Chapter 1
Drug-Resistant Infection: Causes, Consequences, and Responses

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Abstract This chapter provides an overview of the causes and consequences of, and possible policy responses to, the problem of drug resistance. Throughout, we highlight the ways that ethical and conceptual analyses can help to clarify relevant issues and improve policy, especially in public health, broadly conceived. Drug resistant pathogens arise, persist, spread, and produce harm due to a complex set of causes: biological processes (e.g., related to microbial evolution, the transmission of genetic determinants of resistance between microbes, and human host immunity) as well as human behaviors (e.g., antimicrobial use and hygiene practices) and other social factors (e.g., access to clean water, sanitation, healthcare, and antimicrobials). Furthermore, the ethically salient consequences of drug resistance include not only morbidity and mortality from untreatable infections (that are often inequitably distributed), but also broader effects on human freedom, privacy, and well-being. Public health ethicists are ideally placed to identify and weigh the values that might be promoted or compromised by potential policies and/or interventions that aim to address the problem of drug resistance. This chapter concludes by discussing potential policy responses, including those related to surveillance, research, animal and human antimicrobial use, the broader social determinants of health, infection control practices, and vaccination.

Keywords Antimicrobial resistance · Drug resistance · Drug resistant infection · Ethics · Bioethics · Public health ethics

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1.1 Introduction

It is widely acknowledged that drug resistance poses one of the greatest threats to global public health during the coming decades. Drug resistance compromises the treatment of infections (that were commonly debilitating and/or fatal before the development of antimicrobial drugs), and thereby undermines many advances in surgery, cancer treatment, and immunosuppression that depend on our ability to treat infections effectively. Microbes – bacteria, mycobacteria, parasites, fungi, and viruses – have, over billions of years and untold numbers of microbial generations, developed mechanisms (via evolutionary processes) to protect themselves from harm and transmit such portective mechanisms to other microbes (of the same or different species) (Holmes et al. 2016). The rapid increase in antimicrobial drug resistance in the twentieth and twenty-first centuries is a result of these powerful evolutionary mechanisms combined with human activities that affect the microbial world, including the widespread production and use of antimicrobial drugs. Resistance is a matter of degree (for example, low levels of resistance can be overcome with a higher dose or longer course of antimicrobials) and its impact is also relative to the availability of alternative treatments (where second line drugs are readily available, resistance to first line agents may initially be less of a concern). Thus, the recent emergence of strains of clinically important pathogens that are highly resistant to all, or nearly all, available therapies (e.g. extensively drug-resistant tuberculosis (TB) and pan-resistant gram negative bacteria) is an urgent challenge for public health (Schwaber et al. 2011; Birgand et al. 2016; World Health Organisation 2017a).

Drug resistance is an important topic for ethical analysis since (i) human actions and inactions are major contributors to the problem, (ii) the consequences for human health and well-being are highly significant and inequitably distributed, and (iii) policies aiming to reduce the rates of resistant pathogens may involve balancing this reduction in risk with other morally salient risks, burdens, and benefits. Thus, this volume aims to provide a timely exploration of many of the ethical aspects of the phenomenon of drug resistance. This first chapter highlights the complex causes and significant consequences of drug resistance, and the ways in which ethical and conceptual analysis can inform and improve relevant policy responses. We link these discussions with other chapters in this volume, as well as gesturing towards future directions for ethicists, empirical scientists, and public health policymakers.

1.2 Causes

1.2.1 Evolution and Transmission of Resistance Genes

The microbial world is ancient, abundant, ubiquitous, and complex. As a result of random mutation over trillions of microbial generations, bacteria have adapted to their environments, in part by developing genes that code for mechanisms of resistance to various threats – including, for example, heavy metals, naturally occurring

antibacterial compounds (including beta-lactams such as penicillins and carbapenems) and synthetic antimicrobials (e.g. fluroquinolones and sulphonamides) (Holmes et al. 2016; D'Costa et al. 2011). Certain microbes are also able to horizontally transfer genes coding for resistance mechanisms to other microbes (Holmes et al. 2016; Chang et al. 2015). With the dramatic, unprecedented increase in human interventions in the microbial world (especially the widespread use and overuse of antimicrobial agents), strong evolutionary selection pressures have been applied to microbes leading to the emergence, increasing frequency, and persistence of resistant microbes in humans, animals and the environment (Holmes et al. 2016).

