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Review Article

Review on Ethical Approaches to Antimicrobial Resistance

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Abstract

The world is fast approaching a time whereby people will die from infections because there are no longer any effective drugs. This will change the face of medicine, as we know it, since many modern medical procedures are highly dependent upon antimicrobial protection. This might appear to be chiefly a problem for doctors and scientists but the nature of widespread AMR embodies a large number of ethical and moral issues, influencing every aspect of infection management and potentially affecting everyone. The objectives of this review is to introduce and discuss some of the most important ethical approaches associated with AMR and its control, including national and international responsibilities, pharmaceutical companies, prescribing, education, advertising, veterinary and agricultural practices, infection control and patient behaviour. Given the enormous importance of antimicrobial drugs for the functioning and delivery of modern health care, the progressive exhaustion of effective antibiotics presents health care professionals and policy makers with a distributive dilemma that raises complex moral questions of justice, especially how to fairly allocate antimicrobial resources.

ABBREVIATIONS

AMR: Antimicrobial Resistance; AR: Anti Resistance; ABR: Antibiotic Resistance; CDC: Centre for Disease Control; GAP: Global Action Plan; GTAMR: Global Threats Antimicrobial; IDSA: Infectious Disease of society of America; WHO: World Health Organization

INTRODUCTION

Antimicrobial resistance (AMR) is the ability of a microbe to resist the effects of medication that once could successfully treat the microbe [1]. The term antibiotic resistance (AR or ABR) is a subset of AMR, as it applies only to bacteria becoming resistant to Antibiotic. Resistant microbes are more difficult to treat, requiring alternative medications or higher doses of antimicrobials. These approaches may be more expensive, more toxin or both. Microbes resistant to multiple antimicrobials are called multi-resistant. Those considered extensively drug resistant or totally drug resistant are sometimes called “superbugs” [2]. Numerous biological, behavioral, economic, environmental and social factors contribute to the production and propagation of AMR. Resistance arises through one of three mechanisms: natural resistance in certain types of bacteria, genetic mutation, or by one species acquiring resistance from another [3].

All classes of microbes can develop resistance. Fungi develop antifungal resistance. Viruses develop antiviral resistance. Protozoa develop antiprotozoal resistance, and bacteria develop antibiotic resistance. Resistance can appear spontaneously because of random mutations. However, extended use of antimicrobials appears to encourage selection for mutations which can render antimicrobials ineffective [4].

Antimicrobial resistance (AMR) is one of the most serious health threats to individual and population of the 21st century. It challenges effective treatment of infectious diseases, now and in the future. AMR may imply that infections that used to be relatively harmless will pose a severe threat to patients in the future [5]. Many countries have implemented measures to control AMR, including proper use of antimicrobial drugs in humans, minimization of antimicrobial drug use in animals, and prevention of further transmission of resistant microbes within the healthcare system [1]. AMR raises a range of ethical questions which explored ethical issues that arise in relation to carriage of antimicrobial drug resistant organisms [6].

The Centres for Disease Control and Prevention estimate that as much as $20 billion in direct health care costs and $35 billion in lost productivity are associated with AMR to the US economy annually due to ABR [7]. A report commissioned by the UK government last year suggests that the death causalities of AMR could be as high as 300 million people until 2050, with an estimated total financial loss of up to $100 trillion [8].

This calculation includes not only the effect of resistance

against antibiotics but also against antiviral drugs, antimicrobial resistance is certainly indicative of the vast scale and seriousness of the world problem. Antimicrobial agents play a huge role in medical practice. The facility for healthcare services to reliably cure the infected patient has saved countless lives over the last century. Since the discovery of penicillin by Alexander Fleming in 1928, antibiotics have revolutionized patient management, with the 1950-1970's known as the "golden era of antibiotics." Nowadays, increasing resistance is seen as a major problem, since there have been diminishing numbers of novel antibiotics approved since the late 1970's .It appears that the microbial propensity to develop resistance is occurring much faster than man's ability to develop new agents.

The possibility to restrict the use of antibiotics as far as manageable to insure their continued effectiveness [9]. On the other hand, we have not yet managed to ensure the provision of adequate access to antibiotics in many regions of the world, where the price of drugs is often prohibitive for patients and where over-the-counter sales have led to an unregulated and uncontrolled use of antibiotics [10]. Therefore, faced with a situation in which we have to reduce the excessive use of antibiotics in some regions of the world while ensuring access in others. At the same, around half of the world's production of antibiotics are still used in animal and fish farming, which has created reservoirs for resistant bacteria and exacerbates the problem further [11]. Efforts to make progress on antimicrobial resistance issues require us to raise confront and enact some difficult ethical decisions that will affect the lives, relationships and personal projects of millions of people [12].

The ethical approaches of AMR focuses on the way in which drug resistance exacerbates problems associated with infectious disease control, e.g., the restriction of individual liberty for the sake of public health. These are undoubtedly important issues that must be addressed, especially in the context of drug-resistant, where prolonged treatment and decreasing treatment success has led to growing numbers of contagious patients that do not respond to first-line therapy [13]. However, there are various additional ethical approaches, which a comprehensive response to AMR must address, and which have so far not been adequately addressed by researchers, practitioners and policy makers.

The ethical approaches of AMR functions as an introduction for ethical approaches to antimicrobial resistance, which includes contributions exploring various philosophical, political and ethical issues raised by the problem of AMR. The event brought together experts from different academic disciplines, including medicine, public health, philosophy, economics and law, and provided a platform for discussion and the exchange of ideas across disciplinary boundaries AMR.

