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Antimicrobial resistance: what is it?

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Abstract

Antimicrobial resistance is an important concern for public health authorities at a global level. When bacteria, fungi, viruses, and parasites (as well as other microbes) are subjected to antimicrobial drugs that are intended to either kill them or restrict their growth, they develop the ability to resist such drugs, which is known as antimicrobial resistance (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics). As a result, the medications stop working and diseases continue to exist in the body, raising the possibility that they will spread to other people. Antibiotic resistance deals primarily with bacteria that are resistant to antibiotics, whereas antimicrobial resistance refers to all germs that resist medications intended to kill them. Typically, the more frequently antibiotics are taken, the more bacteria adapt and discover new ways to survive, leading to an increase in antibiotic resistance. Some bacteria resist the antibiotics' attempts to destroy them, allowing them to continue growing and causing additional damage. Regarding the quantification of the issue and numerous influencing factors associated with antimicrobial resistance, the structure and operation of the public health care delivery system have gaps. A national plan for the containment of AMR, antimicrobial policy, standard treatment guidelines, and research on the public health aspects of AMR at the community and hospital levels all need to be developed and strengthened immediately.

1. Introduction

Antimicrobial resistance (AMR) is a serious global danger to human health. By 2050, AMR, according to the UK Government-commissioned Review on Antimicrobial Resistance, might kill 10 million people annually (O'Neill, Jim, 2016), although some have criticized these projections, the WHO, numerous other organizations, and researchers concur that the spread of AMR is a serious problem that requires a global, coordinated action plan to address. Antimicrobial resistance is a persistent danger to our ability to treat common diseases due to the creation and spread of drug-resistant bacteria that have developed new resistance mechanisms. The increasing global development of "superbugs," or multi- and pan-resistant bacteria, which cause diseases that cannot be treated with antibiotics or other available antimicrobial medications, is particularly concerning.

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Did you know? Currently, drug-resistant illnesses account for at least 1.27 million deaths worldwide each year.

Drug-resistant bacteria have developed as a result of widespread overuse and abuse of anti-microbial medications. Antibiotics are frequently administered without medical supervision, both to humans and animals, and they are frequently overused. Examples of misuse include giving them to people who have viral illnesses like the flu and colds, giving them to animals as growth boosters, and using them to shield healthy animals from sickness (Porooshat Dagostar, 2019). The number of people whose treatment is failing or who die from infections will rise in the absence of efficient methods for the prevention and sufficient treatment of drug-resistant infections, as well as increased access to both novel and existing quality-assured antimicrobials. Surgery, including cesarean sections or hip replacements, cancer chemotherapy, and organ transplants will all become riskier medical procedures.

1.1 What causes the emergence and spread of antimicrobial resistance to occur more quickly?

AMR develops throughout time, typically as a result of genetic alterations. The environment, humans, animals, food, plants, and the environment all include antimicrobial-resistant microbes (in water, soil, and air). They are contagious both between individuals and between humans and animals, as well as through animal-sourced foods. The misuse and overuse of antibiotics, a lack of access to clean water, sanitation, and hygiene for humans and animals, inadequate infection and disease prevention and control in hospitals and farms, a lack of access to high-quality, reasonably priced medications, vaccines, and diagnostics, a lack of awareness and knowledge, and a lack of legal enforcement are the main causes of antimicrobial resistance.

1.2 Bacterial Drug Resistance

High rates of resistance against the major antibiotics used to treat common bacterial diseases, such as urinary tract infections, sepsis, sexually transmitted infections, and various types of diarrhea, have been documented globally, suggesting that we are running out of effective antibiotics. For instance, the rate of resistance to the antibiotic ciprofloxacin, which is frequently used to treat urinary tract infections, ranged from 4.1% to 79.4% for *Klebsiella pneumonie* a and from 8.4% to 92.9% for *Escherichia coli* in the countries that reported to the Global Antimicrobial Resistance and Use Surveillance System (GLASS). Life-threatening infections brought on by carbapenem-resistant Enterobacteriaceae can only be treated as a last resort using colistin (i.e. *E. coli*, *Klebsiella* spp etc). Additionally, colistin-resistant bacteria have been found in a number of nations and areas, where they are responsible for diseases for which there is