1.2.2 Antimicrobial Use in Humans

In his 1945 Nobel Prize speech, Alexander Fleming (who first discovered the antibiotic properties of penicillin) famously noted 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). If antimicrobial treatment is inadequate, that is, then resistant strains of microbes that otherwise would have been killed off may survive and become more strongly established in the absence of microbal competitors, in the environment of a person's body. Resistant pathogen strains thus selected can then be transmitted to other persons. For pathogens like tuberculosis (TB) and HIV, requiring months (or, for HIV and extensively drug-resistant TB, years) of multi-drug therapy, undertreatment (e.g. due to 'noncompliance' of patients, or inadequate access to medicine, etc.) has played a central role in the emergence and persistence of highly resistant strains (see Chaps. 2, 3, 5, 10 and 26). In the case of malaria – where, for various reasons, parasites may be exposed (in human patients) to sporadic and/or sub-therapeutic concentrations of antimalarials, sometimes as a result of partial treatment – underuse of drugs likewise plays a role in the emergence of antimalarial resistance (White 2017) (See Chap. 4).

In the case of antibiotic resistance in common bacterial pathogens, however, *overuse* of antibiotics is far more important than undertreatment. Despite years of rhetoric regarding the need to 'complete the prescribed course' for common uncomplicated bacterial infections, this now appears, except among a subset of pathogens and specific sites of infection, to have been ill-founded[1] and, on balance (when generalised to all infections), harmful advice (Llewelyn et al. 2017). Overuse and 'appropriate' use are much more dominant causes of resistance. This is because the human body (particularly in the digestive and respiratory tracts, and on the skin) contains billions of bacteria, many of which are indiscriminately exposed to an antibiotic used either appropriately to treat one particular pathogen (e.g. bacterial pneumonia) or inappropriately (e.g. a viral infection mistaken for a bacterial

[1] In part because, until recently, few trials had addressed the question of whether shorter courses for common infections may be just as effective, with less development of resistance (and less side effects) – the few trials that have now been done generally support the use of shorter courses in uncomplicated infections.

infection) (Llewelyn et al. 2017; Carlet 2012). Exposure to more antibiotics in a given individual is predictive of a higher rate of asymptomatic carriage of resistant pathogens (although this rate does decrease over time) (Nasrin et al. 2002; Bryce et al. 2016). These resistant bacteria, although in usual circumstances causing no harm, can lead to invasive (resistant) disease – for example when a person's skin is cut or incised by a surgeon, or when bowel bacteria spread to other locations in a person's body, or when a person becomes immunosuppressed (Tischendorf et al. 2016; Safdar and Bradley 2008). Those who thus become 'carriers' of resistant bacteria can transmit such pathogens to others (whether the initial carrier is symptomatic or not) (Smith et al. 2004; Lerner et al. 2015; Jamrozik and Selgelid 2019).

Overuse of antibiotics in humans is thus a collective action problem – in some respects a classic 'tragedy of the commons' (Hardin 2009), but complicated, *inter alia*, by the transmission of resistance between pathogens and also the transmission of resistant pathogens between humans.[2] The (simplified) structure of the collective action problem is that each doctor or patient seeks individual benefit of the patient (minimising the risk of severe bacterial infection) by, respectively, prescribing and taking antibiotics even in cases where this may have only marginal expected benefits for the patient; but their decisions/actions collectively (in conjunction with other causal factors) bring about high levels of antibiotic resistance – which, in the long term, is a major threat to all.

Problematic treatment decisions (that contribute to resistance) are sometimes related to diagnostic uncertainty. When a patient has symptoms associated with respiratory illness, for example, there is often no sufficiently rapid and accurate test to determine whether it is caused by a bacterial pathogen. As a result of this uncertainty, combined with risk-aversion among doctors and patients, and a (mis)perception that a course of antibiotics 'does no harm' (or that the risks of side-effects and generating resistance are outweighed by potential benefits[3]), millions of antibiotics each year are taken when they are not required. Solutions that rely on individuals acting in accordance with the social optimum (especially if, in doing so, they take on more risk to themselves) are, at best, incomplete or, at worst, doomed.