Therefore, the objective of this study is with the following Objectives:-

To Review on ethical approaches to Antimicrobial resistance To Highlight why AMR is an ethical approach issues

To assess what specific moral questions it raises and

To review how broadly approach the ethical issues raised by AMR

LITERATURE REVIEW

Concept of Antimicrobial Resistance

Antimicrobial resistance (AMR) is one of the most serious health threats to individual and population of the 21st century. It challenges effective treatment of infectious diseases, now and in the future. AMR may imply that infections that used to be relatively harmless will pose a severe threat to patients in the future. AMR is more than a problem that arises as a result of the complications of treating infectious diseases; it is a complex, many-sided global challenge that affects the environment, human and animal health, agriculture and the economy. The impacts of AMR in a present day are a distinctive and significant ethical issue of the world. AMR is putting current and future populations at substantial risk of injury, loss and death. It is going to require a redistribution of resources and a balancing of benefits and burdens, which in turn forces us to make a number of individual and collective sacrifices often for people thousands of kilometers away and for future persons who have not come into existence yet. This will include questions about who is morally responsible for this predicament and whether ascriptions of blame or sanctions should affect who should bear the costs of this problem. It is also going to require us intentionally, and sometimes coercively, shape the institutional structures and individual behaviours of governments, corporations, scientists, clinicians and patients, which raise questions about important moral values such as solidarity, liberty, privacy, reciprocity, fairness and the common good [14].

The worth of AMR explore some of the broad themes that make AMR is a moral issue and how to consider the facing problem of AMR requires recognition of ethical implications and their need to be addressed as part of any successful policy response. The moral implications of an action or non-action of AMR constitute the need for ethical consideration. This encompasses prevention and control of AMR. The risks of AMR are clear to untreatable infection and these risks are well established. The risks of AMR knowledge will comes to the responsibility to act, to slow resistance trends in order to provide time to find new ways of treating infection to control it [15].

Many countries have implemented measures to control AMR, including proper use of antimicrobial drugs in humans, minimization of antimicrobial drug use in animals, and prevention of further transmission of resistant microbes within the healthcare system. AMR raises a range of ethical questions which explored ethical issues that arise in relation to carriage of antimicrobial drug resistant organisms. Because, if nothing is done, then future patients will be deprived of potentially lifesaving drugs. This is unacceptable, especially after humanity has experienced as 'golden era of antibiotics'. Therefore, to reduce the impacts of AMR, it needs the ethical approaches of accountability of governing body [16].

Who is Accountable for Action of Antimicrobial Resistance

There are both individual and institutional responsibilities toward control of AMR. These include healthcare prescribers, their practices and choice of antimicrobial drug; educational organizations that establish the qualifications required to prescribe anti-infective; pharmaceutical companies who develop and market antimicrobial products; drug discovery scientists and/or the academic institutions that support them; veterinary and agricultural industries, ordinary people who request, buy, take (or fail to take) antibiotics; and executives responsible for health regions, or indeed, national bodies including current political rulers. The responsibility clearly encompasses both governmental and professional institutions as well as prescribers and their patients [17].

Whatever actions are chosen to readiness AMR, a balance is required between the needs of the individual and the common good. For example, prescribers may strive to restrict drug consumption, but benefits from decreasing AMR for future use might condemn current patients to serious sepsis. There are additional ethical dilemmas involving antimicrobial prescribing for subsets of patients with specific conditions, none more pertinent than prescribing powerful drugs to terminal or elderly patients [3].

Antimicrobials used to reduce the risk of infection for some (healthy) patient populations should be curtailed, given that these patients are well While physicians have an obligation to help their patients, they are expected to refrain from causing harm [18]. As with all prescribing, a fundamental principle of beneficence may be illustrated by the balance between therapeutic benefit and adverse effects from the drugs prescribed. More pertinent to antimicrobial prescribing, the term non-malfeasance meaning 'to do no harm' or rather inflicting the least harm possible to reach a beneficial outcome, defines the choice between immediate benefit from anti-infective and potential lack of therapies for that patient in the future. This term could also theoretically be applied to current practice of giving antibiotics as surgical prophylaxis, perhaps a privilege in the future [19].

Prescribing restrictions challenge traditional autonomy of individual practitioners. Autonomy itself demonstrates an ethical principle intimating freedom from external control or influence. In this respect, doctors should prescribe what they believe to be best for a patient, justifying empirical decisions with clinical assessment, experience, and sometimes psychosocial reasons [20]. Attempts at influencing medical autonomy means that doctors may not support restrictive policies, particularly if they feel that these short-change a particular patient or condition, or they will consider the cost of antimicrobial to determine therapeutic choices. There remains a fiduciary responsibility to individual patients with shared decision-making balanced against long-term societal interests. Patients themselves have needs, values, and preferences, and their wishes provide a different type of challenges. Directing the medical profession over their right to prescribe requires sensitive diplomacy, underpinned by evidence-based science. Opposing arguments include internet and over the counter sales of antimicrobials, which circumvent the role of licensed prescribing. Antibiotics are a shared global resource and clinicians, patients, public health, and government are bound together by the need to protect these drugs from misuse [20].

