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Antimicrobial and Antibiotic Resistance

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ABSTRACT

Antimicrobial agents have saved the human's from lot of suffering due to infectious diseases. Within 12 years Fleming and others had turned this finding into a wonder drug of its time, which could cure patients with bacterial infections. Sulphonamide resistance was originally reported in the late 1930's. Basically, antimicrobial resistance is developed due to improper and unsafe use of antibiotics and antimicrobials. Antimicrobial resistance had constantly used in order to survive against different conditions. Antibiotic resistance has been called one of the world's most pressing public health concerns. Antimicrobial use is a key driver of the resistance. Some important 626NFI-2011 examples of bacterial species include penicillin-resistant, *Streptococcus pneumonia*, Vancomycin-resistant *enterococci*, methicillin-resistant *Staphylococcus aureus*, multi-resistant *Salmonella typhi*, *Shigella dysenteriae, Neisseria gonorrhoea, Pseudomonas aeruginosa* and multi-resistant *Mycobacterium tuberculosis*. Antibiotics are critical to the success of advanced surgical procedures. There is no perfect antibiotic, and once the most appropriate use of any new compound are identified, it is essential that prescription of the antibiotic be restricted to those users.

INTRODUCTION

In 1928 a piece of mould fortuitously contaminated a Petri dish in Alexander Fleming's laboratory at St Mary's Hospital London, and he discovered that it produced a substance (penicillin) that killed the bacteria he was examining. Within 12 years Fleming and others had turned this finding into a wonder drug of its time, which could cure patients with bacterial infections (1). Since the introduction of the first effective antimicrobials, namely, the sulphonamides, the development of specific mechanism of resistance has plagued their therapeutic use. Sulfonamide resistance was originally reported in the late 1930's and the same mechanisms operate some 70 years later (2). There is no doubt that antimicrobial agents have saved the human race from a lot of suffering due to infectious disease burden. Without antimicrobial agents, millions of people would have succumbed to infectious diseases. Hardly years after the discovery and the use of the first antibiotics was observation made of organisms that still survived the effects of the antimicrobial agents. That was the beginning of the suspicion that different microorganisms were getting a way around previously harmful agents that is known today as antimicrobial resistance (3).

Antibiotic resistance

Antibiotic resistance is the ability of a microorganism to withstand the effects of an antibiotic. Today almost all important bacterial infection in the India and throughout the world are becoming resistant to antibiotics. Antibiotic resistance has been called one of the world's most pressing public health concerns. The rational use of antibiotics is the key to controlling the spread of resistance (4). Antibiotic resistance refers specifically to the resistance to antibiotics that occurs in common bacteria that cause infection. Antimicrobial resistance is a broader term, encompassing resistance to drugs to treat infections caused by other microbes as well, such as parasite, viruses and fungi (5).

Rational use of antibiotics

Development and spread of antimicrobial resistance (AMR) is commonly due to overuse, misuse, and indiscriminate use by doctors, nurses and pharmacist, non-compliance and self medication by patients and use in animal husbandry and agriculture. It is estimated that 70-80% of prescriptions for antimicrobials are probably advised unnecessarily by health professionals. Antimicrobial use is a key driver of the resistance. Poverty and inadequate

access to antibiotics constitute a major factor in the development of resistance. Another common cause of developing resistance is improper diagnosis (4).

The bacterial infections which contribute most to human mortality and morbidity are also these in which emerging antimicrobial resistance is most obvious: diarrhoeal diseases, respiratory infections, meningitis, sexually transmitted disease, and hospital-acquired infections. Some important 626NFI-2011examples include penicillin-resistant, *Streptococcus pneumonia*, Vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, multi-resistant *Salmonella typhi*, *Shigella dysenteriae*, *Neisseria gonorrhoea*, *Pseudomonas aeruginosa* and multi-resistant *Mycobacterium tuberculosis* (4).

Emergence of antibiotic resistance

Reports of penicillin resistant pneumococci have been numerous from developed countries, but such resistance has not been problem in the Indian subcontinent. The arrival of resistant pneumococci was, however, long overdue here, given the degree of inadvertent and irrational use of third generation cephalosporins and other newer antimicrobials in certain trivial infections that ideally required none for example, viral bronchitis, infection of the upper respiratory tract, diarrhoea, and viral croups (7). The damaging effects of antimicrobial resistance (AMR) are already manifesting themselves across the world. Antimicrobial-resistant infections currently claim at least 50,000 lives each year across Europe and the US alone, with many hundreds of thousands more dying in other areas of the world. For instance, in 15 European countries more than 10% of bloodstream *Staphylococcus aureus* infections are caused by methicillin-resistant strains (MRSA), with several of these countries seeing resistance rate closure to 50% (1).

Resistance in tuberculosis

In 2013, there were estimated 480000 new cases of MDR-TB in the world. Globally, 3.5% of new TB cases and 20.5% of previously treated TB cases are estimated to have MDR-TB, with substantial differences in the frequency of MDR-TB among countries (5).

