

## Ethical challenges in the age of bacterial resistance: the threat of indiscriminate use of antibiotics

### Desafíos éticos en la era de la resistencia bacteriana: la amenaza del uso indiscriminado de los antibióticos

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#### Abstract:

The overuse of antibiotics has led to the emergence of antibiotic-resistant bacteria, posing an ethical and public health challenge. Bacterial resistance has become a real threat to the health of populations. It renders treatments for infectious diseases ineffective, increasing the risk of complications during medical interventions and raising the risk of exposure of the population to potentially fatal infections. It is worth mentioning that bacterial resistance is entirely preventable, so it is everyone's responsibility to make conscious use of antibiotics. This article reviews the basic concepts of bacterial resistance and then makes a bioethical reflection on the prescription and use of antibiotics. A non-systematic bibliographic review was carried out in databases such as Pubmed, Google Scholar, and Scopus to identify basic concepts of bacterial resistance. In addition, a database review of bioethics articles was carried out to create a bioethical reflection on the prescription and correct use of antibiotics. The abuse of antibiotics and the resulting bacteria resistant to antibiotics poses an ethical dilemma involving both the medical community and the entire society.

#### Keywords:

*Antibiotics, bacteria, bioethics, bacterial resistance, prescription.*

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#### Resumen:

El uso excesivo de antibióticos ha llevado al surgimiento de bacterias resistentes a los antibióticos, lo que representa un desafío ético y de salud pública. La resistencia bacteriana se ha convertido en una verdadera amenaza para la salud de las poblaciones, pues vuelve ineficaz a los tratamientos de las enfermedades infecciosas, aumentando el riesgo de complicaciones durante intervenciones médicas y aumenta el riesgo de exposición de la población a infecciones potencialmente mortales. La resistencia bacteriana es completamente prevenible, por lo que es responsabilidad de todos hacer un uso consciente de los antibióticos. Este artículo hace un recorrido sobre los conceptos básicos de la resistencia bacteriana, para luego hacer una reflexión bioética sobre la prescripción y uso de los antibióticos.

Se realizó una revisión bibliográfica no sistemática en base de datos como Pubmed, Google Scholar y Scopus para identificar conceptos básicos de la resistencia bacteriana, así mismo se hizo una revisión en base de datos sobre artículos de bioética para crear una reflexión sobre la prescripción y uso correcto de los antibióticos. El abuso en el consumo de antibióticos y la consecuente aparición de bacterias resistentes a los antibióticos plantea un dilema bioético que involucra no solo a la comunidad médica, sino a toda la sociedad.

#### Palabras Clave:

*Antibióticos, bacterias, bioética, resistencia bacteriana, prescripción.*

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## 1. INTRODUCTION

During its report in 2021, the World Health Organization (WHO) declared the growing incidence of infectious diseases caused by resistant bacteria to antibiotics, which is one of the ten places seen as a worldwide threat to health. The bacterial resistance threatens global health, food security, and the economic development of the countries.<sup>[1]</sup>

It has been observed that the consumption of antibiotics occurs in the community area without a prescription or when it is not needed. Similarly, inadequate prescription of antibiotics in human or veterinary medicine is the main factor of resistance to antibiotics (RA).<sup>[2]</sup>

The RA boom presents a phenomenal ethical challenge in terms of shared responsibility between the population and the physicians while correctly using antibiotics. This article will briefly describe the concepts and mechanisms of bacterial resistance and, later on, its effects on health and the population's economy. Lastly, ethical principles will be identified which are associated with the indiscriminate use of antibiotics.

## 2. THEORETICAL FRAMEWORK

### 2.1 RESISTANT BACTERIA: CONCEPTS AND MECHANISMS

A bacteria is resistant when it produces an infectious disease. Once it is treated with an antibiotic with therapeutic concentrations, there is a low or null likelihood of success of the treatment.<sup>[3]</sup>

There are two types of resistance of bacteria:

- **Intrinsic:** it is provoked by innate changes in the bacterial genome that appear before the bacterium has contact with antibiotics and allows it to show structural and functional characteristics that make it insensible to conventional treatments.<sup>[4]</sup>

- **Acquired:** the selective pressure imposed by utilizing antibiotics causes phenomenal stress on bacteria, leading to genetic mutations that let them evade antibiotic action.<sup>[4]</sup>