Mandated restrictions may encompass use of human agents in veterinary and agricultural practices. Growth promotion in animals has been banned in the European Union but not necessarily elsewhere. Aside from food-producing animals, the public expect antimicrobial drugs for sick pets and indeed, wildlife. Antimicrobials are also widely used in business and industry, with products incorporated into paints, sprays, coatings, fabrics, and plastics. Antiseptics, now definitively linked with antibiotic resistance, are present in a huge array of household items. Thus, commerce and profit provide universal challenges to international bodies supporting stewardship [19].

There are further ethical considerations over the distribution of antimicrobial agents. Drugs should be limited to people based on residence in a particular healthcare facility; district; region; or even country [15].Who decides whether some patients should forfeit medicines, even though that decision may conflict with beneficence and indeed, all these need fundamental principles of medical ethics. To a certain extent, this is happening already, due to high pricing of specific drugs and countries facing sanctions, wars, economic disadvantages and lack of public health structures [19].

Antimicrobial resistance raises further economic issues, since increasingly resistant infections encourage clinical demand for more spending on remaining drugs, forcing governing bodies to consider selective funding. Expensive last-resort antibiotics may serve only to accelerate further resistance and could challenge supplier strategies [6].

Indeed, private medicine consortia may decide to act independently of any governmental decree. Universal access to effective antibiotics is essential for tackling antibiotic resistance. A related issue operates at local level, whereby some institutions advise prescribers to choose cheaper options, even if these are therapeutically suspected. Such practices are hardly judicial, since they enhance the risk of persistent or recurrent infection, which itself encourages resistance [21].

Controlling AMR is a current problem with multiple ethical issues, with no possible single solution that does not raise even more questions, which need various analyses of medical practice and autonomy, prescribing, the access of drugs and economic status versus increasing resistance to provide the professional knowledge to the ethical significance at every level. The continuing process of taking action antimicrobial resistance requires much debate regarding the implementation of global initiatives [6]. Restricting antibiotics to benefit one stakeholder will almost certainly affect the same or a different stakeholder further down the line [22].

The Risk of Antimicrobial Resistance

The threat of progressing drug resistance puts the world at a serious risk of harm in our life time and our failure to control and reduce AMR will impose risk on other people and on future generations. The scope of the current AMR problem is perhaps easiest to illustrate by the repeated and growing number of warnings by experts in global health and microbiology, who predict the dawn of a post-antibiotic era and who should fail to act quickly and decisively [23]. While the impact of AMR on future morbidity and mortality is by their nature speculative and dependent on a large number of uncertain variables. Then, it the effects of AMR are likely to be suffering in the near future, if we fail to take an appropriate action [8].

AMR will not only render the treatment of acute bacterial infections more difficult and costly it will also increase the risk for medical procedures in which antibiotics are used prophylactically, such as surgical interventions or some types of chemotherapy. Allowing AMR to progress unchecked would lead to a situation where we might fall short of moral obligations to provide safe medical care, when standard invasive procedures carry high risks of complications or even death [24].

In addition, AMR enhancing the risk of a return of epidemic and pandemic and outbreaks that could be treated with antibiotics in the past correct therapy reduces the risk of spread. Unfortunately, rapid microbiological tests are depending upon available resources and infrastructure of healthcare institutions. While additional funding for expensive molecular tests requires a thoughtful business case in developed countries. Poorer countries lack of sufficient diagnostic laboratories. Arguments for implementing or improving diagnostic provision are dependent upon published evidence, in which company with infection prevention strategies is virtually nonexistent. There is an ethical trade-off between investments in diagnostic facilities versus potential transmission of key resistant pathogens, quite apart from the danger of diagnostic delay for an individual patient [25].

Lack of understanding of educational curriculum on microbiology, infection control and appropriate prescribing, or understand why these are important of AMR the future stewardship initiatives will not achieve ownership [26]. This could be amended by introducing structured feedback on prescribing, which influences adaptive behaviour. Alternatively, senior doctors could take more responsibility for antimicrobial choice. This could be formalized by health boards or even national bodies, since expecting seniors to oversee antimicrobial choice and consumption for their patients cannot be disputed on ethical grounds. Prescribing is often left to junior doctors, who may not have the experience to deal with complex case [27].

Responsibility for Acting

The magnitude of the risk of current problem and future generations are faced with AMR creates ethical problems to the speed and scale with which we must react in order to avert a post-antibiotic age, we are also faced with what constitutes a proportional response and, crucially, who bears responsibility to act. While AMR is a complex challenge with numerous causes, it is the broad use of antimicrobials in health care and agriculture that is the driving force behind the emergence of drug resistance. This means that we are unlikely to find a solution to AMR without substantially changing the way we use antibiotics, and reducing the amount we consume. Drastically reducing the amount of antibiotics will have implications for human and animal health, and raise questions means that we must think seriously about who about the ethical limits of preserving antimicrobial effectiveness [28].

However, recognizing the large part that play in the emergence of AMR also is accountable for the emergence of drug resistance. If the preservation of effective antimicrobials is in the interest of current and future generations, and indeed their lives depend on it, then we should also hold people blameworthy or sanction able for the ignorant, unnecessary or wrongful use of antibiotics, or any other practice that is likely to hasten the emergence of AMR. This may mean that we will be morally justified in imposing greater burdens or costs for their contribution to the current state of AMR [20].