Resistance in influenza

Over the past 10 years, antiviral drugs have become important tools for treatment of epidemic and pandemic influenza. By 2012, virtually all influenza A viruses circulating in humans resistant to drugs frequently used for the prevention of influenza (amantadine and

rimantadine). However, the frequency of resistance to the neuraminidase inhibitor oseltamivir remains low (1-2%) (5).

Resistance in HIV

HIV drugs resistance emerges when HIV replicates in the body of a person infected with the virus who is taking antiretroviral drugs. Even when antiretroviral therapy (ART) programmes are very well-managed, some degree of HIV drug resistance will emerge. Available data suggest that continued expansion of access to ART is associated with a rise in HIV drug resistance. In 2013, 12.9 million people living with HIV were receiving antiretroviral therapy globally. As of 2010, levels of HIV drug resistance among adults had not begun treatment in countries scaling up ART were found to be about 5% globally. However, since 2010, there are reports suggesting that pre-treatment resistance is increasing, peaking at 22% in some areas (5).

Superbugs and super-resistance

It is known that the frequent-flow of genetic material across the whole bacterial species is an inevitable phenomenon that keeps happening in nature as a part of natural selection. This evolutionary process does not respect geographical boundaries, countries or continents. It could just happen anywhere and anytime (8).The term “superbugs” refers to microbes with enhanced morbidity and mortality due to multiple mutations endowing high levels of resistance to the antibiotic classes specially recommends for their treatment; the therapeutic options for these microbes are reduced, and periods of hospital care are extended costly. In some cases, super-resistant strains have also acquired increased virulence and enhanced transmissibility (2). The landmark discovery and introduction of methicillin (the first designer anti-resistant antibiotic) in 1959 were thought to be a sure defense against the penicillinases, but the appearance of methicillin-resistant *S. aureus* (MRSA) within just 3 years led inexorably to other multi-antibiotic-resistant variants, and the acronym now denotes multidrug-resistant *S. aureus* (2).

Established mechanisms of AMR

Bacterial resistance to an antimicrobial agent can occur due to three general mechanisms:

1) **The drug does not reach its target.**

In Gram negative bacteria, many antibiotics enter the cell through protein channels called porins. Mutations or loss of these channels can prevent the rate of antibiotic entry into the cell, effectively reducing drug concentration at the target site. If the drug target is intracellular and the drug requires active transport across the cell membrane a mutation that interferes with the transport mechanism can confer resistance e.g. aminoglycosides. Bacteria can also transport antimicrobial drugs out of the cell through efflux pumps. Resistance to numerous drugs, including fluroquinolones, macrolides, tetracyclines and beta-lactam antibiotics, is mediated by this mechanism (4).

2) **The target site is altered.**

This may be due to mutations in drug binding region of target enzyme e.g. fluroquinolones, target modification e.g. ribosomal protection type of resistance to macrolides and acquirement of a resistant form of the susceptible target e.g., methicillin resistant *Staphylococcus Spp*. Due to production of a low-affinity penicillin-binding protein (PBP) (4).

3) **The drug is inactivated.**

Bacterial resistance to aminoglycosides can be due to a plasmid encoded aminoglycoside-modifying enzymes. Similarly, beta-lactamase production is the most common mechanism of resistance to penicillins and other beta-lactam drugs. A variation of this mechanism is failure of bacterial cell to activate a prodrug e.g. loss of ability of *M. tuberculosis* to activate isoniazide (INH) (4).

Spread of antibiotic resistance

Genetically, antibiotic resistance spreads through bacteria populations both “vertically,” when new generations inherit antibiotic resistance genes, and “horizontally,” when bacteria share or exchange sections of genetic material with other bacteria. Horizontal gene transfer can even occur between different bacterial species. People can pass the resistant bacteria to others; for example, by coughing or contact with unwashed hands. Antibiotic resistance traits can be lost, but this reverse process occurs more slowly. If the selective pressure that is applied by the presence of an antibiotic is removed, the bacterial population can potentially revert to a population of bacteria that responds to antibiotics (6).

Some actions physicians and consumers can take to limit resistance:

Physicians:

1. Wash hands thoroughly between patient visits.
2. Do not accede to patients' demand for unneeded antibiotics.
3. When possible, prescribe antibiotics that target only narrow range of bacteria.
4. Isolate hospital patients with multidrug-resistant infections.
5. Familiarize yourself with local data antibiotic resistance.

Consumers:

1. Do not demand antibiotics.
2. Use soap and other products with antibacterial chemicals only when protecting a sick person whose defences are weakened.
3. Complete the whole course of antibiotic (9).

CONCLUSION

By referencing sources mentioned below, we come to across the facts that we are totally depend on antibiotics for the treatment of infectious diseases, and they shouldn't be considered as mere commodities. Antibiotics are critical to the success of advanced surgical procedures. There is no perfect antibiotic, and once the most appropriate use of any new compound is identified, it is essential that prescription of the antibiotic be restricted to those users. Antibiotic resistance is growing global concern. Given the increasing knowledge of environmental reservoirs of resistance, it should now possible to have early warning of potential resistance mechanisms to new or old antibiotics and thus prepare for problems in the clinic.

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