

REVIEW ARTICLE

Antimicrobial Stewardship-Need of the EraKathavate R. N.¹, Mathews M. A.²**ABSTRACT**

The era of antibiotics started in 1928 when Penicillin was discovered. Since then we are living in a comparatively safe world under the protection of antibiotics from a multitude of infections that were once fatal. We have a multitude of antibiotics at our aid to stop the microbes that want to multiply within us, colonize us and ultimately kill us. We are safe. Or are we really? Emergence of antibiotic resistance is one of the most serious threats faced by humanity since World War II. Today resistance is reported even as soon as within a year of introduction of a new drug. Is the post antibiotic world near? Or are we already in it.

Keywords: Antimicrobial Stewardship, Microbial Resistance, MRSA, Horizontal Gene Transfer, Post Antibiotic World.

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INTRODUCTION

The age of antibiotics starts in 1928 when Scottish scientist and Nobel laureate Alexander Fleming discovered Penicillin.¹ Even though there are various claims that the use of antibiotics had been prevalent before Fleming in some or the other form, the evidence supporting those claims are not comprehensive.² The reign of antibiotics on modern medical practices began by the 1940s when penicillin was used to treat human infectious diseases.³ Antibiotic therapies has come a long from that since 1940s. Various new antibiotics have been discovered and infections once fatal have become a matter of least concern for us. But lurking behind the false pretence of security is one of the most deadly enemies that humanity has ever faced; Antibiotic Resistance. Misuse and more importantly over use of antibiotics is has lead to the

emergence of antibiotic resistance all over the globe. The uncontrolled use of antibiotics in treatment, animal husbandry and agriculture has contributed to this alarming rise of resistant strains.³

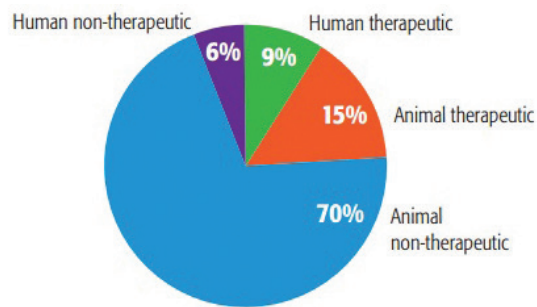
DEFINITION

Antibiotic Stewardship is defined as “The right antibiotic for the right patient, at the right time, with the right dose, and the right route causing the least harm to the patient and future patients.”^{4,5}

The factors which point towards the need of an antibiotic stewardship program are the rapid and uncontrolled rise of resistant strains of bacteria which are repeatedly proving impossible to control and the rise of variant strains with mutated protein expressions. We are now faced with the threat of a post antibiotic era in which even the simplest of infections such as a staphylococcus infection hold within themselves the potential to kill. The major causes of the uncontrolled rise of resistant strains are due to the following reasons⁶:

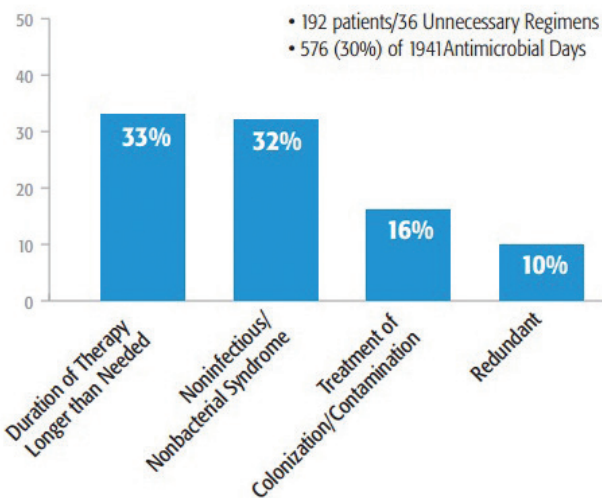
- Use of antibacterial medications for the treatment of syndromes not caused by bacteria;
- One of the major type of this antimicrobial abuse is the prescription of antibiotics for the treatment of diseases of viral origin such as the common cold and over prescription of antibiotics along with analgesics in case of dental pain when the etiology is not bacterial infection.
- Treatment for culture results that reflect colonization or contamination rather than infection
- Administration of broad spectrum antibiotics where narrow spectrum agents are equally effective
- Prescription of antibacterial therapy courses that are longer than necessary
- Prescription of antibacterial agents at inappropriate doses
- Over use of antimicrobial agents in animal husbandry and agriculture³

Antimicrobial resistance is based on the principles of evolution and natural selection. Antimicrobial resistance arises as a result of exposure of microorganisms to antimicrobial agents, especially in sub lethal concentrations. To make the expression “That doesn’t kill you makes you stronger”; the sub lethal concentrations of microbial agents aids the microbes in acquiring such characteristics which in their subsequent generations make them non susceptible to the pre exposed drugs.⁷ Given that the generation time of many microbes is under 24 hours and the time period required for drug discovery, testing and trials, marketing and finally con-



Source: www.pewhealth.org

Figure-1: Current use of antibiotics in the United States



Adapted from Hecker MT. et al. *Arch Intern Med.* 2003;162:972-978.

Figure-2: Unnecessary Antimicrobial therapy;

Figures 1 & 2 Adapted from *Practical Guide to Antimicrobial Stewardship in Hospitals*, Nathwani et al, 2013.

sumption is in years, the threat posed by resistance is quite evident on itself.

