Combating Antibiotic Resistance: How Possible In Bacteria And Cancer Cells?

Nginyu Semuyeh Fabris[1]

1Department of Pharmacology, Faculty of Biomedical Science, Redemption Higher Institute of Biomedical Science (RHIBMS)-Buea. Tel: +237679594289. Email. drnginyu@gmail.com.

Abstract

Antimicrobial resistance has become a major clinical and public health problem. An issue that touches the lives of most people alive today. Antibiotic supplies have increased over the past 50 years, so bacteria have responded to the flood by leaving offspring. That is no longer the case. It contains antibiotics. Resistance genes and the prevalence of resistant bacteria also play an essential role in selecting bacterial resistance and contribute to this problem. The selection of resistant forms can occur during or after antimicrobial therapy. Antibiotic residues can be found in the environment long after treatment. In addition to antibiotics other active ingredients that destroy bacteria are also increasingly used, namely antimicrobial surfactants, which are now found in many household products. These also enter the environment so the stage adapts to altered microbial ecology, not just in terms of resistance. It affects susceptible bacteria and the types of micro-organisms that survive.

Key words: *Antibiotics, Mutation Rate, Public Health Problem, Resistant Bacteria.*

I. Introduction

Antibiotic resistance is when bacteria and/or other infectious organism in the system develop the ability to fight and possibly defeat antibiotics assigned to kill them contrary to the idea that the body itself is resistant to the antibiotic. Bacteria and cancer cells are the leading causes of death worldwide. According to one study, cancer is the second leading cause of death worldwide, killing 8.7 million people in 2015 (Fitzmaurice *et al.*, 2017). Antibiotic resistance, the ability of bacteria to overcome drugs designed to kill them, is also one of our most significant global public health challenges. Antibiotics are one of the most potent tools for fighting life-threatening infections. The mechanisms by which bacteria protect themselves from antibiotics can be classified into four basic types. The most well-known is a modification by antibiotics.

Resistant bacteria retain the same sensitive targets as antibiotic-sensitive strains but use antibiotics. Often, administering low doses of antibiotics that are not potent enough to kill all bacteria promotes survival strategies and the emergence of resistance in some bacteria. Bacteria can evolve ways to fight antibiotics by preventing them from reaching target cells, altering the structure of target cells, or even replacing target cells entirely. Alternatively, produce enzymes that destroy antibiotics. Antibiotics are one of the most effective life-saving treatments in all of medicine. The reduction in mortality with strong antibiotics in all bacterial infections, from superficial skin infections to bloodstream, lung, abdominal, and brain infections, has been significantly reduced (Spellberg *et al.*, 2016).

This happens, for example, with β-lactamases the β-lactamases enzymatically clave the four-membered β-lactam ring, rendering the antibiotic inactive. Most β-lactamases act to some degree against both penicillins and cephalosporins, and others are more specific-namely, cephalosporins, for example AmpC enzyme found in Enterobacter spp, or penicillinases, for example, Staphylococcus aureus penicillinase. β-lactamases are widespread among many bacterial species (both Gram-positive and Gram-negative) and exhibit varying degrees of inhibition by β lactamase inhibitors, such as clavulanic acid.1

Some antibiotic-resistant bacteria protect the target of antibiotic action by preventing the antibiotic from entering the cell or pumping it out faster than it can flow in (rather like a bilge pump in a boat). β-lactam antibiotic in

Gram-negative bacteria gains access to the cell that depends on the antibiotic through a water-filled hollow membrane protein known as a porin. In the case of imipenem resistant *Pseudomonas aeruginosa*, lack of the specific D2 porin confers resistance, as imipenem cannot penetrate the cell. This mechanism is also observed with low tolerance to fluoroquinolones and aminoglycosides. Increased efflux by energy-requiring transport pumps is a known resistance mechanism to tetracyclines. It is encoded by various related genes, such as tet(A), widely distributed in Enterobacteriaceae. Changes in the leading site of action allow the antibiotic to enter the cell and reach its target site. However, conformational changes in the molecule cannot inhibit the target's activity. Enterococci are believed to be naturally resistant to cephalosporins because the enzymes involved in cell wall synthesis, the so-called penicillin-binding proteins, have a low affinity for cephalosporins and are, therefore, not inhibited. Most strains of *Streptococcus pneumoniae* are susceptible to penicillins and cephalosporins. However, taking DNA from other bacteria and modifying the enzyme to have a lower affinity for penicillin is possible (Houndt and Ochman, 2000).