The problems of both antimicrobial overuse and underuse are magnified in some low- and middle-income countries where many people lack access to basic diagnostic testing and antimicrobials—and/or where antimicrobials are commonly available without prescription (Holmes et al. 2016; Laxminarayan et al. 2016; Dar et al. 2016) (see Chap. 5). There is an inherent tension between 'access and excess', i.e. many die because they are unable to obtain diagnosis and/or antimicrobial treatment

[2] In standard commons tragedies, such as overfishing, individuals collectively deplete a common resource (e.g. by fishing), ultimately leading to its collapse. In the case of drug resistance, the resource (e.g. effective antimicrobials) can be depleted (in a way akin to standard depletion) through use of antimicrobial drugs, leading to resistance, but also, for example by the transmission of drug resistant strains from one person to another (regardless of whether either has recently used antimicrobials) – thus the relationships at play may be more complex than standard commons tragedies.

[3] The actual (as opposed to perceived) risks and benefits are rarely quantified 'at the bedside'.

when it is really needed while, at the same time, antibiotics are used when they are not required, leading to resistance. This, in turn, exacerbates problems of access – because the second line drugs required (after first line drugs have been rendered useless) are more expensive/less affordable (Laxminarayan et al. 2016; Dar et al. 2016). In parallel, the transmission of resistant pathogens is amplified by a lack of access to readily available clean water, sanitation, and well-resourced healthcare institutions. The burden of drug-resistant infections thus tracks poverty and social disadvantage both within countries and internationally (Llewelyn et al. 2017; Bryce et al. 2016; Guh et al. 2015) (See Chap. 16).

1.2.3 Transmission

Drug-resistant microbes are transmitted between human beings just like other non-resistant pathogens – via airborne or droplet transmission, skin contact, the faecal-oral route, sexual transmission, contact with infected bodily fluids, contaminated water and food, vector transmission (e.g. mosquitoes in the case of malaria), and so on. The epidemiological significance of transmission of some pathogens in some contexts is relatively well understood, whereas the transmission of the same pathogens in other settings may be different and/or less well-studied. In the case of drug-resistant bacteria, for example, in-hospital transmission is well-documented. Such transmission often occurs via contamination of the clinical environment and via healthcare workers – especially those who fail to adhere to basic hand hygiene practices (see Chap. 6), although controversy surrounds the optimum infection control policies to prevent transmission (Morgan et al. 2017). However, the transmission of resistant bacteria (and antibiotic resistance mechanisms) in the general community (i.e. outside healthcare facilities) is poorly understood, and much more evidence is needed to guide policy (Holmes et al. 2016; Dar et al. 2016). Transmission in the community is facilitated not only by direct human contact, but also general environmental contamination with resistant pathogens, the mobile genetic elements that confer resistance, and even antibiotics themselves – with polluted water systems being a key link in indirect transmission between human beings, and between animals and humans (Pruden et al. 2013; Martinez 2009). This problem is of greatest concern in low-income settings with poor access to clean water and sanitation, further exacerbating the inequitable distribution of harms from drug-resistant infection (Laxminarayan et al. 2016; Dar et al. 2016).

The global spread of drug resistance is greatly facilitated by modern air travel. Millions of people become colonised (usually without symptoms) with resistant pathogens or other (non-pathogenic) microbes containing genetic determinants of resistance every year in locations with high rates of resistance and then fly to regions where (whether or not those colonised are sick) resistant pathogens and/or resistance determinants are directly or indirectly transmitted to others (Kennedy and Collignon 2010; Östholm-Balkhed et al. 2013).

1.2.4 Antimicrobial Use in Animals and Agriculture

The widespread use of antibiotics in industrial agriculture and aquaculture, either as 'growth promoters' or in other mass prophylactic uses, has lead to pathogens developing resistance to the agents used. This has had consequences for both animal and human health. Consequences for humans occur when clinically significant pathogens (and/or resistance determinants) are transmitted from animals to humans (either directly via animal contact or consumption of animal products, or indirectly via environmental contamination with resistant pathogens and/or resistance determinants), when humans are themselves exposed to antibiotics used in the food chain (either in the products they consume, or because antibiotics and antibiotic residues are released into the environment), or when humans are exposed to pathogens (or other microbes) that become resistant (and/or carry resistance determinants) as a result of exposure to antibiotics in enviroments contaminated by agricultural use (Holmes et al. 2016; Schwaber et al. 2011; Birgand et al. 2016; Chang et al. 2015; Martinez 2009).[4] The links between animal and human health via our shared microbiome are complex, and the relative importance of different causal pathways in a particular setting is often difficult to quantify (Chang et al. 2015) (See Chap. 7). Likewise, although the agricultural industry uses more antibiotics in total tonnage than human healthcare, the relative contribution of agricultural antibiotic use to the epidemiology of resistant bacterial disease in humans is difficult to study, often unknown and likely varies widely in different settings (Holmes et al. 2016).

