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A Review on Antibiotic Resistance in Microorganisms

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ABSTRACT

Antibiotic resistance occurs when microorganisms develop mechanisms that protect them from the effects of antibiotics. Resistant microorganisms are more difficult to treat, require higher doses or alternative therapies may be more toxic, as well as more expensive. Microorganisms that are able to resist many antibiotics are called multi-resistant. All kinds of microorganisms can develop this ability to resist; Fungi develop resistance against antifungals, viruses develop resistance against antivirals, protozoa develop resistance against protozoa, and bacteria develop resistance against antibiotics. Resistance arose naturally either through genetic mutations or through the transmission of resistance from one sex that has acquired it to another that has not yet acquired it, in particular. Accordingly, it is urgent to reduce the misuse of antibiotics by not using them only when they are really needed.

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1. Introduction

Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria change themselves in response to the use of these medicines (Alter, 2015). Bacteria, not humans or animals, are resistant to antibiotics and may cause infections in humans and animals that are more difficult to treat than those caused by their non-antibiotic resistant counterpart (Dadgostar, 2019). Antimicrobial resistance (AMR) occurs when microbes develop mechanisms that protect them from their antimicrobial effects. The term antibiotic resistance is a subcategory of antimicrobial resistance, as it applies to bacteria that develop resistance to antibiotics. Resistant microbes are difficult to treat and may require higher doses or alternative, more toxic types of drugs. These methods may also be more expensive. Microbes that are resistant to many antimicrobials are called multidrug resistance (MDR) (Kwon & Powderly, 2021).

All classes of microbes can develop resistance. As fungi develop resistance to antifungals, viruses develop resistance to antivirals, protozoa develop resistance to antiprotozoal, and bacteria develop resistance to antibiotics. Bacteria that are broad-spectrum-resistant (XDR) or fully drug-resistant (TDR) are called “superbugs” (MacGowan & Macnaughton, 2013). Bacteria resistance can arise naturally through genetic mutations or through the transmission of resistance from one type to another. Resistance can arise spontaneously due to random mutations. However, prolonged use of antimicrobials appears to encourage selection for mutations that would eliminate antimicrobial efficacy (Gerber, et al, 2017).

Antibiotic resistance increases medical costs, extends hospital stay, and increases mortality. The world urgently needs to change the way antibiotics are prescribed and used, and even if new drugs are developed, antibiotic resistance will remain a major threat unless it changes behaviors in the use of these drugs. A change that must also include taking measures to limit the spread of infections thanks to vaccination and washing Hands, have safe sex, and take good care of food hygiene (Murray, et al., 2022). Antibiotic resistance is rising to dangerous levels worldwide and new resistance mechanisms are emerging and spreading globally that threaten our ability to treat common infectious diseases. There is a growing list of inflammatory infections - such as pneumonia, tuberculosis, septicemia and gonorrhea - that are becoming more difficult, and

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sometimes impossible, to treat due to the low efficacy of antibiotics (Cirz et al., 2005).

1.1. Causes of Resistance

Antibiotic resistance emerged because of evolution by natural selection. The effect of the antibiotic puts an environmental pressure on the bacteria, but mutations that appear in some bacterial cells cause them to survive the action of the antibiotic (Holmes et al., 2016). Then, this feature is passed on to the next offspring, which is characterized as a generation that is completely resistant to the antibiotic. Several studies have shown that the way antibiotics are used greatly affects the development of the number of resistant microorganisms. Overuse of broad-spectrum antibiotics, such as second- and third-generation cephalosporins, accelerates the development of methicillin resistance. There are other factors represented in the inaccurate medical diagnosis, the doctor prescribing unnecessary drugs, the inappropriate use of antibiotics by the patient, in addition to the use of antibiotics as additional materials to feed livestock to encourage their growth (Cirz et al., 2005).

1.2. Mechanism of Antibiotic Resistance by Pathogenic Bacteria

Antibiotic resistance occurs in four ways (Boyle-Vavra & Daum, (2007):

1. Inhibition or alteration of the antibiotic: Such as the enzymatic inhibition of penicillin G in some penicillin-resistant bacteria by synthesizing beta-lactamases
2. Changing the site of the target (the site of antibiotic activity): Such as changing the PBP - the site of penicillin activity - in a type of bacteria called MRSA, as well as in other bacteria that are resistant to penicillin
3. Altering the metabolic pathway: PABA is an important factor for the synthesis of folic acid and nucleic acids in bacteria. This factor can be inhibited by sulfonamide. However, some bacteria resistant to sulfonamide dispense with this essential factor by using ready-made folic acid (by taking it directly from their surroundings, for example), just like animal cells
4. To reduce antibiotic buildup: by decreasing the permeability of the antibiotic into the cell and/or accelerating the active flow (pumping to the periphery) of drugs across the bacterial cell membrane.