The altered enzyme continues to synthesize peptidoglycan but now has a different structure. However, penicillin-resistant, laboratory-altered *S. pyogenes* variants have not been observed in patients. This is probably because the cell wall can no longer bind the antiphagocytic M protein. The ultimate mechanism by which bacteria protect themselves from antibiotics is to generate alternative targets. These enzymes are usually resistant to antibiotic inhibition while continuing to generate the original sensitive target. This allows bacteria to survive despite selection (Grahn and Holm, 1987).

Alternate enzymes circumvent the action of antibiotics. The best-known example of this mechanism is an alternative penicillin-binding protein produced by methicillin-resistant *Staphylococcus aureus* (MRSA) and the normal penicillin-binding protein. The mecA gene encodes a protein. Since PBP2a is not inhibited by antibiotics such as flucloxacillin, cells continue synthesizing peptidoglycan and have structurally healthy cell walls (Nord, 1986).

The emergence of vancomycin-resistant enterococci in 1987 generated tremendous interest because the genes involved could be transferred to Staphylococcus aureus, theoretically causing vancomycin-resistant MRSA. This mechanism is also a variant of the alternative targeting mechanism of resistance. In vancomycin-sensitive enterococci, the average target of vancomycin is a cell wall precursor containing a D-alanine-D-alanine-terminated pentapeptide that binds vancomycin. Therefore, further cell wall synthesis is prevented. However, when enterococci acquire the vanA gene cluster, they can make another cell wall precursor that terminates in D-alanine-D-lactose, to which vancomycin does not bind (Spratt, 1994).

A vaccine to reduce troll colonisation and subsequent infection. Gram-positive cocci have become established in the last two decades among the causative agents of nosocomial infections. This trend is associated with these pathogens.

Evolutionary natural selection will eventually lead to the emergence of antibiotic resistance, but antibiotic abuse and overuse exacerbate the process dramatically. When antibiotics are misused in human or veterinary medicine (too short, too low in dose, not strong enough, or used for the wrong disease), they do not kill bacteria; their survival properties may be passed on too many bacteria. This leads to more severe infections, more illness, and even death. Rising resistance is also caused by the overuse of antibiotics, including prolonged treatment at intensities insufficient to kill all bacteria commonly found on industrial farms. Antibiotics are used in cattle, poultry, pigs, and other livestock not only to treat individual diseases but also to prevent disease in whole herds and herds living in cramped and unsanitary conditions and to promote growth. It also improves feed efficiency. Up to 70 percent of all antibiotics manufactured in the United States are administered to livestock, not humans. According to the World Health Organisation, the widespread use of antibiotics to control disease and promote growth in animals has increased the resistance of bacteria, often expelled from animals through diet. It can infect animals. Infectious diseases are caused in humans (Rodríguez *et al*,. 2000).

The problem of drug resistance is a global health challenge that demands consistent scientific work to combat the bacteria and cancer cell resistance to antibiotic and cancer chemotherapy, respectively.

The objectives of this study are:

- This study will be geared at looking at some manifestations of antibiotic antibacterial resistances and cancer cell resistance chemotherapy.
- Understanding their mechanisms of action of antibacterial resistances and cancer cell resistance chemotherapy.
- Asserting how possible the resistances can be combat.

This paper is organised into four different sections. Section 1 focuses on the introduction. Section 2 gives a literature review of the subject under investigation. Section3 focuses on the methodology. Section 4 will give a detailed account of the findings. The paper ends with section 5 where summary, conclusion and recommendations are given.

I. Literature Review

Several commercial antibiotics are produced by bacteria or fungi in nature as part of their repertoire of secondary metabolites. Probably, the most well know is the production of penicillin by the Penicillium mold, with most of our commonly used antibiotics, among them streptomycin and tetracycline, being products of soil bacteria belonging to the genus Streptomyces (Procópio *et al.*, 2012). Esnault *et al.* (2017) suggested that 'antibiotics are part of the physiological function of the producing organism by being involved in the regulation of the cellular growth rate'.