1.3 Consequences

1.3.1 Direct Harms to Human Beings

The true global burden of death and disease due to resistant infection is unknown, and from both ethical and scientific points of view there is an urgent need for more accurate estimates. One prominent appraisal published in 2015 suggested that at least 700,000 deaths occur each year due to drug-resistant infection worldwide, and that this annual death toll could rise to ten million by the year 2050 (Antimicrobial resistance: Tackling a crisis for the health and wealth of nations 2015). However, this analysis included only 6 pathogens and acknowledged that the true number is probably already far higher, especially given that more of the burden of disease falls on poor communities that often have incomplete disease surveillance systems and limited access to relevant diagnostic technology (Laxminarayan et al. 2016).

[4] In (1) microbes become resistant due to their exposure to antibiotics in animals' bodies; in (2) microbes become resistant due to their exposure to antibiotics in people's bodies (resulting from people's exposure to antibiotics in contaminated environments); in (3) microbes become resistant due to their exposure to antibiotics in contaminated environments.

The inequitable distribution of harms from resistant disease mirrors the inequitable distribution of infectious disease burden more generally. In both high- and low-income countries, the heavy burden disproportionately shouldered by impoverished people and communities is largely explained by 'social determinants of health' (e.g. lack of access to clean water, sanitation, wealth, education, access to a robust health system, etc). On many accounts of justice, wealthy individuals and societies have strong moral reasons to improve these basic determinants of public health for all (Selgelid 2008). Furthermore, since resistant pathogens (like other pathogens) spread across borders, the wealthy have increasingly strong self-interested reasons to provide assistance to others and to prevent others from developing resistant disease.

High rates of resistant pathogens (especially common bacterial species) undermine many of the advances of modern medicine – because the successes of surgery, transplantation, cancer treatment, immunosuppression, intensive care, and obstetric and neonatal care are very often contingent on being able to treat and cure infections. Increasing drug resistance thus has widespread implications for health and healthcare. Although patients who are unwell with other comorbidities are at the highest risk (both of carrying resistant pathogens – due to recurrent treatment and hospitalisation – and of invasive disease from these pathogens), even relatively healthy people are, and will increasingly be, harmed by resistant infectious disease.

Before the advent of antibiotics, a simple skin wound could lead to untreatable sepsis, amputation and/or death, and a 'post-antibiotic era' would entail a return to similarly grim prospects. Increasing drug resistance thus severely threatens the entire global population and, in addition, future generations.

1.3.2 Economic Consequences

Along with direct harms, drug resistance has severe economic consequences. Drug-resistant infections are more difficult (sometimes impossible) and more expensive to treat and cure, and they are more likely to result in incapacitation of the patient and significant economic losses for society. One estimate suggested that total global losses due to resistant infection between now and 2050 could total over $US 100 trillion (O'Neill 2015), meaning that there are powerful economic reasons to devise and implement effective measures to curb the problem (See Chap. 17).

As noted in several chapters in this book, the *availability of effective antimicrobials* has many features of a 'public good' in economic terms. Standard economic models predict (more or less accurately) that a free market in antimicrobials (i.e. with little or no regulation of access apart from price) leads to 'market failure' and the erosion of the good in question (i.e. availability of effective antimicrobials). In most societies, since access to antimicrobials occurs via healthcare practitioners, the 'market' is relatively controlled (as opposed to free). The incentive structures that lead to a collective action problem for doctors and patients (discussed above)

nevertheless lead to a similar erosion of antimicrobial effectiveness – albeit at an attenuated rate, depending upon the degree to which regulations on prescriptions succeed. Private healthcare providers, in any case, can be difficult to regulate (see Chap. 5), especially where they are not part of a centralised and/or universal healthcare system.