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now no efficient antibiotic treatment. *Staphylococcus aureus* is a prevalent cause of infections in both the general population and healthcare settings. It is a component of our skin flora. Methicillin-resistant *Staphylococcus aureus* (MRSA) infections increase the risk of death by 64% compared to infections that respond to treatment. Sulphonamides, penicillins, tetracyclines, macrolides, fluoroquinolones, and early-generation cephalosporins are among the antibiotics for which resistance has arisen quickly. Although not the only problematic pathogens, the ESKAPE pathogens (Enterococcus faecium, *Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter* species) have been identified as needing special attention because they are in charge of the majority of hospital-acquired infections each year and exhibit high rates of AMR (Rice 2008).

1.3 viral drug resistance

Antiviral drug resistance is a growing concern in populations of immunocompromised patients because persistent viral replication and extended drug exposure select resistant types of viruses. The majority of antivirals, including antiretroviral (ARV) medications, have developed resistance. Due to the advent of drug-resistant HIV, all antiretroviral (ARV) medications, even newer classes, run the risk of going partially or completely inactive (HIVDR). HIVDR can develop in patients undergoing antiretroviral medication, and persons can contract HIV that is already drug-resistant.

1.4 Fungal drug resistance

Drug-resistant fungal infections are becoming more common, which makes the already challenging treatment environment worse. There are now problems with treating many fungi, such as toxicity, especially in patients with concomitant underlying infections (e.g. HIV). One of the most prevalent invasive fungal diseases, drug-resistant *Candida auris,* is already pervasive, with rising reports of resistance to fluconazole, amphotericin B, and voriconazole as well as growing caspofungin resistance. This results in fungal infections that are more challenging to treat, treatment failures, lengthier hospital stays, and significantly more expensive treatment alternatives.

2. Resistance mechanisms

Antimicrobial resistance mechanisms can be divided into four groups: (1) reducing drug uptake; (2) altering drug targets; (3) inactivating a drug (4) active drug efflux. Limiting drug uptake, drug inactivation, and drug efflux are examples of intrinsic resistance strategies; drug target modification, drug inactivation, and drug efflux are examples of acquired resistance strategies. There are differences between the types of processes utilized by gram-negative bacteria and gram-positive bacteria due to changes in structure and other factors. Gram-positive bacteria less frequently employ restricting the uptake of a drug

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(don't have an LPS outer membrane) and don't have the capacity for some forms of drug efflux mechanisms, whereas gram-negative bacteria use all four primary methods (Chancey *et al.*,2012 and Mahon CR *et al.*,2014).

2.1 Reducing drug uptake

Certain kinds of chemicals are blocked by the gram-negative bacteria's LPS layer's structure and activities. Because of this, certain bacteria have an inbuilt resistance to specific classes of powerful antimicrobial medicines (Blair JM, Richmond GE, Piddock LJ.,2014). Due to the high lipid content of the outer membrane of mycobacteria, hydrophobic drugs—such as rifampicin and fluoroquinolones—have easier access to the cell than hydrophilic ones (Kumar A, Schweizer HP.,2005 and Lambert PA., 2002). Therefore, all medications that target the cell wall, including -lactams and glycopeptides ones, are intrinsically ineffective against bacteria that lack a cell wall, such as Mycoplasma and related species. Drug access restrictions are less common for gram-positive bacteria because they lack an outer membrane. Polar molecules have trouble entering the cell wall of enterococci, which results in inherent resistance to aminoglycosides. *Staphylococcus aureus*, a different gram-positive bacterium, has recently gained vancomycin resistance. Out of the two defense mechanisms S. aureus employs against vancomycin, one causes the bacterium to create a thickened cell wall that makes it challenging for the medication to penetrate the cell and confers an intermediate level of resistance to vancomycin. These strains have the VISA designation (Miller WR, Munita JM, Arias CA.,2014).

