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REVIEW ARTICLE

# Antimicrobial Resistance – its Causes, Effects and Preventive Measures

G V Narasimha Kumar[1]*,P Deepishka[2], Chitikela. P. Pullaiah[3], G. Dayanand Reddy[4]

[1, 3 ,4]*Department of Pharmacology, Siddha Central Research Institute, Arumbakkam, Chennai, India*
[2]*Department of Pharmacy practice, Sri Padmavathi school of Pharmacy, Tirupathi, Andhra Pradesh.*

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## ABSTRACT

Antimicrobial agents are the drugs that kill or suppress the growth of microorganisms. The discovery of antimicrobial agents in 1928 marked the origin of antibiotic era. They were widelyused in the treatment of dreadful infectious diseases and their use has made possible the therapy of cancer and surgical transplantations without facing the death. The infections that were once controlled by antimicrobial agents are turning unresponsive due to the development of antimicrobial resistance. Activities like irrational antibiotic use, use of antimicrobial agents for non-therapeutic purposes isfavoring the development of antimicrobial resistance. The spread of antimicrobial resistance is influenced by various ecological, environmental behavioural and financial factors. The rise in antimicrobial resistance contributes to alarming effects like development of pan resistant infections which are not treatable even with rarely used antibiotics like Colistine and Tigecycline resulting in increased healthcare costs. The further development of antimicrobial resistance can be prevented through workable and effective interventions like reducing the need of antibiotics, eliminating their non-therapeutic use, providing educational approaches and surveillance of antimicrobial resistance. Also, reducing gaps in antibiotic discovery pipeline by promoting novel innovations and also implementation of antimicrobial steward ship programmers reduces the impact of antimicrobial resistance.

**Key words:** Antimicrobialresistance, Antimicrobial agents, Antibiotics, Infections, Chemotherapy

## INTRODUCTION

Antimicrobial agents are the drugs that kill or suppress the growth and replication of bacteria, fungi and viruses. [1]In 1928 Penicillin was discovered by Sir Alexander Fleming which had turned in to a wonder drug, curing dreadful bacterial infections including Plague, Tuberculosis (TB), Pneumonia etc. Further, more antimicrobial agents were discovered which revolutionized the health care.[2]These microorganisms that were once controlled by anti-microbial agents are now turning unresponsive towards these agents due to the development of resistance.[3]The first incidence of antimicrobial resistance was quoted by Paul Erlich in 1907 when he developed arsenic therapy against trypanosomiasis. Following then there was a surge inanti-microbial resistance leading to emergence of sulphonamide resistant streptococcus pyogenes in 1940's, streptomycin resistant mycobacterium in 1950's, ampicillin resistant hemophilus influenzae, chloramphenicol resistant hemophilus in 1970's etc. [3]Now, we have entered in to an era after the golden age of anti-microbial agents where there is an alarming increase in anti-microbial resistance.[2]Various factors that cause emergence of anti-microbial resistance in the environment are irrational prescribing of anti-microbial agents, OTC dispensing, self-medication and unjustified use for human, animal, and industrial consumption.[4] The ecological, environmental, epidemiological, cultural, social and economic factors also influence the spread of anti-microbial resistance.

The anti-microbial resistance had emerged as a global concern particularly in the developing countries where anti-microbial agents are readily available as OTC medications, burden of infectious disease is high due to poor sanitation conditions and health care spending is low.[3] In countries like India, irrational prescribing of antimicrobial agents by physicians and "more drug better doctor" aspect of patients had worsened the problem.[5] Developing antimicrobial resistance coincided with the collapse in the antibiotic discovery pipeline had become a global, clinical and economic

***Corresponding Author:**G V Narasimha Kumar, **Email:**narasimha.spsp@gmail.com

threat.[6]Increasing antimicrobial resistance presents a major threat to public health as it reduces the efficiency of anti-microbial therapy leading to increased treatment cost, morbidity, mortality and health expenditure.[7]

However, the appropriate use of antimicrobial agents to patient clinical needs, in correct dosesand measures like preventing the infection spread, tracking the surveillance of infection, developingrapid diagnostic tests, vaccination, promoting the research and development of novel antibiotics etc, are need to be put in to action to fight against the alarming effects of increasing anti-microbial resistancefor a better tomorrow.[2-6]