1.3.3 Burdensome Public Health Interventions

The consequences of drug resistance for human beings are more than just matters of physical health and wealth. In many cases, public health surveillance and related public health practices have ethically salient implications for other aspects of well-being, including psychological well-being (e.g. due to experiences of stigma among carriers of resistant microbes – see below), as well as privacy and other freedoms (e.g. which are compromised by mandatory physical/social distancing measures such as isolation and quarantine). Well-designed public health surveillance and research should be conducted in order to clarify the health risks and costs of resistant infection and the risks, benefits, and burdens of potential public health interventions. High quality data would help policymakers determine whether imposing certain burdens on individuals would be justified as a means to improve public health (e.g. by reducing infectious disease due to resistant organisms) (Fairchild and Bayer 2004). Unfortunately, investment in surveillance for resistance has, globally, been very low and is only just starting to be improved, particularly in wealthy settings.

Those identified by surveillance as carriers of resistant pathogens while inpatients in healthcare settings sometimes experience stigma (Rump et al. 2017) as well as a wide range of effects on well-being, which some argue are best understood through a capabilities approach that explores the broader implications of public health policies for the flourishing of individual lives (see Chap. 13). Such an approach may also help to illustrate the broader aspects of human life that are jeopardised by the lack of access to effective antimicrobials, especially among children, for whom early severe infection may impair long term development (see Chap. 14).

Indeed, as more people become aware of resistance, and more community surveillance is conducted, apparently healthy individuals in the community may be increasingly identified as asymptomatic carriers of resistant organisms (See Chap. 12). Furthermore, such individuals might be monitored, offered or required to undergo treatment, and have other liberties (freedom of movement, free choice of occupation) curtailed by public health policy (Houston and Houston 2015). Those who have had recent contact with carriers might be tested and/or quarantined. There is thus frequently a tension between the aim to protect public health (by identifying infected individuals and reducing transmission of (resistant) disease) and the aim to avoid imposing significant burdens (in terms of compromised well-being, privacy and/or liberty) on individuals in order to prevent the spread of disease to others (Viens et al. 2009).

1.4 Responses

1.4.1 New Drugs

For many decades, even where the emergence of drug resistance was recognized, much of the response (or lack thereof) by individual clinicians as well as policymakers was grounded in (apparently unfounded) confidence that new antimicrobial drugs would be discovered and developed, meaning that resistance to older drugs was of limited significance. Despite early warnings of the consequences (Holmes et al. 2016; Honigsbaum 2016) – profligate use continued and indeed accelerated in humans, animals, and agriculture. Meanwhile, the restricted use of new antimicrobials as 'reserve' agents – although it may help to slow the emergence of resistance – means that there are disencentives to (profit-motivated) research and development of new antimicrobials. For this and other reasons, few new antibiotic classes or agents have been developed in recent decades (Norrby et al. 2005). Boosting more relevant research and development may thus require more public effort/funding and/or realignment of pharmaceutical companies' incentive structures (i.e. so that profit making becomes more compatible with developing products that are most important to global public health) (Banerjee et al. 2010).

New drugs (or other means of treatment/prevention) are arguably most urgently needed for infections that have become nearly pan-resistant (e.g. extensively drug-resistant TB, or multi-resistant gram negative bacteria). Vis-à-vis other responses that target particular causal pathways (e.g. restrictions on prescriptions practices or agricultural use) they would provide a cross-cutting solution to the problem of drug resistance – i.e. addressing the problem regardless of the specific mechanisms by which it was brought about.

It is clear, however, that policymakers (and, indeed, patients) cannot rely on new drugs to 'fix' the problem(s) of drug resistance, since (i) the development of new antimicrobial drugs has, in recent decades, been slow and/or relatively unsuccessful, (ii) the challenges underlying difficulties with drug development have thus far proven difficult to overcome, and (iii) without other interventions to curb the increase in drug resistance, we face a never-ending problem of finding new drugs. Thus, drug resistance requires a multi-faceted and global policy response – yet one that is also tailored to the specific problems and mechanisms of resistance in a given microbe and a given context.

1.4.2 Research and Surveillance

Apart from finding new treatments, other kinds of research are urgently needed, including empirical research in diagnostics, microbiology, vaccines (and other non-drug interventions), as well as social science and public health systems research (Dar et al. 2016). As a starting point, there are large gaps in our knowledge of the

epidemiology of most resistant pathogens. Improving local and international public health surveillance would help to determine the impact of various resistance mechanisms and evaluate the cost-effectiveness of interventions. Yet this, in turn, requires development of cost-effective and publically acceptable surveillance mechanisms that can be more widely implemented, including in LMICs, and political and scientific agreement on which data will be collected and shared (Tacconelli et al. 2017). It also requires careful attention to the ethical conduct of public health surveillance (World Health Organisation 2017b).

