot be guaranteed. Hence, unlike precise diagnostics, suboptimal diagnostics is not only coupled with lots of uncertainty, but also often leads to inappropriate medication and the doctors resort to broad-spectrum antibiotics due to a lack of knowledge about the specific infection.

(d) Exactly such handling is part of the so-called *irrational* use of antibiotics, as opposed to a *rational* one in which “patients receive the appropriate medicines, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost both to them and their community.” (World Health Organization 2004: 75). Irrational use of antibiotics is widespread and there are various ways to address it, ranging from an introduction of quota regulations or taxation to legal restrictions on accessibility or intended use. Ultimately, the point of all this is to make it more difficult to sell and purchase antibiotics by strict requirements for prescriptions and according monitoring processes (cf. Davies et al. 2013: 65-66). However, the most prominent means to prevent irrational use of antibiotics seems to be so-called Antibiotic-Stewardship-programs, which promote “both the appropriate use of antimicrobials when they are indicated, as well as avoiding unnecessary use” (Dyar et al 2017: 794). Although there is still room for improvement, especially in terms of global coverage, the results of these programmes are remarkable. As the European Centre for Disease Prevention and Control, for example, has been able to show, such programmes are significantly associated with a lower incidence of antibiotic resistance. Accordingly, institutions such as the World Health Organization pledge to expand them, because they have not yet been (sustainably) established in many places and progress in this regard does only come in small and slow steps (cf. WHO Regional Office for Europe/European Centre for Disease Prevention and Control 2022: xii-xiv).

For an optimally tailored therapy, knowledge of the exact pathogen is required. Otherwise, the right medication as well as the assessment of the optimal treatment duration, the possible change and specification of therapy or the administration of the drugs cannot be guaranteed. Hence, suboptimal diagnostics often leads to inappropriate medication and the doctors resort to broad-spectrum antibiotics due to a lack of knowledge about the specific infection.

(e) Ultimately, such programmes help “minimising the use of antibiotics when they are not necessary to improve human health” (Antimicrobial Resistance Collaborators 2022: 649). However, for this to actually succeed, *all* antibiotic consumption must be reduced, and this includes proper usage of antibiotics. Such a reduction can by no means be limited to applications for humans, but must also include other uses, such as agricultural use in animal husbandry. The reasoning behind this is not only a more thoughtful general use, but also the possible “[s]pread and cross-transmission of antimicrobial-resistant microorganisms between humans, between animals, and between humans and animals and the environment.” (European Centre for Disease Prevention and Control 2008). Although there remain some uncertainties about those

interactions in detail, such as questions of causality (cf. e.g., Antimicrobial Resistance Collaborators 2022: 649), considering them could prove proactive in delaying or stopping the development of resistant bacteria. An overall more frugal use of antibiotics, where appropriate, might help prevent further harm to the public good of antibiotics.

(f) While this certainly could be associated with unpleasant experiences, e.g. in the form of longer rest periods, many bacterial infections can be cured without the use of antibiotics and without actual risk to patients. Education on this topic is key, as it could improve the antibiotic knowledge of practitioners, but especially of patients. Because, as of now, “[c]onsumers have positive attitudes towards antibiotics, but paradoxically [...] poor knowledge about these drugs and diseases.” (Merrett et al. 2016: 4). People are often unaware of the negative side effects of antibiotics as well as the basic mechanisms of these drugs, especially that not every antibiotic is suitable to treat every bacterial infection, but also the fact that we all contribute to the increasing resistance. Education could not only help to stop the demand for and granting of antibiotics when not medically indicated and clarify misconceptions, such as a benefit for colds or flu (cf. Davies et al. 2013: 48, 50), but also increase compliance so that treatment instructions are strictly adhered to in situations where antibiotics are necessary. Currently, patients regularly intervene in therapies by, for example, discontinuing medication prematurely, which, contrary to popular belief, is a major problem (cf. Antão/Wagner-Ahlf 2018: 500; Davies et al. 2013: 26) regarding antibiotic resistance, or by storing and reusing drugs without consultations.

But as important as the aforementioned possibilities are, the first step to address antibiotic resistance and a post-antibiotic era is anything but high-tech: “Minimizing the need for antibiotics through preventive health care and improved sanitation, housing, and access to clean water is achievable, as is ensuring that the right antibiotic is available and given at the appropriate dose for the appropriate duration.” (Palmer 2022: xi). Especially when it comes to patient health, stopping the spread of bacteria and sparing people from potentially deadly infections is a top priority. Measures to achieve this include not only social distancing and quarantining of infected individuals, but also simple aspects of personal hygiene that reduce or prevent transmission. This holds particularly true for proper hand hygiene, which is practiced by only a fraction of people (cf. e.g., Davies et al. 2013: 47).

Although the rampant antibiotic crisis is a serious problem, it does not necessarily have to reach catastrophic proportions. A closer examination reveals a whole spectrum of possible ways that humanity could try tackle antibiotic resistance.

Especially the last-mentioned aspects may appear very basic, but they are not only highly effective and sustainable, but also seem to be the most realistically implementable. In sum, there are several possible ways to address antibiotic resistance, but the issue’s high complexity requires “concerted efforts of microbiologists, ecologists, health care specialists, educationalists, policy makers, legislative bodies, agricultural and pharmaceutical industry workers, and the public to deal with.” (Aminov 2010: 3). Thus, if we agree on the general guideline of ensuring humanity’s access to antibacterial treatment in the future, this will require a broad range of actions and collective efforts by virtually everyone, as non-participation will hinder the necessary global endeavor. At the same time, however, these efforts must be adapted to specific regional

or geographic needs, as this may require better hygiene or sanitation in some areas, reduced use of antibiotics in animal husbandry in others, or simply better medical training (cf. Palmer 2022: x, Antimicrobial Resistance Collaborators 2022: 649, Davies et al. 2013: 70).

Conclusion: The (un)avoidable era of deadly bacteria upon us?

Overall, it is not impossible to avert the grim post-antibiotic era in which millions of people die each year from untreatable bacterial infections that scientists and organisations like the World Health Organization keep warning the global community about. Therefore, *Combating Antimicrobial Resistance and Protecting the Miracle of Modern Medicine* (National Academies of Sciences, Engineering, and Medicine 2022) is not a lost cause. At present, however, success is unlikely, and realistically, the goal of the initiatives taken can only be to reduce or at least slow down the problems at hand, not to completely avert the dangers outlined. Given the problem's current scope, it is not a question of whether antibiotic resistance is going to hit humanity, but only of how hard it will hit it and how much of an existential threat this poses. The past omissions in areas such as research and development, as well as the widespread failure to use antibiotics rationally, demonstrate a lack of political and societal commitment to a serious change in the way antibiotics are used. Furthermore, attempting to stop antibiotic resistance does come at a price – the most pressing one being the potential exposure of current patients to health risks in order to spare future ones.

Given the problem's extent, humankind does not only face the already difficult global and intergenerational challenge of providing „access to effective antimicrobials for all who need them, today and tomorrow“ (Dyar et al. 2017: 797), but possibly more extreme hardships in form of “the subordination of present advantages to the long-term exigencies of the future.” (Jonas 1984: 142). Antibiotic resistances and the horizon of a post-antibiotic era confront us with the question of whether it is morally imperative to restrict or withhold antibiotic therapies from patients *today* in certain situations, or even in general, in order to make them available to the same or other patients *in the future*. Addressing such questions, however, may lead to the realisation that intergenerational justice can only be achieved with a paradigm shift away from the idea of providing the best possible care for today's patients towards treatment that is sufficient to make sustainable antibiotic therapy more likely.

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