Antibiotic resistance can be achieved through horizontal acquisition of resistance genes carried by transposons or plasmids, recombination of foreign DNA into chromosomes, or mutations at different chromosomal locations. In the study of molecular evolutionary biology, the term mutation rate refers to the mutation rate on a nucleotide-by-nucleotide, locus-by-locus, or ultimately genome-wide basis, selectively considering favorable, unfavorable, or neutral mutations. Used to estimate the Moving away from this concept, mutation frequency measures all mutants present in a given population regardless of whether the mutation event occurred early or late in population growth. Thus, Mutant frequencies provide a cross-section of the bacterial population at a given time. It reflects not only the mutation rate but also the history of the population prior to selection. For antibiotic resistance, the mutation rate is often defined as the in vitro frequency at which detectable mutants emerge within a bacterial population in a specific antibiotic concentration (Edlund Nord, 1993).

The method to distinguish observed resistance frequency values cannot be compared by simply applying the mutation rates and mutant strains. Variation tests were developed to analyse the presence of pre-existing mutant jackpots in the tested population. The problem is further complicated in the case of antibiotic resistance, as the phenotype may only reflect the identical genotype of all selected mutants. Finally, mutations in different genes can result in similar antibiotic resistance phenotypes (Edlund and Nord, 1993).

In this respect, the calculated 'phenotypic mutation rate' results from several different 'genotypic' mutational events. It is well-known that mutations at different sites lead to different MIC changes and stably maintain heterogeneous antibiotic resistance expression classes in bacterial populations. The mutation rate of a particular antibiotic can vary depending on its concentration at selection (Gahm-Hansen, 1987). Physiological conditions, such as the availability of mutagenesis phenotypes in bacteria and the ability of some antibiotics to increase mutability, greatly complicate studies on the effects of population dynamics on the emergence of antibiotic-resistant mutants in bacteria. These variables pose significant challenges to our ability to predict mutation rates using only simple experimental procedures commonly used in laboratory experiments (Hoiby *et al*., 1997).

Clinical studies have shown that approximately 4% of infectious organisms resist treatment. There is also a relationship between the amount of antibiotic used and the resistance level. Such penicillin-resistant pneumococcal clones are spreading regionally and internationally under selective pressure. The rapid increase of resistant strains in the commensal flora is less widely recognized (Jarlov and Hoiby, 1998). However, there is growing evidence that normal flora provides a pool to select resistance genes that can spread to other species and genera by horizontal transfer by conjugation, transduction, or transformation. Swallowing penicillin and other oral antibiotics exposes the normal oral and pharyngeal flora to the antibiotic, along with the excretion of the antibiotic from the salivary glands, viridans group streptococci, and other components of the normal flora is suppressed. When the bacterium is lysed by an antibiotic such as penicillin, its DNA is released, facilitating horizontal gene transfer through transformation. Some pneumococci acquire penicillin resistance through penicillin-binding protein 2 (PBP2) alterations, resulting in decreased penicillin levels (Zhang *et al.*, 2017).

II. Methodology

Food animals shed resistant bacteria in their skin, in the case of Staphylococcus infections. Once there, antibiotic-resistant bacteria in contaminated manure can migrate around a farm, in slaughter and meat processing, into neighbouring farms and the environment, and even across long distances. Therefore, they are easier to control once harmful resistant bacteria are generated (Rule *et al.*, 2008).

Several direct routes of human exposure to antibiotic-resistant bacteria develop in industrial food animal production: Improper handling or consuming inadequately cooked contaminated meat. Contact infected farm workers, meat processors, or perhaps their families, doctors, and others with whom they interact—drinking

contaminated surface or groundwater and eating contaminated crops, and contacting air vented from concentrated animal housing or released during animal transport (Mellon *et al.*, 2001).