1.4.2.1 Reducing Use in Humans

There is an urgent need to reduce antibiotic use in human patients. The most ethically straightforward cases are those in which a person is prescribed (or purchases without prescription) an antibiotic (with a risk of side-effects and resistance) for a condition for which it will provide no benefit (e.g. a viral illness) or where a shorter course of antibiotics is as effective as a longer course but the latter confers an increased risk of resistance and/or side-effects. In such cases, antibiotic use constitutes a net harm to the individual and, through the risk of transmission of resistant organisms, to others.

One strategy to reduce use is to develop new diagnostics, so that patients and doctors can avoid using antibiotics where they are not required. But in the absence of perfect tests, changes in professional and public culture are also required. For example, doctors should address their own cognitive biases (see Chap. 8) as well as patient concerns about avoiding the complications of infection, and public awareness campaigns must emphasize that antibiotics are often not required and can themselves entail significant risk (to individuals and public health) (World Health Organisation 2015). International data suggest that some countries have made significant progress in reducing antibiotic use without a significant increase in severe infections (Bronzwaer et al. 2002).

Yet, as effective antibiotics become more and more scarce, there are more difficult ethical tradeoffs to be considered, involving greater uncertainty. For example, if antibiotics become reserved for severe and/or complicated infections – so that use is banned or dramatically reduced for patients with simple infections – many patients with a simple bacterial infection (e.g. mild pneumonia) may end up being more unwell for longer, or even at a small risk of severe outcomes (even though the vast majority will ultimately recover without specific curative treatment), because they do not have access to antibiotics.

Policy to reduce use in either the low risk or the higher risk cases cannot rely entirely on individuals, since the structure of the underlying collective action problem leads to strong incentives to ‘free-ride’ on others’ reduction in use. Thus, some form of regulation is required – e.g. through antimicrobial stewardship (which has been a successful but resource intensive approach in healthcare institutions), and/or restrictions on physician prescribing. How best to design and enforce such regulation is an important matter for debate in public health ethics.

1.4.2.2 Reducing Use in Animals and Agriculture

As argued in later chapters of this volume (see Chaps. 7 and 18), antibiotic use and overuse in agriculture must also be reduced. First and foremost, many have argued that the widespread use in animals of agents that are critical to human health should be dramatically reduced and/or prohibited, especially when such agents are employed for non-therapeutic purposes (e.g. as 'growth promoters') (Marshall and Levy 2011; World Health Organisation 2017c). But even other drugs (and non-drug agents) may lead to the co-selection of resistance determinants for critical drugs among bacteria (and fungi) shared between animals and humans. The overuse of antibiotics in agriculture in part represents a palliative for the high rates of infection in crowded 'factory farms', suggesting that reforming farming practices would have the dual benefits of reducing animal cruelty and reducing drug resistant infections. Reducing or eliminating meat consumption would also obviate many of the dangers to humans of resistance in animals (although not all, since companion animals can also transmit drug-resistant infection (Guardabassi et al. 2004)). The fact that some wealthy countries have dramatically reduced or eliminated profligate antibiotic use in farm animals (in part by giving animals more space and improving infection control practices) often at little or no long term economic cost suggests that it is possible to minimise this driver of drug resistance (McEwen et al. 2018). Whether such practices will be successfully implemented in lower income countries remains to be seen (Dar et al. 2016).

1.4.2.3 Addressing Social Determinants of Health

Infectious diseases, in general, are more prevalent among poor people and communities in both high and low-income countries. Many aspects of social organization and the built environment (water and sanitation systems, health systems, etc.) alter the risk of acquiring infection, and the risk of transmission of resistance mechanisms. Historically, improvements in living conditions arguably contributed more to the decline in infectious diseases in developed/industrialised countries than discoveries of vaccines or antimicrobial treatments (McKeown 1976). One way of reducing the prevalence of drug resistant infection would be to reduce its incidence and transmission by addressing these (and other) such social determinants of health.