## HISTORY

In the 19th century, before the discovery and wide spread use of anti-microbial drugs, mortality in women was common due to spread of post child birth infections and dreadful infections like TB, cholera. Farmers have lost their crops, livestock with infectious diseases which lead to a condition called famine. In 1928, the discovery of penicillin, an antimicrobial drug growing on petri dish accidentally by the scientist Sir Alexander Fleming marked the antibiotic era. It showed a remarkable ability in killing many bacterial strains including staphylococcus and streptococcus species responsible for infections.[8] Thus the discovery and introduction of antibiotics have saved the lives of millions of people and animals, revolutionized the disease therapyand gave the ability of preventing the disease tragedies.[1] The development of resistant strains of staphylococcus to penicillins developed Methicillin, a semi synthetic derivative of penicillin.[8] With the development of broad spectrum antimicrobial agents like Streptomycin, Chloramphenicol and Tetracycline in 1940's and 1950's, the antimicrobial chemotherapy fully came in to existence.[8]The use of antimicrobial agents have made possible of cancer therapy and surgical transplantations without facing the threat of death due to infections .The advancements in anti-infective therapy have created a optimistic view that the curbing of infections would become possible. However, in reality the continuous development of infectious strains and their counter action called antimicrobial resistance against antibiotics had remained the problem unsolved.[9]The microbe is said to be resistant if it is unresponsive to its antimicrobial agent at the normal dose achievable. It can also be described as the fall in an antibiotic's minimum inhibitory concentration.[8]After 90 years of penicillin discovery, the world is facing the worrying effects of antimicrobial resistance. The antimicrobial resistance has raised in such a way that drug resistant bacteria kills about 700,000 people each year and this number will increase to 10million by 2050 according to an UK report released in May (1999), necessitating the importance of rational use of antibiotics.[9]

## SPREAD

Acquiring resistance to an antimicrobial agent is the characteristic feature of microbes during their process of evolution.[2] Microbes show resistance to antibiotics by mechanisms like producing chemicals to destroy antibiotics, building efflux pumps to send antibiotics out, making their cell wall less permeable to antibiotics, altering targets within the cell, creating alternative pathways to the anti-microbial targetsetc. This resistance is mobile and spreads through genetic elements such as bacteriophages, plasmids, naked DNA, or transposons etc. Not only single gene bearing resistance to a family or a type of antimicrobial agent, but also multiple genes each resistant to a single drug may accumulate in the same organism making it multiple drug resistant.[3]The spread of antimicrobial resistance is influenced by ecological, environmental, behavioural and financial factors.[10] Ecologically the antimicrobial agents are unique from others as they exhibit "societal effect" i.e the use of antimicrobial agent by one individual affects its effect in other individual.[3]Therefore, effective antimicrobial therapy is a shared social property and it is not acceptable to abuse this causing harm to others.[11]With regard to environmental influence, the wide spread use of antimicrobial agents in the agriculture, domestic animals, aquaculture, and dusting of fruit trees for non-therapeutic uses makes antimicrobialresistant strains enter in to the environment. [10]The behavioural patterns of physicians, patients, and retailers from large pharmacies to local drug stores have part in contributing to anti-microbial resistance. The irrational prescribing patterns of antimicrobial agents by the physicians i.e. prescribing at incorrect dose, duration, for incorrect indication,influence the spread of antimicrobial resistance.[12]Misuse of anti-microbial agents by patients for treating viral infections, under-use of antimicrobial agents through non adherence or substitution with sub therapeutic doses, over-use with desire for instant gratification, self-

medication and unwilling to undergo microbial tests had led to increase in the development of anti-microbial resistance.[10]The behaviour of retailers or pharmacists in selling large volume of anti-microbial agents as over the counter (OTC) drugs is a worst scenario especially in the developing countries for the progression of anti-microbial resistance.[3]With respect to all the above factors that influence the spread of anti-microbial resistance, the levels of its spread is worryingly high having its impact on therapeutic outcomes and economic consequences.[11]