These mutations can be transferred to other bacteria through acquiring resistance genes due to vertical or horizontal heritage.<sup>[5]</sup>

On one side, horizontal heritage is the most alarming since resistance genes can be displaced quickly and effectively. There are three mechanisms of horizontal heritage to spread resistance genes:

- **Conjugation:** requires contact from cell to cell, in which a receiver bacteria acquires genetic material from a donor bacteria.<sup>[6]</sup>

- **Transformation:** includes genetic material retained in the extracellular environment originating from the lysis of other bacteria.<sup>[6]</sup>

- **Transduction:** the capture of genetic elements transported to bacteriophages or by gene transfer agents from a donor bacterium.<sup>[6]</sup>

The bacteria are resistant to antibiotics due to the presence of resistance mechanisms, which can be classified into four categories:

- **Efflux system:** the cytoplasmic removal of the antibiotics is carried out through bombs that go through the cellular membrane, composed of a pore in the external membrane connected to a periplasmic protein. These bombs limit the intracellular concentration of antibiotics to provide an exchange of extracellular protons.<sup>[6-7]</sup>
- **Enzymatic inactivation:** the bacteria own the capacity to produce enzymes that inactivate the antibiotics when attacking its ring through hydrolysis or by turning on functional groups.<sup>[6-7]</sup>
- **Alteration of the union site:** the mutations of the bacteria genome cause miniature changes in the sequences of amino acids, which alters the structure of proteins, resulting in the modification of bacteria receiving those antibiotics. This translates into a loss of affinity and action. Another mechanism is the catalyzed modification for enzymes that adjust the structure of ribosomal subunits, producing a blockage of union receivers.<sup>[6-7]</sup>
- **By-pass of the objective:** the bacteria have created strategies for antibiotics that can avoid the production of objective enzymes, such as the overproduction of final compounds, and the prevention of that the antibiotic is together with its union site.<sup>[6-7]</sup>

The bacteria can be resistant to a family of antibiotics through various mechanisms of resistance or, on the contrary, only one type of mechanism can make them resistant against more than a family of antibiotics.<sup>[8]</sup>

### 2.2 BACTERIAL RESISTANCE: CONCEPTS AND IMPLICATIONS

RAM is defined as the capacity of bacteria to acquire mechanisms that allow them to survive and multiply even with the use of antibiotics that are regularly effective in their inhibition or removal.<sup>[9]</sup>

To have a better understanding of RAM, in 2012, an international terminology was created, which classifies resistance into:

- **Multiresistance (MDR):** the absence of sensibility of a bacteria or at least an antibiotic of three used families for its treatment.
- **Extended resistance (XDR):** the absence of sensibility of a bacteria to all the families of antibiotics, except one or two utilized for its treatment.
- **Pan-resistance (PDR):** the absence of sensibility of all the antibiotics of all families that are usually used in treating a specific bacterium.<sup>[10]</sup>

The bacterial resistance has modified from being a simple condition of the bacteria to being a threat to health. The danger of RAM focused on the increase in the number of annual deaths due to non-treated infections. Moreover, it raises the risk of complications during medical procedures. For instance, surgeries, organ transplants, and chemotherapies. On one side, it expands the lethality of common and treatable infections. On the other side, it enlarges the costs of the treatments due to prolonged hospital stays, the need to use intensive care units, and the implementation of specialized drugs.<sup>[11]</sup>

According to the Center for Disease Control and Prevention (CDC) Report on Antibiotic Resistance Threats mentioned in 2019, there were registered more than two thousand deaths per day globally because of resistant infections to antibiotics. Based on the same report in the United States of America, there were more than 2,8 million cases of resistant infections and more than 35000 dead people as a result of the first year of the pandemic of COVID-19.<sup>[12]</sup>

The data gathered from WHO is the same as concerning since it reported in 2021 that there were more than 700,000 dead people worldwide. Based on its forecasts of the incidence of these infections not decreasing, the number of deaths will extend to more than 10 million, even raising the number of deaths caused by cancer.<sup>[13]</sup> In Mexico, the scenery is not distinct since in 2021, there were three million eight hundred cases of resistant infections in the treatments, prompting 48 thousand deaths.<sup>[14]</sup>