At the same time, however, we must remember that there may be no truly sustainable way of using antibiotics in the long-run, as microorganisms have shown to be almost infinitely adaptable since the first introduction of antibiotics. This means that our struggle to keep abreast of AMR will most likely be a continuous and vicious cycle of resistance and obsolescence [29]. While this does not absolve current generations of their responsibility for their inappropriate use of antibiotics, it should make us reconsider what kind of policy problem AMR represents. If it is not easily solvable, then our moral obligations to future generations may not so much be to fix but rather to manage the problem. We have argued elsewhere that due to its complexity, AMR can be understood as a so-called super- wicked problem, a policy challenge to which no singular solution exists [30].

Proposing ethical approaches to antimicrobial resistance is the one way of re-focusing the debate to consider AMR as to reduce emerging disaster. This would not only account for the scale and severity of the problem for humanity, it would also draw attention to the ways in which a potential post-apocalyptic world would impact on many kinds of human interaction, resulting in uncertainty and increased vulnerability of livelihoods. Understanding AMR as a slowly emerging disaster highlights a number of ethical and legal challenges that will become increasingly it to acute. Therefore, understanding the risk of AMR as a slowly emerging disaster also emphasizes the need for policies that build resilience and better to reduce the risk of AMR for a world population lifespan are available [15].

The Cost of Antimicrobial Resistance

AMR is one of the major threats to individual and population health in the 21st century, and national and international organizations have repeatedly underlined the urgent need for action. The WHA call a new global action plan on AMR and the

topic was discussed as one of the priorities for policy action at a current problem of AMR. The Centers for Disease Control and Prevention estimate that as much as $20 billion in direct health care costs and $35 billion in lost productivity are associated with understanding of the consequences of AMR and its ethical implications annually [7] and also the UK government suggests that the death causalities of AMR could be as high as 300 million people until 2050, with an estimated total financial loss of up to $100 trillion [8].

AMR not only uses more resources and increases the cost of health care delivery, by increasing the risk of complications or treatment failure and lengthening the recovery time, it also leads to productivity losses which are commonly not fully taken into account and have led to an underestimation of the true cost of AMR in the past. Moreover, there are associated social and economic costs that arise from resultant obligations to care for relatives or friends who have fallen ill from AMR-related disease, which may not be fully incorporated in cost models. Unless drastic measures are taken to prevent or at least slow down a further progression of AMR, health care expenditures associated with drug resistance, both direct and indirect, will continue to grow substantially. This will put pressure on public spending and necessitate a re-allocation of public funds from other areas, sparking concerns about fair resource distribution and health care rationing and the development of cost models for AMR creates its own set of ethical problems [24].

Solidarity against Antimicrobial Resistance

Prescribers in community-based practices are less well-supported than hospital colleagues, since they often operate in isolation. Despite an excess of prescribing guidance, there are many opportunities for incorrect choice of anti-infective as well as over or defensive prescribing. Patients not only desire the best and most modern of treatments, they expect a medication for every ill. This makes it difficult to withhold antimicrobial drugs from the worried well, especially those who are paying for their treatment. Doctors are more likely to prescribe drugs for private patients, because they feel obliged to do so. There may well be an ethical responsibility to challenge prescribers over their management of private versus public patients, while acknowledging the tension between patient autonomy and stewardship requirements [31].

Solidarity is important because it underlines the fact that we will only be able to effectively deal with AMR through collective and collaborative activities. A focus on solidarity seeks to re-orient our ethical focus towards our common interests and vulnerabilities, individually and collectively, and these considerations should make the distribution of health and risk a joint concern of all levels and sectors of our global society. The solidarity constitutive of a moral community of health justice will confer a mutual recognition, respect and reciprocal concern that requires stand up for and stand besides those most affected by AMR [32,33].

Antimicrobial resistance and questions of justice: Following on the previous point, the problem of AMR will require a fair balance of benefits and burdens among affected by AMR. Therefore, any solution to AMR will create Questions of justice to give response to AMR through developing new drugs and technologies, enhancing surveillance and reporting systems and conducting research in areas that aligned with their current national priorities. At the same time, a response to AMR will also require to provide better access to high quality drugs, diagnostic tools and expert care, since AMR is as much a problem of overuse as it is a problem of insufficient access in many low and middle-income countries [34].

Therefore, AMR does not only raise ethical questions about reducing the use of antibiotics, crucially it will also require a substantial extension of access to antibiotics in many regions of the world. This also involves the quality assurance of drugs that are made available in low- income regions, and the availability of new, patent-protected medicines that may be drugs of last resort. The ethical consideration of AMR poses challenging questions about how distributive fairness is to be incorporated and balanced with considerations of effectiveness. For instance, if resistance to antibiotics of last resort is likely to emerge quicker the more equally we provide access to justify restricting access to antibiotics [10].

The Ethical Dimensions of Antibiotic Resistance

Given the complexity and dimension of ABR, as well as the many ways in which it affects people, there are numerous ethical problems that arise in its wake. At the most fundamental level, these can be distinguished into four different sets of problems.

Ethical challenges in infectious disease control: These well-known challenges are exacerbated by ABR. For example, whether social distancing measures or mandatory reporting of patients with contagious bacterial infections is ethically acceptable has remained controversial (as illustrated by the problems surrounding the treatment of multidrug-resistant tuberculosis).With an increasing number of drug- resistant infections that are more difficult to treat or that no longer respond to treatment, such measures could be considered more frequently. Their inherent ethical conflict between patient autonomy and control, and the protection of others, will thus have to be addressed. Moreover, owing to increased healthcare costs and longer hospital stays, ABR will also further increase existing resource limitations in hospitals, leading to conflicts in the allocation of already scarce medical resources [35].