Bacterial genetic adaptation to antibiotics can be achieved through two distinct pathways: (I) by a spontaneous genetic change in the chromosome or (II) by the acquisition of a resistance-conferring gene encoded on a foreign piece of DNA through horizontal gene transfer. Genetic changes in ChromosomeA spontaneous genetic change in the chromosome could be a point mutation, insertion or deletion in a gene or regulatory element, or amplifying a genetic segment. A genetic change could have several consequences in the cell, including deactivating a gene or altering its expression level. These two events are relatively frequent since they can happen through several different avenues, such as amino acid substitutions, deletions, insertions, and amplifications that affect a gene directly or its regulators. For example, antibiotic resistance is often acquired through increased expression of an efflux pump due to a disruption in a gene that represses the expression of the pump or through amplification of the genetic segment that encodes the pump (Piddock, 2006). Other possible consequences could be an alteration of the conformation of the gene product or a change in the antibiotic binding site. Telenti *et al., in 1993*, described the first scenario where a point mutation provides silver resistance by ostensibly changing the conformation of the sensor protein. Resistance to rifampicin is achieved by mutations in the binding site of the RNA polymerase preventing the antibiotic from binding its target (Campbell *et al*., 2001; Brandis *et al.*, 2015). An altered protein conformation or a changed binding site would be less frequent since they require specific mutations in a restricted genetic region (Schaaper *et al.*, 1986; Drake, 1991; Abdulkarim & Hughes, 1996). Despite the lower frequency, these mechanisms are of greater clinical importance since the resistance levels are higher and are associated with lower fitness costs (Huseby e*t al*., 2017). A chromosomal genetic change is stable and is inherited by the next generation. When the change provides a benefit, such as resistance during antibiotic exposure, the bacteria that possess it will survive and reproduce.

Mechanisms of bacterial antibiotic resistance acquisition. Antibiotic resistance can develop by internal changes in the chromosome or horizontal gene transfer (yellow).

(i) Internal mechanisms include spontaneous genetic changes in amino acid substitutions, insertions, deletions, or amplifications in the bacterial chromosome. Horizontal gene transfer includes

(ii) The uptake of naked DNA from the environment (transformation),

(iii) The transfer of genetic material by phage infection (transduction), and

(iv) The uptake of a mobile genetic element such as a plasmid (conjugation).at a higher rate than their competitors. The change gets fixed in the local bacterial population even without the antibiotic.

Notable exceptions to this stability are gene amplifications that rapidly segregate without selection pressure (Sandegren & Andersson, 2009; Reams *et al*., 2010). Horizontal Gene TransferHorizontal gene transfer is a common way to acquire a resistance-conferring gene. This happens by obtaining a foreign piece of DNA by (I) the uptake of naked DNA from the environment (transformation) (II) infection by a bacterial phage (transduction) the uptake of a mobile genetic element by conjugation (Soucy *et al.*, 2015). Mobile genetic elements are pieces of DNA that, as the name suggests, can move independently of the cell. The most significant mobile genetic elements are transposons and plasmids. A transposon is a DNA segment that can integrate into the bacterial chromosome. Transposons in the Tn21 family are great drivers in the spread of antibiotic resistance because they carry an array of antibiotic-resistance genes that are spread among bacteria as the transposon moves within and across species barriers (Liebert *et al.*, 1999). Transposons can also integrate into the other mobile genetic element mentioned, plasmids. Plasmids are circular extra-chromosomal entities of DNA that contain the genes necessary for their proliferation and often also their intracellular transfer mechanism. They carry genes that are not essential to the growth of the cell under normal conditions, but that can confer benefits to the cell in certain circumstances, such as antibiotic and metal resistance genes. Plasmids can harbor resistance genes to several antibiotics and metals, making the cell multi-drug resistant. Thus, acquiring one plasmid can render a bacterium resistant to various compounds. This way, plasmids can often greatly benefit their bacterial host cell, giving it a competitive advantage and tremendous reproductive success in a set environment. The drawback for the plasmid-carrying bacterium is the fitness cost or decrease in growth rate that a plasmid often confers on a cell. The slower growth rate will place the cell at a disadvantage in environments lacking direct selective pressure on the plasmid (Dahlberg & Chao, 2003). The presence of plasmids is to a great extent, responsible for the rapid spread of clinical resistance among Gram-negative bacteria. Resistance to several classes of antibiotics, among them β-lactams (including carbapenems), has been identified in plasmids present in Enterobacteriaceae isolated from clinics (Kumarasamy *et al.*, 2010), and plasmid-encoded β-lactamases such as the extended-spectrum β-lactamase (ESBL) CTX-M group and carbapenemases cause outbreaks of infections worldwide (Carattoli, 2009). Plasmid is an example of an ESBL-encoding plasmid with clinical relevance. It was isolated from a Klebsiella pneumonia strain that caused nosocomial outbreaks among elderly and immune-compromised patients at Uppsala University Hospital between 2005 and 2007. This plasmid consists of a backbone similar to another Klebsiella pneumonia-associated plasmid, pKPN3, and it encodes a cassette of antibiotic resistance genes also found in plasmids in the recognized outbreak strain E. coli ST131 (Woodford *et al*., 2009; Sandegren *et al.*, 2011). The gene cassette includes resistance to aminoglycosides, macrolides, sulfonamides, tetracyclines,

