Infectious diseases are common and most of these are caused by bacteria. The disease burden is seen more in low - income countries where they account for 45% of all deaths. The mainstay of treatment for these diseases is antibiotics. Today, antibiotics are the most widely used category of drugs in the world, accounting for over one quarter of hospital drug costs. Wide spread and indiscriminate use of antibiotics has resulted in almost all bacteria pathogenic to humans developing resistance to all available antibiotics. Although antibiotics are prescribed individually, the impact of bacterial resistance is seen at a population level and since microbes do not respect boundaries, all countries in the world are affected. Antibiotic resistance therefore has become a global public health problem. Its impact is felt more in developing countries with sparse resources and the resultant economic and societal issues have no easy solutions.

Antibiotic resistance

Antibiotic resistance occurs when an antibiotic has lost its ability to effectively control or kill bacterial growth. Bacteria then become "resistant" and continue to multiply in the presence of therapeutic levels of the antibiotic. Some bacteria have developed mechanisms which make them resistant to many of the antibiotics normally used for their treatment (multi-drug resistant bacteria -MDRB). Treatment of infections caused by these MDRBs need more potent and broad spectrum antibiotics. At times they cause infections for which no treatment options are available.

Antibiotic resistance occurs with both appropriate and inappropriate use of antibiotics due to the selective pressures exerted on bacteria. It is now a global problem which is spreading to new clinical niches.

Inappropriate prescription could be due to many causes and more than one cause may be seen in an individual. These include:

- Selection and prescription of the wrong antibiotic for the particular infection
- Antibiotic prescribed at a sub therapeutic dose
- Antibiotic administered through an inappropriate route
- Antibiotic prescribed for a shorter duration than what is needed
- Prescribing antibiotics for non - bacterial infections
- Non-adherence to dosing regimens by patients
- Inappropriate self-medication by patients

Increasing resistance can result in clinicians frequently using broad spectrum therapy to empirically cover the pathogens, paradoxically contributing to a higher incidence of MDRBs. In 2014 there was a high proportions of antibiotic resistance in bacteria that cause common infections (e.g. urinary tract infections, pneumonia, bloodstream infections) in all regions of the world. Resistance to fluoroquinolones used for treatment of urinary tract infections caused by E. coli was widespread. An increase in new cases of multidrug-resistant tuberculosis (MDR-TB), a high percentage of hospital-acquired infections caused by highly resistant bacteria such as methicillin-resistant Staphylococcus aureus (MRSA) or multidrug-

resistant Gram-negative bacteria were also seen. Resistance to the treatment of last resort (ie carbapenems) for life-threatening infections caused by Klebsiella pneumoniae had spread to all regions of the world.

Sri Lanka is no exception to the problem of MDROs. The recent data from the Antibiotic Resistance Surveillance Project (ARSP) and the National Laboratory Based Surveillance of Antimicrobial Resistance of significant urine culture isolates (NLBSA) show that MDROs are increasing at an alarming rate. Most of these organisms were resistant to both commonly used first line antibiotics as well as broad spectrum, high end antibiotics such as carbapenems.

According to the data from the Medical Supplies Division, the government of Sri Lanka has spent a staggering Rs 2.6 billion on antibiotics in 2011, which accounted to 26.6% of the total drug expenditure on medicines for the state sector. MSD data also show a steady increase in the use of newer broad spectrum agents with a decline in the use of some of the first line older antibiotics.

There is no data with regards to antimicrobial resistance patterns or total amount of spending on antibiotics in the private health sector institutions. However, the situation is unlikely to be different, if not worse from that of the state sector institutions given that there are no restrictions for the use of antibiotics in the private sector.

As there are no new antibiotics in the pipeline of antibiotic development and there is pressing need to optimize and extend the effectiveness of currently available agents. It is in this backdrop that rational use of antibiotics becomes a priority for all health care professional and patients to reduce emergence of antibiotic resistant strains and resultant health care costs.