2. Pathogenic and Resistant Microorganisms

2.1. Staphylococcus aureus

Staphylococcus aureus, or for short, *staph aureus* or *staph* infection, is one of the most important pathogenic and resistant microorganisms. These bacteria are present on the skin and mucous membranes of approximately one third of the population. This type of bacteria is highly adaptable to the pressure of antibiotics. *Staphylococcus aureus* is the first bacteria that developed resistance against penicillin in 1948, a few years (four years) after selling penicillin in large quantities (Maree et al., 2007; Larsen, 2022). After developing resistance to penicillin, methicillin was used instead of penicillin, but due to the emergence of a dangerous side effect, which is toxicity to the kidneys

because of the use of methicillin, it was also replaced by oxacillin. MRSA was first discovered in Britain in 1961. Methicillin-resistant *Staphylococcus aureus* is responsible for 37% of fatal cases of septicemia in Britain in 1999, after it was no more than 4% in 1991. Now, this phenomenon has become acutely prevalent in hospitals (Albrich et al., 2004; Larsen, 2022).

Half of all cases of *S. aureus* infection in the United States are resistant to penicillin, methicillin, tetracycline, and erythromycin. Therefore, vancomycin is the only effective antibiotic in our time. Although vancomycin-resistant *Staphylococcus aureus* was discovered in Japan in 1996. It was also found in some hospitals in Britain, the United States of America and France. Vancomycin-resistant *Staphylococcus aureus* has been given other names such as glycopeptide-mediator *Staphylococcus aureus* or Vancomycin-insensitive *Staphylococcus aureus*. This clearly indicates resistance to all antibiotics of a peptidoglycemic nature (Ferri et al., 2017).

A new class of antibiotics, oxazolidinone, was developed that became available in the 1990s. The first oxazolidinone to be introduced to the market is linezolid, which is comparable to vancomycin in terms of efficacy against MRSA. Unfortunately, the first case of *Staphylococcus aureus* resistant to linezolid was reported in 2003 (Ayukekbong et al., 2017). Community-acquired MRSA has emerged as an epidemic causing progressive and fatal diseases such as necrotizing/necrotizing pneumonia, severe sepsis, and necrotizing fasciitis.

The epidemic of infection with methicillin-resistant *Staphylococcus aureus* is changing rapidly. There are two clones of MRSA in the United States of America, these two clones are USA400 (MW2 strain, ST1 strain) and USA300, and they are considered responsible for community outbreaks. The two clones most often contain the Pantone-Valentine-Lucocidin (PVL) genes and the presence of these pathogens was related to the presence of these two strains Associated with the skin and soft tissues (Harris et al., 2019).

2.2. Enterococcus Faecium

Enterococcus faecium is another highly resistant bacteria found in hospitals. Penicillin-resistant was observed in 1983, vancomycin-resistant was observed in 1987, and linezolid-resistant was observed in the late 1990s (Tang et al., 2017).

2.3. Streptococcus Pyogenes

Group A streptococcal (GAS) infection can be treated with different antibiotics. Early treatment can reduce the risk of death from infection with group A invasive streptococci. For people with very serious infections, intensive care is essential. People with necrotizing fasciitis need surgery to remove the damaged tissue. *Streptococcus pyogenes* species have emerged that are resistant to the antibiotic macrolide, but all *Streptococcus pyogenes* are sensitive to penicillin (Innes et al., 2020).

2.4. Streptococci Pulmonary

Streptococcus pneumoniae resistance to penicillin and beta-lactam antibiotics is on the rise worldwide. One of the most important mechanisms of the resistance process is genetic mutations in genes that transcribe penicillin-related

proteins. Selective pressure plays an important role and the use of beta-lactam antibiotics is a risk factor for infection. *Streptococcus pneumoniae* is responsible for the following diseases: pneumonia, septicemia, otitis media, meningitis, sinusitis, peritonitis, arthritis. Penicillin-resistant *Streptococcus pneumoniae* was first discovered in 1967 (Chisti et al., 2021).