trimethoprim, and β-lactams, including the extended-spectrum β-lactamase gene CTX-M-15 that breaks down cefotaxime. In addition, the plasmid carries genes for resistance to quaternary ammonium compounds and the metals silver, copper, and arsenic (Sandegren *et al.*, 2011).

Mechanisms of Resistance; The mechanisms of antibiotic resistance involve interfering with or preventing the action of the antibiotic molecule. The bacterial cell has many potential strategies; multiple mechanisms can sometimes work against the same antibiotic. A ubiquitous and general mechanism of resistance is (I) decreasing the cellular concentration of the antibiotic by preventing uptake or enhancing efflux. The uptake of antibiotics can, for example, be reduced by deleting membrane porins through which the antibiotics enter the cell (Nikaido, 2001; Nikaido, 2003). The unspecific efflux pump, AcrAB-TolC, spans the membranes of many clinical Gram-negatives and transports a wide array of toxic substances out of the cell, including the antibiotics ciprofloxacin, tetracycline and chloramphenicol. Genetic changes that lead to pump overexpression increase the resistance level (Baucheron *et al*., 2004; Keeney *et al.*, 2007; Swick *et al*., 2011). Another common strategy is (II) preventing the antibiotic from binding to its cellular target. This can be achieved by altering the antibiotic binding site in the target molecule (by mutation or enzyme activity) (Hooper, 2000; Brandis *et al.*, 2015), by the presence of a "protective" molecule that competes with the antibiotic for binding the target (Connell *et al.*, 2003) or by enzymatic alteration or destruction of the antibiotic molecule itself (Bonnet, 2004; Robicsek *et al.*, 2005). Both rifampicin and quinolone resistance is achieved by mutations in the cellular target, RNA polymerase, and DNA gyrase, respectively, that inhibit the binding of the antibiotic molecule (Telenti *et al*., 1993; Heisig & Tschorny, 1994; Piddock *et al.*, 1999; Marcusson et al., 2009; Brandis *et al.*, 2015). Ribosomal protection proteins, such as TetM, protect the ribosomes from tetracycline binding (Connell *et al.*, 2003; Dönhöfer *et al.*, 2012), and topoisomerase protection proteins can confer resistance to fluoroquinolone antibiotics (Tran *et al*., 2005; Garoff *et al.*, 2018) Resistance to the important β-lactams is provided by destruction of the antibiotic molecule by β-lactamases (Bonnet, 2004). Furthermore, the cell can (III) bypass the harmful action of the antibiotic. This can be done by abandoning the use of the target molecule by finding alternative proteins to perform the same biochemical function as the target molecule or by increasing the expression of the target molecule. An example of the use of an alternative protein is MecA-mediated methicillin resistance in MRSA (Stapleton & Taylor, 2002), and overexpression of MurA, the target of the antibiotic fosfomycin, can confer clinical resistance levels (Couce *et al*., 2012). Mechanisms of antibiotic resistance include; Reduced cellular drug concentration by decreasing uptake or increasing efflux, prevention of drug binding by altering the binding site on the drug target, prevention of drug binding by the presence of a protein that competes for the same binding site on the drug target, Prevention of drug binding by enzymatic destruction of the drug, bypassing the harmful effect of the drug by the presence of an alternative protein to perform the same biochemical function as the drug target and bypassing the harmful effect of the drug by increasing the level of expression of the drug target