## IMPACT OF ANTI MICROBIAL RESISTANCE

Greater use of anti-microbial agents over the past 50 years as main stay of many lifesaving and life improving therapies like joint replacement surgeries, organ transplantations, cancer chemotherapy, and in management of chronic diseases like diabetes, asthma, rheumatoid arthritis etc focused selective pressure on susceptible strains causing emergence of anti microbial resistance[11] due to which the effect of antibiotics may be decreased partially or fully, that undermines their ability to prevent infectious complications. Hence it is a serious global health problem requiring immediate attention.[5]Due to poor surveillance studies the impact of rising antimicrobial resistance has remained largely unknown but now it is seen as a distant risk[12] as already the resistance has acquired to antibiotics used in treatment of common infectious diseases like urinary tract infections (UTI), diarrhoea, pneumonia, skin infections.[13]The increase in anti-microbial resistance is at a higher rate that pan resistant infections have not become treatable even with rarely used antibiotics like Colistin and Tigecycline.[11]Compared to infections susceptible to antibiotics, treatment of antimicrobial resistant infections requires prolonged and/or costlier treatments, extended hospital stays, necessity of additional doctor visits and increased medication or health care use which eventually results in considerable rise of human and health care costs.[11]The emergence of resistance to antibiotics is not a major health problem as long as new, alternative therapies are available to replace less effective pharmaceuticals.[14] But the antibiotic discovery pipeline has collapsed completely that only one antibiotic has been discovered and developed for use in humans for the last 50 years.[1] We currently face the threat of multi drug resistant infections which are difficult or impossible to treat causing additional side effects, decreasing quality of life of patients, imposing economic and social burden on families. If the anti-microbial resistance continues to increase at the same rate, it will return our society to pre-antibiotic era when one in ten patients died with pneumonia, one in three patients died with skin infections and death rates are greater than tenfold higher compared to antibiotic era. Thus the impact of rising antimicrobial resistance is important economically and ecologically [1] which is measured in terms of consequences arising from illness and death, specifically the added cost of treatment. [14]

## PREVENTION OF ANTI MICROBIAL RESISTANCE:

Prevention of anti-microbial resistance can be achieved through developing workable and effective interventions. The major steps to be taken for antimicrobial resistance prevention include: reducing the irrational use of antibiotics, eliminating their non-therapeutic use, tracking the surveillance of anti microbial resistance, providing education approaches, and responsible use of antibiotics. [12]

- Reducing the irrational use of antibiotics:
  Promoting the use of diagnostic tests through behavioural changes and improvement in microbiology laboratory capacity reduces the irrational use of antibiotics to patients. Establishing infection control interventions in hospitals, developing standard treatment guidelines in the therapy of infections, preparing surgical safety checklists to control infections during surgeries, increasing vaccination programmes promotes the responsible use of antibiotics.[12]

- Eliminating the non-therapeutic use of antibiotics:
  Non-therapeutic usage of antibiotics for promoting growth in livestock releases antimicrobial resistant strains in to environment.[12]Thus, reducing and controlling the antibiotic use in the veterinary sector prevents the rise in the antimicrobial resistance.

- Tracking the surveillance of antimicrobial resistance and antibiotic use:
  Conduction of surveillance programmes and tracking the rise in antimicrobial

resistance provides better information to underpin the decisions on rationalisation of antibiotic use and to monitor all the time. [3] Anti microbial resistance can be lowered through improved antimicrobial targeting through rationalised use.[12]

- Educational approaches:
  Educating patients regarding the use of diagnostic tests before therapy, disadvantages of self-medication improves responsible use of antibiotics decreasing antimicrobial resistance.[12] Providing education to farmers and stake holders about the effects of inappropriate use of antibiotics in livestock reduces antimicrobial resistance. Educating prescribers, paramedical and patients about various treatment policies to be followed for rationalisation of antibiotic therapy reduces the emergence of antimicrobial resistance.[10]Also, novel innovations reducing gaps in research and development of antibiotics, antimicrobial agent stewardship programmes are necessary to control the development of antimicrobial resistance.

## CONCLUSION

Antimicrobial resistance is a global public health concern that is increasing at alarming rate. It will result in increased hospital stays, health care costs and decreased quality of life of the patients if necessary measures are not taken. Rational uses of antibiotics, educational approaches, use of accurate diagnostic tests are some of the preventive measures to prevent the effects of anti-microbial resistance.

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