2.5. Proteus

Proteus can cause urinary tract infections as well as hospital-acquired infections. *Proteus* is unique in that it is highly mobile and forms irregular colonies. In fact, *Proteus* forms what are known as irregular, climbing colonies when grown on uninhibited medium. It is one of the most important members of the family of Proteobacteriaceae wonderful, which causes wound infections and urinary tract infections. Most species of *Proteus* versicolor are sensitive to penicillin and cephalosporins. However, Ordinary *Proteus* is not sensitive to these antibiotics, and they are few and far between in immunosuppressed people. Normal *Proteus* is found naturally in the human intestines as well as in various types of animals, compost, soil and contaminated water (Davey et al., 2017).

More than 80% of UTIs in humans are due to the presence of *Escherichia coli* bacteria but UTIs due to *Proteus mirabilis* are also common. When *Proteus glaucoma* attaches to the walls of the urinary tract, there is a greater chance that *Proteus* vera infects the kidneys than of *E. coli*. *Proteococcus mutans* belongs to the family Amanoea, which is a Gram-negative bacterium that is also mobile and climbing. *Proteus terrific* is present as free micro-organisms in water and soil, but it is considered parasitic if it is present in the upper urinary tract of humans (Fleming et al., 2016).

2.6. Pseudomonas Aeruginosa

Pseudomonas aeruginosa is an ideal model for opportunistic pathogens. One of the disturbing characteristics of *Pseudomonas aeruginosa* is its lack of sensitivity and its susceptibility to antibiotics. This feature is due to the pumps located at the level of the cell membrane, which work to pump several drugs, including antibiotics, out of the cell. In addition, *Pseudomonas aeruginosa* develops resistance easily acquired, through genetic mutations in chromosomal genes, or by horizontal transfer of antibiotic resistance genes from cell to cell (Chan et al., 2011). Some recent studies have shown that typical resistance related to biofilm formation or the emergence of small and varying colonies may be necessary for the response and extent to which *Pseudomonas aeruginosa* is affected by antibiotic therapy (Reygaert, 2018).

2.7. Prevention of Antibiotic Resistance

Avoiding the use of antibiotics can, in some cases, reduce the chances of infection with antibiotic-resistant bacteria. One study demonstrated that the use of fluoroquinolone is clearly associated with *Clostridium difficile* infection, which is the main cause of nosocomial diarrhea in the United States of America and a serious cause of death in the third world country (Duval, 2018). Vaccines have no problems with resistance because the vaccine increases the body's natural immunity, while the antibiotic works in isolation from this immunity. However, new bacterial species are evolving to escape the immunity caused by the vaccine. Some anti-staphylococcal vaccines have shown limited

efficacy due to the immune change between different staphylococcal strains in addition to the limited duration of activity of the antibodies produced. Development and testing of more effective vaccines is underway (Reygaert, 2018).

3. Useful Applications of Antibiotic Resistance

Antibiotic resistance will serve as a useful tool in genetic engineering. For example, a plasmid is made that contains an antibiotic resistance gene in addition to the genes desired to be translated. In this way, the researcher can ensure that when bacterial cells multiply, only bacteria carrying the plasmid can live, while the others die due to the effect of the antibiotic (Visser et al., 2014).

Thus, this method can ensure that the genes desired for translation are transmitted through cells as they multiply. Mostly, the antibiotics used in the field of genetic engineering are old and are no longer used to treat patients, such as Ampicillin, kanamycin, Tetracycline, Chloramphenicol. The use of the method of antibiotic resistance is not preferred in the industrial field, as it consumes huge quantities of antibiotics. Alternatively, axotrophic bacteria can be used because it is unable to make an organic compound important for their growth (Reygaert, 2018).

4. Conclusion

There are many types of microbes, especially pathogenic bacteria that have the ability to resist antibiotics and reduce and skip their effectiveness, which causes a major problem that affects human health. There are multiple reasons for this resistance, including those related to microbes and their possession of specific enzymes and mechanisms that enable them to resist antibiotics. In addition, the excessive use of antibiotics without a doctor's prescription is one of the reasons for the emergence of antibiotic resistance in pathogenic bacteria.

Competing Interests

The authors have declared that no competing interests exist.

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