Origin of Antibiotic Resistance Genes despite the current problem of clinical antibiotic resistance, it has been well established that antibiotic resistance determinants originated long before the human antibiotic era. Cultured Gram-negatives and Gram-positives from a New Mexico cave that had been isolated for 4 million years collectively exhibited resistance to more than a dozen commercially available antibiotics, including streptomycin, clindamycin, sulfamethoxazole as well as semisynthetic macrolides and the last-resort drug daptomycin (Bhullar *et al*., 2012). Similarly, 30 000-year-old permafrost contained bacterial genes for resistance to vancomycin, beta-lactams, and tetracycline. Interestingly, the vancomycin resistance determinant, vanA, resembled modern versions (D'Costa *et al.*, 2011). These studies demonstrate that a wide range of antibiotic resistance determinants before human-induced selection had any influence on bacterial evolution. Since antibiotics are themselves produced by microorganisms, this may not be surprising. However, the role of antibiotic-resistance genes in nature is unclear, as is the case for antibiotics. They could have evolved to interfere with signaling or to ward off the toxic effects of antibiotics in the producing organism itself or competitors. β-lactamases might initially be proteins involved in cell wall synthesis, the antibiotic resistance activity being an unintentional side effect (Massova & Mobashery, 1998). The collective reservoir of bacterial antibiotic resistance genes, referred to as the resistome, has most likely served as the origin of resistance determinants that have been introduced into pathogenic strains. Environmental Resistome and Human Pathogens Antibiotic resistance genes are widespread and diverse in environmental bacteria. However, to pose a clinical threat to humans, they must enter and be expressed in strains belonging to the mammalian commensal flora or that can colonize the mammalian gut, nasopharynx, lungs, or urinary tract and potentially cause infection. A proposed scenario is that anthropogenic use and distribution of antibiotics create artificially high concentrations in human habitats and thus facilitate the process of gene transfer from environmental bacteria to mammalian pathogenic strains. Several studies surveying resistance frequencies in commensal bacteria from wild animals point towards a connection between resistance and exposure to humans or human activities. In one study, fecal E. coli was sampled from animals in distinct groups according to the human population density within the animal's habitat. There was a clear trend where resistance increased with human population density, and the highest frequencies were found within farm animals and pets (Skurnik, 2006). Two separate studies show that enteric bacteria from gorillas whose habitat overlapped with humans and livestock, as well as from baboons that resided near a tourist

lodge, exhibited more antibiotic resistance than enteric bacteria from gorillas and baboons living in isolated areas with minimal human contact (Rolland et al., 1985; Rwego *et al.*, 2008). Similarly, rodents living close to human populations in the U.K. were found to have a high prevalence of resistance to β-lactams in their commensal Enterobacteriaceae (Gilliver *et al*., 1999). In contrast, Enterobacteriaceae isolated from moose, deer, and vole in remote areas of Finland harbored almost no antibiotic resistance (Österblad *et al.*, 2001). These studies are all observational and do not show the underlying mechanisms of the observed pattern. However, they correlate human contact and antibiotic resistance in animal enteric bacteria. Thus, they offer indications that (I) residual concentrations of antibiotics in populated areas select for resistance in enteric strains and (II) that the resistance genes and resistant enteric strains spread and are shared between creatures residing within the geographical area where the selective antibiotics are present. The resistance circulating within animal populations in this manner could originally have been selected for among human patients or in clinics and subsequently spread into the surrounding animal habitat. Alternatively, the genes could originate from the environmental resistome. As such, the "artificial" selection pressure by residual antibiotics released by human activities would have transferred resistance genes from environmental bacteria to enteric bacteria to establish themselves within the enteric bacteria. A metagenomic study identified resistance genes in bacteria from various U.S. soils identical to genes encoded in human pathogenic strains. The genes conferred resistance to beta-lactams, aminoglycosides, amphenicols, sulfonamides, and tetracyclines (Forsberg *et al*., 2012). Plasmid-borne beta-lactamases belonging to the CTX-M group have also been found on the chromosomes of the soil and water-dwelling Kluyvera, indicating that this clinically relevant resistance has environmental origins (Poirel *et al.*, 2002). Aquatic Shewanella has been identified as the reservoir of the ciprofloxacin resistance gene and the oxacillinase group of beta-lactamases (Poirel *et al*., 2004; Poirel *et al.*, 2005). Two separate studies also present evidence that the exchange of antibiotic-resistance genes happened through mobile genetic elements such as integrons (Skurnik, 2006; Forsberg *et al*., 2012).