Ethical challenges for the fair distribution of global resources: Since the burden of ABR disproportionately affects low- and middle-income countries, it has the potential to widen existing discrepancies in health outcomes between regions. Weak healthcare systems are less likely to be able to address the challenge of ABR by themselves, and whilst it is important to curb the use of antibiotics, it should also be noted that more people die from lack of access to high-quality antibiotics in low-income countries than die from ABR in high-income countries [36]. Since many healthcare systems are insufficiently equipped to deal with

ABR themselves, an ethical policy response to ABR will have to be explicit about the degree of international assistance and capacity-building that resource-poor healthcare systems are entitled too.

The Ethical Use of Veterinary and Human Antibiotics: Whilst it is acknowledged that large savings in the use of antibiotics can be achieved in the veterinary sector, where more than one-half of the world's total production of antibiotics is used, the related ethical issue of animal welfare is rarely addressed. If entire classes of antibiotics are exclusively reserved for human use, certain treatable infections would no longer be curable in the veterinary sector. At the same time, a more restrictive use of antibiotics also necessitates a frank discussion of animal welfare standards in food production, especially where current modes of production are only attainable due to the widespread prophylactic use of antibiotics to compensate for overcrowded farming conditions [37].

Antibiotic resistance is a growing problem among humans and wildlife in terrestrial or aquatic environments. In this respect, the spread and contamination of the environment, especially through water pollution "hot spots" such as hospital wastewater and untreated urban wastewater, is a growing and serious public health problem [38]. Antibiotics have been polluting the environment since their introduction through human waste (medication, farming), animals, and the pharmaceutical industry [35]. The contribution of the pharmaceutical industry is so significant that parallels can be drawn between countries with highest rate of increasing antibiotic resistance and countries with largest footprint of pharmaceutical industry. Along with antibiotic waste, resistant bacteria follow, thus introducing antibiotic-resistant bacteria into the environment. Already in 2011, mapping of sewage and water supply samples in New Delhi showed widespread and uncontrolled infection as indicated by the presence of NDM-1positive enteric bacteria [39].

As bacteria replicate quickly, the resistant bacteria that enter water bodies through wastewater replicate their resistance genes as they continue to divide. In addition, bacteria carrying resistance genes have the ability to spread those genes to other species via horizontal gene transfer [39]. Therefore, even if the specific antibiotic is no longer introduced into the environment, antibiotic resistance genes will persist through the bacteria that have since replicated without continuous exposure [35]. Antibiotic resistance is widespread in marine vertebrates and they may be important reservoirs of antibiotic resistant bacteria in the marine environment [40].

The production process of antibiotics itself raises a number of ethical problems, including the substantial environmental impact and pollution caused by dumping by-products into wastewater, there by affecting rivers and groundwater supplies and ultimately contributing to the emergence of AMR. An ethical policy response to AMR must focus on all aspects of the drug development process and the end products of antibiotic produced [41].

Ethical challenges of intergenerational and intergenerational justice: With decreasing antibiotic effectiveness, an ethical conflict emerges for the fair distribution both within and across generations. How should we allocate this increasingly scarce public good? Is it fair if we leave future generations without effective antibiotics? These are ethical challenges that exist because of the unique properties of antibiotics, as we will explain below. We believe that they are commonly overlooked in policy-making and clinical practice, but deserve more attention because they affect both patients and prescribers.

To date, what little discussion there has been about ethical implications of ABR has been focused on the first three challenges. The first falls into the traditional realm of public health ethics. At its heart lie concerns about the patient's autonomy and its trade off against public interests, either due to limitations of individual liberty or as a lack of informed consent [42].It is vital that the proper balance between patient and public interests is achieved at the international, national and regional levels. However, this issue as such is not unique to the case of ABR, but only exacerbated by it. An established literature exists on the trade-off between patient rights and public health that can and should be used to establish such balance in practice. The same is true for categories, both of which constitute complex ethical and political challenges in themselves that also exist in the absence of ABR and are the subject of expansive and ongoing discussion. Category on the other hand, is distinct from the other three categories because it constitutes a set of ethical challenges that are not merely exacerbated by ABR, but exist as a direct result of the properties of antibiotics. We will therefore focus on these properties and the ensuing challenges for the remainder of the paper [11].

Lack of new drug investigation: The dilemma AMR face is the more extensively we use antibiotics, the faster we will create antibiotic resistance. From an ethical approach, the lack of new antibiotics poses a number of problems. Perhaps most pressing is the question of who manage to tolerate responsibility for the development of new drugs and tests, and how these should be made available, once they enter the market. Since both the burden of infectious disease and the prevalence of AMR are disproportionately higher in low- and middle-income countries, there is an urgent need for the provision of low cost, high-quality drugs and tests to be made widely available to finance the development of new diagnostic and therapeutic agents [43].

On the other hand, they also include measures to improve surveillance and diagnostic tools for bacterial infections, to promote antibiotic stewardship and crucially, to minimize the global uncontrolled sales of antibiotics. In countries with developed health and regulatory systems, a restrictive antibiotic prescribing policy is needed that limits the use of antibiotics for human and animal use to instances where their use is clearly indicated and offers a measurable therapeutic benefit. Similar policies need also to be implemented in low- and middle-income countries to the extent possible without reducing access to essential antibiotics. As commendable as many of the current policy efforts to curb drug resistance are, they have so far failed

to address sufficiently the ethical challenges that arise as a consequence of ABR. In this paper, we will describe these ethical challenges and outline their relevance for patients, physicians and policy-makers [21].