2.2 Alterations to medication targets

There are numerous parts of the bacterial cell that could be targeted by antimicrobial substances, and just as many targets could be altered by the bacterium to confer resistance to those medications. Eg; Changes in the structure and/or quantity of PBPs are one method by which gram-positive bacteria are resistant to the -lactam medicines they almost exclusively employ (penicillin-binding proteins). The amount of drug that can bind to that target is affected by changes in the number of PBPs (increase in PBPs with decreased drug binding ability or decrease in PBPs with normal drug binding. (Beceiro A, Tomás M, Bou G.,2013).

2.3 Drug inactivation

Bacteria can inactivate medications in one of two ways: by actually degrading the drug, or by adding a chemical group to the drug. The broad category of drug-hydrolyzing enzymes is known as -lactamases. Tetracycline is another medication that can be rendered inactive by hydrolyzation through the tetX gene (Kumar S, Mukherjee MM, Varela MF.,2013 and Blair JM *et al.*,2015). The β -lactamases,

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which were formerly known as penicillinases and cephalosporinases, inactivate β -lactam medications by hydrolyzing a particular location in the ring structure, which results in the ring opening. The target PBP proteins cannot be contacted by the open-ring medicines.

2.4 Drug efflux

Most bacteria have a wide variety of efflux pumps. The ATP-binding cassette (ABC) family, the multidrug and toxic compound extrusion (MATE) family, the small multidrug resistance (SMR) family, the major facilitator superfamily (MFS), and the resistance-nodulation-cell division (RND) family are the five main families of efflux pumps in bacteria, which are categorized based on structure and energy source. Most bacteria have a wide variety of efflux pumps. The ATP-binding cassette (ABC) family, the multidrug and toxic compound extrusion (MATE) family, the small multidrug resistance (SMR) family, the major facilitator superfamily (MFS), and the resistance-nodulation-cell division (RND) family are the five main families of efflux pumps in bacteria, which are categorized based on structure and energy source (Poole K.,2007).

3. Methods for reducing antimicrobial resistance

Everybody has a responsibility to play in the urgent need to address the major public health problem of AMR.

3.1 Personal

- Only take antibiotics as directed by a licensed physician.
- Wash your hands frequently, prepare food properly, stay away from ill people, and stay up to date on your vaccines to prevent infections.
- Never distribute or utilize unused antibiotics.

3.2 Government officials

- Increased monitoring of illnesses with antibiotic resistance.
- Regulate and encourage the proper disposal of potent medications.
- Disseminate knowledge about antibiotic resistance's effects.
- Make sure the national action plan is effective.

3.3 Healthcare experts

- Discuss the risks of improper usage, antibiotic resistance, and proper antibiotic use with your patients.
- Keep your hands, instruments, and surroundings clean to prevent infections.
- Only dispense and administer antibiotics when necessary.
- Report infections with antibiotic resistance.
- Discuss infection prevention with your patients.

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3.4 Healthcare sector

- Make investments in the study and creation of fresh antibiotics, vaccines, diagnostics, and other instruments.

3.5 Agricultural industry

- To limit the demand for antibiotics, vaccinate animals.
- Avoid giving healthy animals antibiotics to promote growth or prevent disease.
- Only administer antibiotics to animals while a veterinarian is present.
- Encourage the implementation of measures put in place to stop AMR from spreading in the environment.

Conclusions

Antimicrobial resistance poses a hazard to both human health and biosecurity, hence it is important to comprehend its methods and causes. Antimicrobial resistance selection has been influenced by antimicrobial exposure in healthcare, agriculture, and the environment, despite the fact that the emergence of antimicrobial resistance in microbes is a natural phenomenon. Standards of infection control, sanitation, access to clean water, availability of antimicrobials and diagnostics of guaranteed quality, travel, and migration all have an impact on onward transmission. As diverse as the bacteria themselves are, so are the mechanisms discussed here. There are definitely additional resistance mechanisms out there that we have not yet characterized, and these bacterial weapons essentially cover all of the antimicrobial drugs that we have. To guarantee ongoing, universal access to efficient antibiotics, intelligent, coordinated procedures that are conscious of potential unintended consequences are required.

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