Antibiotic resistance: genetics and mechanisms

Antimicrobial resistance occurs when a microorganism such as bacteria, viruses or parasites acquire the ability to disable the effects of a drug designed to kill them or stop their growth (CDC, 2018). As a consequence the treatments to get rid of infections failed and the risk to spread to others increased (WHO, 2018).

Antibiotic Resistance is a global issue due to the fast and easy way of spreading. According to the CDC in 2013, around 2 million people were getting ill with bacteria that have the characteristic of being resistant to antibiotics. A minimum of 23, 000 people dies every year because of this threat. In most of the cases, people cannot be treated correctly so the infections caused by these bacteria get worse (CDC, 2013).

The excessive use of antibiotics is one of the main causes of the evolution of antibiotic resistance. The antibiotics is one of the most used drugs in the world and in many cases are not prescribed in the right way when treating diseases in humans. They are also used to prevent and treat diseases in animals and in some countries to promote growth (CDC, 2013).

All people are exposed to this type of threat, however the population that is most at risk are those with chronic diseases (CDC, 2018). This includes people under cancer treatments, diabetes, asthma, rheumatoid arthritis, organ transplants and so on. These sorts of people depend on the effectiveness of antibiotics to treat possible complications caused by infections during their treatments (CDC, 2013). The cost of medical care provided to patients with antibiotic resistant infections is higher than in patients with common illnesses, this is because they can be prolonged and in

many cases more expensive drugs are used (WHO, 2018). The total cost to treat infections related to antibiotic resistance in the United States is difficult to calculate and may vary, however by 2013 it was estimated that the cost could reach up to 20 billion dollars per year (CDC, 2013).

Genetic Basis of the Acquisition of Antibiotic Resistance

The bacteria use two main strategies to adapt to the attack of the antibiotics: Mutations in the gene and by the obtaining of DNA coding for resistance through the horizontal gene transfer (HGT). In the case of gene mutations, a group of bacteria susceptible to a certain antibiotic develops one or more resistance genes that make the effectiveness of the drug reduced or disappear. Once the resistance gene is expressed within the host, the antibiotic eliminates the susceptible community and resistant ones predominate. This type of mutations that result in antimicrobial resistance modifies the mode of action of the antibiotic using the following mechanisms: Reduction in the ability of absorption of the drug, activation of efflux mechanisms or overall changes in the metabolic pathways through the regulatory networks of the cell (Munita and Arias, 2016).

The acquisition of the antibiotic resistance gene through horizontal gene transfer is one of the most important vehicles in the development and evolution of bacteria. In general, this method is the main responsible for the antimicrobial resistance. When the transfer of resistance genes occurs, in most cases it is due to the bacteria being in an environment where intrinsic resistance genetic factors are lodged (Munita and Arias, 2016).

Three main ways in which bacteria acquire genetic material from the environment are known:

1. Transformation, which consists of acquiring DNA from the environment in which it is located, it is also known as incorporation of naked DNA. In general, a donor microorganism releases DNA into the environment and is catch by host bacteria. This is the simplest method in how a bacterium can acquire resistance genes (Munita and Arias, 2016).
2. Conjugation or “ bacterial sex”. Cell-to-cell contact is essential for the transfer process and it is presumed that it can occur at high rates within the digestive tract of humans who are in treatments that involve the ingestion of antibiotics. This method uses mobile genetic elements (MGE) as a vehicle for the distribution of genetic material, although it is also characterized by using direct transfer from chromosome to chromosome. Among the most important MGE are the plasmids and transposons, which play a key role in the distribution of microbial resistance in microorganisms of importance for human health (Munita and Arias, 2016).
3. Transduction, this mechanism involves genetic transfer through a virus particle (phage) to a host bacterium. The DNA is located in the phage and is responsible for the dissemination of the gene (Parkinson, 2016).

Mechanism for Antimicrobial Resistance

1. Impermeability: Decrease in number of porin channels lead to decrease in the entry of antibiotics into the cell. The molecules of an antibiotic can enter the cell through porins that are found in the outer membrane of gram-negative bacteria. As the number of porins

channels decrease the outer membrane becomes less permeable, preventing the passage of antibiotics such as β-lactams (Kapoor, 2017).