Lack of hygiene: Raw meat, vegetables, and other foods may be contaminated by pathogens at the point of sale [44]. If there is insufficient washing or cooking of products organisms are ingested that both infect, and/or colonize, for later complications. Even non-infective microbes pose a risk from contaminated foods, because they may harbour AMRs, which the consumer could retain for years to come. This compromises future management of infection for that individual. The gastrointestinal tract offers an ideal environment for microbial gene exchange. Here is specific moral responsibility for food suppliers and distributors to manage contamination of foodstuffs at every point in the food chain. The same applies for dirty water, although water quality usually depends upon existing public health and sanitation structures.

The organization has a comprehensive hand hygiene strategy including:-Hand hygiene education for all staff, Senior leader in the organization encouraging and supporting implementation of hand hygiene education and training for all staff, Hand hygiene product availability for staff including alcohol-based hand rub at point of care and service delivery, Hand hygiene practices audited with the results shared with staff and used to make improvements in hand hygiene practices. O Hand hygiene compliance meets existing guidelines and standards, Communication of hand hygiene rates throughout the organization together with processes for improvement, Development and implementation of an antimicrobial stewardship program, Comprehensive environmental control program.

Defined roles and responsibilities for cleaning and disinfecting the environment o Policies and procedures outlining: How to clean specific areas (e.g. patient rooms, bathrooms, common areas) Cleaning schedules, assigned responsibility and expectations for frequency of cleaning, Choice of cleaners or disinfectants (e.g. hospital grade disinfectant with valid DIN), ensuring application of disinfectant follow manufacturer's recommendations, Education for staff involved in cleaning/ disinfection of equipment and the environment regarding cleaning policies and procedures as well as IP&C practices on an ongoing basis, A quality assurance program for monitoring cleaning/disinfection of the environment with analysis and feedback to improve practice.

Prescribing guidelines: There are many differences types of antimicrobial guidelines and these guidelines are contradictory, which tend to be launched in technical terms and aimed at professionals such as doctors, scientists, and pharmacists.

Prescriber will not know the full range of prescribing guidelines. Most guidelines focus on hospitals, rather than community, since the risk of generating resistance is assumed to be greater in environments that are heavily exposed to antimicrobials. Guidelines might exhort prescribers to prescribe more carefully but these are not mandatory policy. Doctors can still prescribe their preferred drug without recourse, unless they can be held accountable for their choice. The quality of guidance itself is important, since conflicting advice provides justification for using 'favourite' antibiotics [31]. While there may be a strong moral argument to choose unusual or second-line drugs, a prescriber could be placed at risk of penalty unless relevant and timely confirmation is received from the diagnostic laboratory. This demands a degree of courage among prescribers, as well as the necessary diagnostic support. There is good evidence to show that restrictive and enabling interventions empower doctors to both reduce and improve antimicrobial prescribing, although the most effective behavioral techniques do not yet seem to be widely implemented.

Ethics

The ethics of AMR require new ideas and analysis subject matter and the apparently infinite contributing factors. AMR is not a problem that tends itself to the straightforward application of well-established basic principles of bioethics. As a result, further work will be needed from moral and political philosophers on transferring moral concepts of bioethics to the population level and elucidating the rational and socially embedded normative concepts to reduce the current problem of AMR. In addition to conceptual work on AMR, the aims to clarify and analyse, the fruits of moral and political thought ethics of AMR must also be addressed in policy terms, as well as in public health and medical practices.

Ethics of new policy, law and regulation: The response to AMR will be approached via the use of governance mechanisms within both public and private institutions, especially instruments such as policy, law and regulation. Going forward, it is going to be exceedingly important that these mechanisms and instruments recognize and address the many ethical issues involved in responding to AMR. These issues also have to be addressed in a way that has normative legitimacy not only do we want our governance mechanisms to be morally justified, we also know that being viewed as morally justified increases the likelihood that people will comply with law and policy [45].

The progression of AMR in many countries suggests that current policy efforts are falling short goal to stop or even reverse the effects of AMR and The WHA call for the development of national response plans to AMR is a crucial first step in extending and improving existing legislation. However, it will be important that new policies take into account the ethical challenges posed by AMR [46].

AMR is framework policy rather than describing term is a purely medical challenge and policy makers should seek to promote greater collaboration between sectors and research areas to better address AMR as the social challenge. Similarly, by focussing on the aspects of mitigation and management, rather than creating an unrealistic and false hope of an imminent technological fix, health policy makers and regulators can help in managing expectations of AMR [47].

Ethics of health care workers and public health practitioners: As prescribers or dispensers, medical practitioners, health care workers and pharmacists play a crucial role not only in regulating access to antibiotics, but also educating patients' access to AMR. If healthcare workers and public health practitioners are not aware or not feel to address the ethical dilemmas of AMR, they cannot be expected to AMR respond appropriately. Ethics of education, training and guidance need to be provided for professionals to help them to navigate the moral issues they will encounter about AMR [42].