On one hand, it has been observed that the most affected population due to bacterial resistance are people older than 70 years. Three of two deaths are produced at this age. Moreover, minors of one year have a higher risk of danger.<sup>[15]</sup> On the other hand, the economic impact of resistant infections of antibiotics is also distressing. Hence, it is estimated that the costs to treat the complications of bacterial resistance exceed 28,900 million dollars each year. Most of this resource will be utilized for financing extended hospital stays because they bring on more than 32.5 million additional days of the year.<sup>[16]</sup>

The global bank estimates that countries with low income will designate more than 5% of the Gross Domestic Product (GDP) in treating resistant infections, and 28.3 million people will become poor by 2050 if there is no implantation of plans to mitigate bacterial resistance. According to WHO projections, a resistant infection could cost up to 100 billion dollars to the worldwide economy during the same year.<sup>[17-18]</sup>

## 2.3 ANTIBIOTICS

The term antibiotic was first used by Selman Waksman in 1941 to describe a molecule prompted by microorganisms that can inhibit other microorganisms' growth. Nowadays, antibiotics are defined as compounds of natural or synthetic origin in treating infectious diseases produced by bacteria.<sup>[19-20]</sup> According to its mechanisms of action, antibiotics are classified into five main groups:

- The ones that disable the biosynthesis of wall cells.
- The ones that alter the integrity of the cell membrane.
- The ones that suppress the synthesis of nucleic acids.

- The ones that disrupt the metabolic processes.
- Finally, the ones that inhibit the synthesis of proteins.<sup>[21]</sup>

## 2.4 ANTIBIOTICS AND BACTERIAL RESISTANCE

The discovery of antibiotics is one of the most exceptional achievements of medicine. Therefore, they have been beneficial in treating infectious diseases, reducing morbidity induced by the same..<sup>[22]</sup> By taking a journey through time, we can ascertain that from the time of 1922 with the discovery of penicillin until the middle of the nineties with the development of tetracycline and chloramphenicol, it can be called the golden age of antibiotics. Nonetheless, the efficiency of those original antibiotics. Similarly, the following are under threat because of the growth of pathogenic-resistant bacteria. Whether replacements are not found or measurements that guarantee the adequate use of the same, the golden age will soon come to an end.<sup>[23]</sup> Not only are antibiotics misused in humans and veterinary medicine. But also in agriculture and food plants, being the last ones, the ones that have contributed more to enlarging resistant bacteria.<sup>[24]</sup>

On one side, WHO has made an effort to establish a reduction of 60% of the consumption of antibiotics as an essential objective for the nations, but more than a third of the countries that are part of OECD do not fulfill the goal of WHO.

On the other side, antibiotic sales for human beings have expanded by almost 2% since 2000 to date. The high indexes of indiscriminate consumption of antibiotics are still disturbing. It estimates irrational consumption, which has led to one to five infections induced by resistant bacteria. Furthermore, the most distressing is foreseen by 2035 and the bacterial resistance to antibiotics of the third generation(the last tool to treat complicated infections) will rise 2 times more.<sup>[25]</sup>

The progress of RAM and its complications in the health of the populations can be stopped if they guarantee the suitable use of antibiotics due to well-constructed policies. Based on the OECD, three of every four deaths provoked by RAM can be prevented. For instance, the health systems provide two annual dollars per person to create campaigns emphasizing the cautious prescription and consumption of antibiotics. In addition to teaching the correct technique to wash the hands.<sup>[25]</sup>

## 2.5 BIOETHICS AND ITS PRINCIPLES

Bioethics has been around since its formation in the 1970s when American oncologist Van Rensselaer Potter utilized the term for the first time in his article *Bioethics, the Science of the Survival* has had an acclaimed development since this discipline considers all the ethical issues of research, and medical practice until trying to explain itself from the diverse models.<sup>[26]</sup>

Presently, bioethics can be defined as a branch of applied ethics whose objective is to create reflections related to the health sciences to create regulatory approaches and public policies that regulate and solve conflicts of life for both the present and future generations.<sup>[27]</sup>

As stated before, bioethics has suffered diverse changes; however, it is the foremost movement with the most success. It

states that during the resolution of ethical conflicts, research, and clinical practice, it is necessary to apply four principles:

- **Autonomy:** is the person's right to decide according to his values and personal beliefs about any intervention that will be performed on him.<sup>[28-29]</sup>
- **Non-maleficence:** establishes the obligation of not violating a damager over doing the well.<sup>[28-29]</sup>
- **Benefit:** defines the right and maintains a close relationship with the previously stated. It sets an obligation to prevent or eliminate damage and seeks to do well for others.<sup>[28-29]</sup>
- **Justice:** ascertain that all human beings are equal in dignity and rights during an intervention. Getting everyone what they deserve. In other words, when faced with similar situations, act similarly and differently when the situation warrants it..<sup>[28-29]</sup>