The rise of untreatable infections provides a new, and urgent, rationale to ensure universal access to the social conditions that enable healthy living. Even basic measures, especially if provided to all, could help minimize the transmission of resistance (e.g. by providing access to clean water and sanitation) and reduce the use of antimicrobial drugs (e.g. by providing access to high quality, and well-regulated, health systems). Since resistant infections routinely spread via international travel, wealthy nations have reasons not only to act locally but also to act globally by assisting others with less resources (see Chap. 21) – to reduce the incidence and international transmission of resistant infection (Selgelid 2008).

1.4.2.4 Infection Control

Infection control involves measures that aim to reduce the transmission of pathogens in an institution or community. In healthcare institutions, this typically involves screening of patients, monitoring of those carrying (and/or suffering disease from) resistant pathogens, use of personal protective equipment, and social distancing measures such as isolation and quarantine. In some cases, it also involves decolonization of patients. Methicillin-resistant *Staphylococcus aureus* (MRSA) decolonization, for example, involves the use of antibacterial solutions on the skin, hair, and nasal membranes. More dramatically, recent studies have reported successful use of faecal transplantation to decolonize those with highly resistant bowel organisms (Freedman and Eppes 2014; Crum-Cianflone et al. 2015). In many cases, screening for resistant pathogens in hospital does not involve/require informed consent of patients, on the grounds that screening and control measures are required in order to prevent harm to others. Such policies should nonetheless be based upon careful ethical justification as well as, where possible, evidence of cost-effectiveness (see Chap. 6), especially insofar as they infringe on the lives of individual carriers (who may or may not be symptomatic) in significant ways (see Chap. 13).

Infection control policies become more complex when they are applied in the general community. As more people in the community are identified as carriers of highly resistant pathogens, it remains to be seen what kinds of restrictions of individual liberty would or shoud be considered justifiable. When, if ever, for example, should travellers be screened on arrival from high-risk regions – and when should those who test positive for resistant organisms be offered (or required to have) decolonization – and/or be subject to monitoring and/or social distancing measures? Important questions such as these need to be considered (and re-evaluated) as more is learned about community and international transmission of drug-resistant organisms.

1.4.2.5 Vaccines

Vaccines are a cross-cutting intervention with the potential to obviate the need to prescribe antimicrobials for a range of pathogens. In some cases, furthermore, vaccines can prevent infections that would otherwise be untreatable/uncurable (e.g., due to high levels of drug resistance). Existing vaccines against tuberculosis and some bacterial infections (e.g. *Streptococcus pneumoniae, Haemophilus influenzae*) reduce the incidence of infections due to these pathogens and thereby reduce the use of relevant antimicrobials (Dar et al. 2016). Vaccines against specific resistant strains may also lead to their replacement (e.g. in a given ecological niche in the human body) by strains that are easier to treat (Dar et al. 2016), although longitudinal surveillance data regarding strain epidemiology and disease burden are needed to confirm whether such effects lead to a long-term net public health benefit.

Even effective vaccines against viral infections (e.g. influenza, common cold viruses) can lead to a marked reduction in antibiotic use since viral infections are often erroneously treated with antibiotics (Neuzil et al. 2000). New vaccines against malaria and typhoid may help to reduce antimicrobial use and resistance relevant to these pathogens. Because there is a great number of resistant pathogens for which we lack vaccines, however, this is an important area in need of further research and development.

Of course, discovering an effective vaccine may lead to the replacement of one collective action problem (antimicrobial overuse) with another (assuring high vaccination rates) – meaning that even this 'technical fix' would have limitations. Like the development of new drugs, in any case, new vaccines would form only one part of the multi-pronged approach needed to control the problem of drug resistance.

1.5 Conclusions

Drug-resistance is widely recognised to be one of the greatest threats to global public health in the coming decades. Its causes are complex, and more work is needed to determine the relative importance of different causes. The consequences for human health are already highly significant, and, if left unchecked, will be even more dramatic in the near future. These harms, taken together, represent a large, likely underestimated, and ethically salient burden of disease that disproportionately affects underprivileged people and communities worldwide. Yet the presence of untreatable and potentially fatal pathogens and the prospect of such infections becoming more common is a threat to all. Despite current uncertainties and urgent gaps in our knowledge regarding drug-resistant infection, there is a pressing need to develop and implement ethically informed policies to reduce rising levels of resistance and thereby mitigate or avert future harms and injustices. We hope that the subsequent chapters of this volume will make a significant contribution to this important area of public health ethics.

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