Education, public awareness, and media campaigns: Governing boards responsible for a particular institute, national organizations to impose specific recommendations on importance of AMR, education on hygiene, infection control, microbiology and prescribing need more focus within universities, hospitals and colleges, ideally supported by hygiene teaching in schools [48].These will introduces an important ethical consideration for bodies such as the GMC, Departments of Health and Education, Royal Colleges, veterinary sciences, medical and nursing defences unions [49]. Publicizing awareness of AMR and infection prevention will help GPs and pharmacists explain antibiotic use to frustrated and uninformed customers, who fail to realize the consequences from taking antimicrobial drugs. An appropriately targeted awareness campaign is justifiable because it might influence socially conscious citizens [8].

Ethics of civil society and industry: Industry also needs to be more collaborative and willing to assist to a greater extent without waiting for government regulation to reduce AMR. Current pricing strategies for antimicrobials, especially for drugs of last resort and new medicines that make them unaffordable for a majority of the world's population, would be a good place to start. Showing more concern and solidarity in these matters can only help industry's public relations and stave off the feeling that increased regulation of industry should be undertaken to force them to do more.

CONCLUSIONS AND RECOMMENDATIONS

Antibiotic resistance accounts for hundreds of thousands of deaths annually and its projected increase has made the WHO recognize it as a major global health threat. Conventionally, the struggle against antibiotic resistance development has mainly taken place in clinical, community, and in more recent years also agricultural settings aiming to reduce transmission and prevent selection of resistant bacteria during antibiotic treatment. Over the past years, the role of the environment as an important source and dissemination route of resistance has been increasingly recognized. AMR need for greater international collaboration and accountability distribution, with broader engagement of countries and to foster global intersectoral action on AMR. This includes agreed definitions for surveillance and support for analyses and reporting of trends on a worldwide basis. Control of disease and its causes is impossible without surveillance and international licence. More understanding of AMR help to drive health behaviours on antimicrobial use would benefit policy makers and stewardship strategies. The complexity of ABR as a policy challenge is reflected in the multitude of practical and ethical problems. However, more often than not, ethical issues of ABR are not explicitly addressed in policy development and discussion, even though they are becoming increasingly relevant for prescribing physicians, patients, pharmacists and policy-makers. This paper has highlighted a number of pressing ethical challenges that effective and credible future policy should address. In particular, if and when it is ethical to withhold antibiotics when this would constitute a risk to patients remains an open question. Therefore, AMR need urgent discussion, Governing body and the present representatives of political rulers must transparently debate including clinicians and researchers as well as ethicists and policy must be implemented.

Based on the above conclusions, the following recommendation should be forwarded:

- Uniform and Strong Ethics of legal framework is needed to antimicrobial use standards,
- Strong command of chain is needed in international, national and regional level of the countries prevent and control antimicrobial resistance.
- Regular surveillance systems to regulate antibiotic marketing before use
- Implement ethics of one health approach at local, national and global level to combat the spread of AMR and to protect the world population.
- Awareness creation on challenges antimicrobial resistance for stake holders and working on the gap

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REFERENCES

1. Siegel D, Rhinehart E, Jackson M and Chiarello L. Healthcare Infection Control Practices Advisory Committee and Management of multidrug-resistant organisms in health care settings, 2006. Am J Infect Control. 2007; 35: S165-193.
2. Shlaes DM, Gerding DN, John JF, Craig WA, Bornstein DL, Duncan RA, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. Clin Infect Dis. 1997; 25: 584-599.
3. Leibovici L, Paul M. Ethical dilemmas in antibiotic treatment: focus on the elderly. Clin Microbiol Infect. 2015; 21: 27-29.
4. Goossens H, Ferech M, Vander R, Elseviers M. Outpatient antibiotic use in Europe and association with resistance. A cross-national database study. Lancet. 2005; 365: 579-587.
5. Macnaughton E, MacGowan A. Antibiotic resistance. Medicine. 2017; 45: 622-628.
6. Littmann J. Antimicrobial resistance and distributive justice (doctoral thesis). London: University College London. 2014.
7. Centers for Disease Control and Prevention. Antibiotic Resistance and Threats in the United States Washington: CDC. 2013.

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

9. Littmann J, Buyx A, Cars O. Antibiotic resistance: an ethical challenge. Int J Antimicrob Agents. 2015; 46: 359-361.

10. Laximinarayan R, Duse A, Wattal C, Zaidi A, Wertheim HF. Antibiotic Resistance and the Need for Global Solutions. Lancet Infect Dis. 2013; 13: 1057-1098.

11. Bengtson B, Greko C. Antibiotic resistance consequences for animal health, welfare, and food production. Ups J Med Sci. 2014; 119: 96-102.

12. Heyman G, Cars O, Bejarano M, Peterson S. Access, Excess, and Ethics towards a Sustainable Distribution Model for Antibiotics. Ups J Med Sci. 2014; 119: 134-141.

13. World Health Organization. Global Tuberculosis Report. Geneva: WHO Press. 2014.

14. World Health Organization. Global action plan on antimicrobial resistance. 2015.

15. Littmann J, Viens AM. The ethical significance of antimicrobial resistance. Public Health Ethics. 2015; 8: 209-224.

16. Millar M. Can antibiotic use be both just and sustainable... or only more or less so? J Med Ethics. 2011; 37:153-157.

17. Haire B, Kaldor JM. Ethics of ARV based prevention: treatment-as-prevention and PrEP. Dev World Bioeth. 2013; 13: 63-69.