MOLECULAR MECHANISMS OF RESISTANCE⁸

The ability of microbial organisms to resist different types of antibiotics is genetically encoded. There are various methods in which the microbe is capable of exercising resistance to the chemical compounds. The mechanism by which microbes acquire resistance is broadly classified into two:

1. **Intrinsic Resistance:** It is that type of resistance which is naturally coded and expressed by almost all strains of particular bacterial species. Example is the natural resistance of anaerobes to aminoglycosides and Gram-negative bacteria against vancomycin.
2. **Extrinsic Resistance:** Changes in bacterial genome through mutation or horizontal gene transfer,^{9,10} leading to change in the type/nature of proteins expressed by the organisms. This would result in the loss of antigen markers which would leave the host defenses incapable of effectively neutralizing them and also reduce the

affectivity of antibiotic compounds manifold. This type of resistance is generally limited to selected isolates of that particular species or group of microorganisms. For example, we know that methicillin resistance of *Staphylococcus aureus* is primarily due to changes that occur in the penicillin binding protein (PBP), which is the protein which beta-lactam antibiotics bind and inactivate to consequently inhibit cell wall synthesis. This change is actually rendered by the expression of a certain *mecA* gene in some strains of these bacteria, which is hypothesized to have been induced by the excessive use of Penicillin. Expression of this *mecA* gene results in an alternative PBP (PBP2a) that has a low affinity for most β -lactam antibiotics, thereby allowing these strains to replicate in the presence of methicillin and related antibiotics.¹¹

REASONS FOR OVER-PRESCRIBING OF ANTIMICROBIALS¹⁶

- Lack of knowledge – limited coverage in medical schools and lack of formal training
- Influence of senior colleagues
- Inadequate diagnosis or lack of diagnostic facilities
- Incorrect selection, dose, duration and route of administration of drugs
- Compliance with patients' inappropriate demand or pressure to prescribe antibiotics
- Fear of litigation or adverse outcomes
- Financial gain from pharmaceutical companies in countries where physicians are underpaid, or response to promotional pressures of drug representatives

WHAT CAN BE DONE?

The growing incidences of antimicrobial resistance have warranted global attention and strategies are being formulated in different parts of the world. Some of the basic processes that we can follow as medical practitioners are as follows:¹²

- Prescribe antibiotics correctly – get cultures, start the right drug promptly at the right dose for the right duration. Reassess the prescription within 48 hours based on tests and patient exam.
- Document the dose, duration and indication for every antibiotic prescription.
- Stay aware of antibiotic resistance patterns in your facility.
- Participate in and lead efforts within your hospital/clinic to improve prescribing practices.
- Follow hand hygiene and other infection control measures with every patient.
- A national expert committee on antibiotic policies should be established.¹³ Professional organizations like MCI, DCI, IAP, API, Association of Microbiologists, Society for Infectious Diseases, Association of Preventive Medicine Specialists etc should take a lead. They-

Name of Site /Sponsor	URL
American Society Of Health-System Pharmacists (ASHP)	www.ashp.org
Association For Professionals In Infection Control And Epidemiology	www.apic.org
California Antimicrobial Stewardship Program Initiative	www.cdph.ca.gov
Centers for disease control and prevention	www.cdc.gov/
Clinical and Laboratory Standards Institute	www.clsi.org
Infectious Diseases Society of America	www.idsociety.org
The joint commission	www.jointcommission.org
MAD-ID Making a Difference in Infectious Diseases Pharmacotherapy	http://mad-id.org
National Foundation for Infectious Diseases	www.nfid.org
Society of Infectious Diseases Pharmacists	www.sidp.org
U.S. Department of Health and Human Services (HHS)	www.hhs.gov
Society for Healthcare Epidemiology of America	http://www.shea-online.org/
Premier Inc Antimicrobial Stewardship website	www.premierinc.com
The Nebraska medical center	http://www.nebraskamed.com/careers/education-programs/asp
UCLA health system	http://www.asp.mednet.ucla.edu/pages/
The Ohio state university medical center	http://wexnermedical.osu.edu
Table-1: Sources for Antimicrobial Stewardship guides/action plans	

should consider both hospital and primary care settings as well as veterinary and agriculture use.

- Develop guidelines for creating and auditing antibiotic prescriptions as well as considerations of content.^{13,14,15}

RESOURCES FOR STEWARDSHIP INITIATIVES

There are ample resources available for further study, analysis or research about antibiotic resistance and antibiotic stewardship procedures. Some of these resources are shown in table 1.A.^{17,18} These resources provide a comprehensive outline for the process as well as guide in implementation of stewardship practices in the clinical as well as public health setting.

CONCLUSION

The threat of antimicrobial resistance is very real and it is a ticking clock. Every single wrong prescription will have long lasting effects in the fight against antibiotic resistance. The simple steps such as confirming the source of infection and undertaking patient education as a part of normal consultations can go a long way in combating this hidden enemy. The effects of a post antibiotic world would be catastrophic. Even though the phenomenon of antibiotic resistance cannot be prevented as it is a process of nature itself, all we can do is hasten it and figure out our way through it. In that process, antibiotic stewardship will be our key in preventing the emergence of a post antibiotic world.

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