III. Findings and Discussions

Increase drug resistance to most antibiotics like streptomycin, chloramphenicol and trimethoprim are substantial, displaying that exposure to QACs (Quaternary Ammonium Compounds) are capable of causing significant cross-resistance to antibiotics. Though the degree of increased resistance in many cases is relatively low, any increase in resistance gives the bacterium an advantage over fully susceptible strains. This advantage can serve as a springboard in the development of higher levels of resistance. Not surprisingly, efflux mechanisms account for many of the genetic changes that were identified. Changes in genes related to translation/ transcription and membranes.

Moreover, the environment consists of minute concentrations of antibiotics and metals which would be contaminated with human or animal faeces containing potential pathogenic bacterial strains as well as the plasmids they carry. Thus, the use and distribution of antibiotics and metals is a concern in many external environments where the lower concentrations were previously assumed to be insufficient for selection of antibiotic resistance (Albrecht, 2018).

In addition, are brought about due to incomplete treatment of a particular disease or repeated administration of a particular medication over prolong administration.

Conclusion and Recommendation

Antibiotic resistance is when bacteria and/or other infectious organism in the system develop the ability to fight and possibly defeat antibiotics assigned to kill them, contrary to the idea that the body itself is resistant to the antibiotic. Bacteria and cancer cells are the leading causes of death worldwide. Antibiotic resistance, the ability of bacteria to overcome drugs designed to kill them, is also one of our most significant global public health challenges.

Resistant bacteria retain the same sensitive targets as antibiotic-sensitive strains but use antibiotics. Often, administering low doses of antibiotics that are not potent enough to kill all bacteria promotes survival strategies and the emergence of resistance in some bacteria. Some antibiotic-resistant bacteria protect the target of antibiotic action by preventing the antibiotic from entering the cell or pumping it out faster than it can flow in (rather like a bilge pump in a boat).

Changes in the leading site of action allow the antibiotic to enter the cell and reach its target site. Enterococci are believed to be naturally resistant to cephalosporins because the enzymes involved in cell wall synthesis, the so-called penicillin-binding proteins, have a low affinity for cephalosporins and are, therefore, not inhibited.

The ultimate mechanism by which bacteria protect themselves from antibiotics is to generate alternative targets. These enzymes are usually resistant to antibiotic inhibition while continuing to generate the original sensitive target.

The best-known example of this mechanism is an alternative penicillin-binding protein produced by methicillin-resistant Staphylococcus aureus (MRSA) and the normal penicillin-binding protein. The emergence of vancomycin-resistant enterococci in 1987 generated tremendous interest because the genes involved could be transferred to Staphylococcus aureus, theoretically causing vancomycin-resistant MRSA. In vancomycin-sensitive enterococci, the average target of vancomycin is a cell wall precursor containing a D-alanine-D-alanine-terminated pentapeptide that binds vancomycin. However, when enterococci acquire the vanA gene cluster, they can make another cell wall precursor that terminates in D-alanine-D-lactose, to which vancomycin does not bind (Spratt, 1994).

Antibiotic resistance can be achieved through horizontal acquisition of resistance genes carried by transposons or plasmids, recombination of foreign DNA into chromosomes, or mutations at different chromosomal locations. For antibiotic resistance, the mutation rate is often defined as the in vitro frequency at which detectable mutants emerge within a bacterial population in a specific antibiotic concentration (Edlund Nord, 1993).

The method to distinguish observed resistance frequency values cannot be compared by simply applying the mutation rates and mutant strains. The problem is further complicated in the case of antibiotic resistance, as the phenotype may only reflect the identical genotype of all selected mutants. Finally, mutations in different genes can result in similar antibiotic resistance phenotypes (Edlund and Nord, 1993).

Physiological conditions, such as the availability of mutagenesis phenotypes in bacteria and the ability of some antibiotics to increase mutability, greatly complicate studies on the effects of population dynamics on the emergence of antibiotic-resistant mutants in bacteria. When the bacterium is lysed by an antibiotic such as penicillin, its DNA is released, facilitating horizontal gene transfer through transformation.

Since it has been seen or observed that it is quite difficult to deal away completely with drug resistance due to its versatile modes of action and natural environmentally influencing factor, the following recommendations can be made;

Drug analogues should not be encouraged because since they take a longer time to deliver the desired responds, it potentially leads to drug resistance.

Patient monitoring to probably complete the required medication within the desired time frame (according to prescription) should be encouraged to ensure the proper eradication of the bacteria leading to elimination of the bacteria completely which could lead to developing resistance.

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