18. Gillon R. Medical ethics: four principles plus attention to scope. Journal of the American Medical Association. 1994; 309: 2345-2352.

19. Dancer SJ. Infection control in the post antibiotic era. Healthcare Infect. 2013; 18: 51-60.

20. Spellberg B, Bartlett JG, Gilbert DN. The Future of Antibiotics and Resistance. New England Journal of Medicine. 2013; 368: 299-302.

21. Daulaire N, Bang A, Tomson G, Kalyango JN, Cars O. Universal access to effective antimicrobials: an essential feature of global collective action against antimicrobial resistance. J Law Med Ethics. 2015; 43:17-21.

22. Dancer SJ. How antibiotics can make us sick: the less obvious adverse effects of antimicrobial chemotherapy. Lancet Infect Dis. 2004; 4: 611-619.

23. Davies SC, Gibbens N. UK Five Year Antimicrobial Resistance Strategy. London: Department of Health. PP: 2013–2018. 2013.

24. Smith R, Coast J. The True Cost of Antimicrobial Resistance. BMJ. 2013; 346: 1493.

25. Cars O, Högberg LD, Murray M, Nordberg O, Sivaraman S, Lundborg CS, et al. Meeting on the Challenge of Antibiotic resistance. British Medical Journal. 2008; 337:1438.

26. Owens R, Shorr F, Deschambeault A. Antimicrobial stewardship: shepherding precious resources. Am J Health Syst Pharm. 2009; 66: S15-S22.

27. McLellan L, Dornan T, Newton P, Williams D, Lewis P, Steinke et al. Pharmacist-led feedback workshops increase appropriate prescribing of antimicrobials. J Antimicrob Chemother. 2016; 71: 1415-1425.

28. Cars O, Nathan C. Antibiotic Resistance Problems, Progress, and Prospects. N Engl J Med. 2014; 371:1761-1763.

29. Aiello AE, Larson EE. What is the Evidence for a Causal Link between Hygiene and Infections? Lancet Infect Dis. 2002; 2:103-110.

30. Littmann J. Antimicrobial Resistance and Distributive Justice. London: University College (PhD dissertation). 2014.

31. Duane S, Domegan C, Callan A, Galvin S, Cormican M, Bennett K, et al. Using qualitative insights to change practice: exploring the culture of antibiotic prescribing and consumption for urinary tract infections. Special Euro barometer: Antimicrobial Resistance. Brussels: European Commission. 2016;6: e008894.

32. Dawson A, Verweij M. Solidarity: A Moral Concept in Need of Clarification. Public Health Ethics. 2012; 5:1-5.

33. Jennings B. Relational Liberty Revisited: Membership, Solidarity and a Public Health Ethics of Place. Public Health Ethics. 2015; 8: 7-17.

34. Baker S. A Return to the Pre-Antimicrobial Era. Science. 2015; 347:1064-1066.

35. Martinez JL, Olivares J. Environmental Pollution by Antibiotic Resistance Genes. Antimicrobial Resistance in the Environment 2012; 151- 171.

36. Laximinarayan R, Duse A, Wattal C, Zaidi AKM, Wertheim HFL, Sumpradit N. Antibiotic resistance the need for global solutions. Errata in: Lancet Infect Dis. 2014; 14:182.

37. Dawson A, Verweij M. Ethics, prevention and public health. Oxford, UK: Oxford University Press. 2009.

38. Marti E, Variatza E, Balcazar JL. The role of aquatic ecosystems as reservoirs of antibiotic resistance. Trends Microbiol. 2014; 22: 36-41.

39. Walsh TR, Weeks J, Livermore DM, Toleman MA. Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. Lancet Infect Dis. 2011; 11: 355-362.

40. Rose JM, Gast RJ, Bogomolni A, Ellis JC, Lentell BJ, Touhey K, Moore M. Occurrence and patterns of antibiotic resistance in vertebrates off the Northeastern United States coast. FEMS Microbiol Ecol. 2009; 67: 421-431.

41. Larsson D. Pollution from Drug Manufacturing: Review and Perspectives. Philos Trans R Soc Lond B Biol Sci. 2014; 369: 20130571.

42. Coleman C, Jaramillo E, Reis A, Selgelid M. Guidance on ethics of tuberculosis prevention, care and control. Geneva, Switzerland: WHO. 2010.

43. Outterson K, Pogge T, Hollis A. Combating Antibiotic Resistance through the Health Impact Fund. In Boston University School of Law Working Paper No: 2011; 11-30.

44. Fox C. Resisting Antibiotic Resistance: Legal Strategies to Maintain Man's Dominion over Microbes. Houston Journal of Health Law and Policy. 2011; 12: 35-62.

45. Anomaly J. Combating Resistance: The Case for a Global Antibiotics Treaty. Public Health Ethics. 2010; 3:13-22.

46. World Health Organization. Antimicrobial Resistance Global Report on Surveillance. Geneva: WHO Press. 2014.

47. Tyler TR. Why People Obey the Law. Princeton, NJ: Princeton University Press. 2006.

48. Lecky DM, McNulty CA, Adriaenssens N, Herotová T, Holt J, Kostkova P, et al. Development of an educational resource on microbes, hygiene and prudent antibiotic use for junior and senior school children. J Antimicrob Chemother. 2011; 66: 23-31.

49. Torjesen I. Doctors who prescribe antibiotics online face GMC investigation. BMJ. 2016; 355: i5423.