### 3. METHODOLOGY

A non-systematic literature review was implemented considering data such as Pubmed, Google Scholar & Scopus to know concepts about bacterial resistance, antibiotics, and bioethics. Additionally, words like mechanisms of bacterial resistance of antibiotics and bioethics principles were considered. At the same time, there was a search in the principal data basis of the articles on bioethics to generate a bioethical reflection about the prescription of antibiotics and bacterial resistance. To obtain statistical data, it proceeded with a search of distinct official sources of information.

## 4. RESULTS

### 4.1 MEDICAL PRESCRIPTION

Prescription is when administering drugs or performing medical procedures based on established criteria and guidelines, and the objective is to provide treatment. Likewise, a medical prescription is one of the most significant responsibilities of health professionals, and it comes from scientific knowledge, which means that the physician diagnoses from a cognitive process that involves knowledge and judgment previously acquired after determining the course of action, in case a therapeutic one, emerges prescription.<sup>[30-31]</sup> Currently, physicians face an expansive challenge when prescribing because the availability of information sources leads to informed patients who demand specific treatments. Similarly, the requirement of offering treatments that generate quick results and commercial strategies of the pharmaceutical industry might produce pressure to prescribe certain drugs..<sup>[30-32]</sup>

Bioethics proves giving the doctor the freedom to prescribe without considering his interests or impositions by others, taking the following steps:

- **Maximizing efficiency:** The prescription must be effective after being evaluated to other therapeutic options and the most helpful according to the patient's clinical characteristics.<sup>[33-34]</sup>
- **Minimizing the costs:** taking into account the economic situation of each patient.<sup>[33-34]</sup>
- **Reducing the risks.**<sup>[33-34]</sup>

- **Respecting the patient's decision:** getting his consent beforehand.<sup>[33-34]</sup>

Bioethics verifies a medical prescription that must be given based on the individual needs, guaranteeing the collective well-being. It implies that physicians must encourage the rational use of antibiotics, besides being aware that each prescription might influence building resistant bacteria to antibiotics. For this reason, bioethics not only protects the patient from an incorrect prescription but also safeguards the therapeutic resources for future generations to have a rationalized use.<sup>[35]</sup>

### 4.2 THE MOST PROMINENT

The beneficence principle demands that physicians act for the benefit of their patients, and the one with non-maleficence obligates them not to cause damage. The treatment using antibiotics has the objective to treat infectious diseases or avoid complications during medical procedures. Regarding bioethics, this action is doing well; nevertheless, the physician must prescribe antibiotics taking into account the dosage, duration, and antimicrobial coverage of antibiotics, the clinical characteristics of the patient, microbiological analysis (antibiogram samples), and antibiotics that have confirmed inefficiency due to bacterial resistance in the hospital or clinic where the person works to avoid spreading resistant bacteria and with that avoiding prompting damage to population or future generations.<sup>[35-36]</sup>

The autonomy principle highlights the patient's right to make informed decisions about his treatment. Bioethics states that the physician must offer clear and respectful communication based on scientific evidence concerning implementing antibiotics, emphasizing that deficient use of the same can favor the spread of bacterial resistance, which threatens populations' health to make informed and conscious decisions about their treatments.<sup>[35-36]</sup> Justice implies an equal distribution of resources and benefits. The bacterial resistance threatens this principle. As a result, it limits access to efficient treatments and raises the costs of medical attention to treat infections that formerly were resolved with traditional antibiotics.<sup>[38-39]</sup>

## 5. CONCLUSIONS

The bacterial resistance represents a challenge to bioethics and public health, especially in the excessive use of antibiotics in medicine, veterinary, and the rest of the economic activities where they are utilized. The spread of resistant bacteria to antibiotics compromises the efficacy of the treatments and puts pressure on the health systems.

Facing this hazard requires adopting a bioethical perspective that guarantees the informed and conscious use of antibiotics based on the individual characteristics of the patients and the scientific evidence. It would be possible to decrease the impact of bacterial resistance during our age and the next ones only by using a multidisciplinary approach that includes a bioethical reflection shared between the health personnel and the population.

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