2. Pumping out (efflux pumps): The efflux pumps are proteins of the membrane that are located in the cytoplasm and are responsible for exporting the antibiotics of the cell. When an antimicrobial agent tries to enter, it is expelled by the efflux mechanisms before they can reach their target. All classes of antibiotics are susceptible to this type of mechanism with the exception of polymyxin (Kapoor, 2017).
3. Modification: Target site changes due to unexpected mutations of a bacterial gene located on the chromosome. These mutations prevent the binding of the antibiotic and the target site from taking place (Kapoor, 2017).
4. Antibiotic inactivation: There are three main enzymes that are responsible for the inactivation of antibiotics: β-lactamases, aminoglycoside-modifying enzymes, and chloramphenicol acetyltransferases. These enzymes are responsible for completely inactivating the function of the antibiotic inside the cell (Kapoor, 2017).

How Antibiotic Resistance Spreads

In countries where people have high incomes, the use of antibiotics has increased in hospitals, the agricultural area and the community in general. Many antibiotics are used indiscriminately and this has resulted in a decrease in their effectiveness (Laxminarayan, 2013).

The increase in the use of antibiotics in the community has made the weaker bacteria disappear and only the strongest prevail. It is known that as the

antimicrobial resistance increases, the consumption of antibiotics also increases. While bacteria have become champions of evolution, efforts in the development of new antibiotics have stalled, because the pharmaceutical industry has focused on the development of more lucrative drugs, used to treat diseases such as cancer or diabetes (Weckx, 2012)

The antibiotics are medicines that are used to eliminate bacteria that are causing some type of infection, however if this drug is given to people or animals that do not need it, the bacteria can develop resistance. One of the ways in which the microorganism can be prevented from developing resistance to antibiotics is through proper prescription. All people and animals have bacteria in the intestinal tract. When either of the two is treated with antibiotics, many of the bacteria will die, but those that are resistant will survive and multiply. Therefore, antibiotics should be used responsibly in humans and animals (CDC, 2018).

One of the critical points at the time of the dissemination of bacteria from animals is during slaughter and processing. At this point bacteria can contaminate meat and other products intended for human consumption. Another way in which bacteria can spread is through animal feces. These can contaminate the water and soil used to cultivated fruits and vegetables. People can acquire resistance infections through the manipulation or consumption of raw meat or products that have not been subjected to an adequate thermal process. It can also be contaminated by direct contact with animal feces or by drinking or swimming in pollutes water (CDC, 2018).

Some of the preventive actions taken by the CDC to prevent the transmission of antibiotic-resistant bacteria are: to track, study and analyze how the infection emerged and spread, identify and investigate as quickly as possible the outbreaks related to antimicrobial resistance, determine the source of contamination, educate people about preventive methods that include good hygiene practices when handling and consuming food, and promote the responsible use of antibiotics in humans and animals (CDC, 2018).

Regarding the preventive actions mention before, the CDC has established four main cores of actions to prevent antibiotic resistance, which includes: preventing infections and the spread of resistance, tracking, improving antibiotic prescribing and development of new drugs and tests. The main purpose of these cores is to control and prevent the spreading of resistance among the population (CDC, 2013).

The last report issued by the CDC on antibiotic resistance threat in 2013, reported the 18 principals threats (bacteria and fungi) of concern in human health. In each one, the minimum number of morbidity and mortality was evaluated, people who are at high risk for contracting resistant infections and actions that were being carried out to combat this threat. Among the microorganisms of greater relevance and that represented greater risks to health are: *Clostridium difficile* (*C. difficile*), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance). The CDC is working in issuing a new report of antiotic threats by fall 2019 (CDC, 2018).

The National Antimicrobial Resistance Monitoring System (NARMS)

NARMS is a public health monitoring system in the United States established in association with the Food and Drug Administration (FDA), Center for Disease Control and Prevention (CDC) and the U. S. Department to track antibiotic resistance in foodborne and enteric bacteria from humans, retail meats and food animals.

- https://www. cdc. gov/drugresistance/about. html
- https://www. who. int/antimicrobial-resistance/en/
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