Rational use of antibiotics
Rational use of antibiotics include identification of appropriate indication based on sound medical consideration, selection of appropriate antibiotic considering efficacy, safety, suitability for the patient and cost, and prescribing the appropriate dosage of antibiotic in quantities sufficient to last for duration of treatment. It also includes the provision of appropriate information to the patient to ensure that the prescribed antibiotics are taken correctly. This would necessitate the prescriber to have a sound knowledge of the causative microbe for a particular disease including its pattern of antibiotic sensitivity.

Rational use of antibiotics also requires appropriate quality of antibiotics to be maintained along with proper dispensing of antibiotics.

Rational use of antibiotics is dependent on many independent factors. All these will have an allotted role which when correctly performed will lead towards rational use of antibiotics.

Antimicrobial stewardship is a key component of a multifaceted approach to prevent or reduce emergence of resistant bacteria. It involves coordinated interventions designed to improve and measure the appropriate use of antimicrobials. These include

- selecting an appropriate drug
- optimizing its dose and duration to cure an infection
- minimising toxicity
- minimising conditions for selection of resistant bacterial strains

Measures that can be taken to improve antibiotic use
There are many measures that can be taken, each complementing the other, to improve use of antibiotics. These have been tried in different countries with varying successes. Prescriber education, formulary restriction, prior approval, streamlining, antibiotic cycling and computer-assisted programs are some of them.
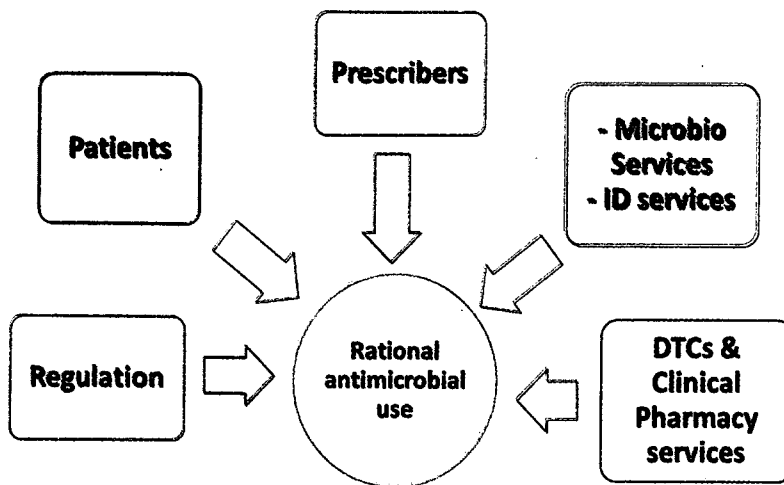
Figure 1. Factors that affect antibiotic use
ID - Infectious diseases, DTCs - Drugs and Therapeutic committees

Selecting the appropriate antibiotic is an evidence based and not an eminence based process. Selection should be backed by sound microbiological information which includes knowledge of the likely causative organism/s and likely antibiotic sensitivity pattern. Knowledge of the pharmacokinetics and pharmacodynamics is also needed to select the appropriate antibiotic to a patient. However, the most crucial decision that a prescriber needs to make is whether an antibiotic is indicated or not in a particular patient.

A wide range of education methods are available to improve the knowledge and practices of prescribers. These vary from one-on-one instruction at work place to more formalized and less personalized approaches such as staff conferences, lectures, mailing of instructional material and drug utilization evaluations. The last helps prescribers to understand what antibiotics are being used for different clinical situations and how they conform to available guidelines or policies. Clinical pharmacy consultations, hospital–pharmacy committee newsletters and dissemination of clinical guidelines both national and institutional are some of the other ways in which prescriber education and knowledge can be improved.

Peer reviewed national and institutional guidelines are useful in streamlining decision-making processes for clinicians. They assist in the implementation of appropriate antibiotic use taking into consideration the microbial flora and their local sensitivity patterns. Guidelines therefore need to be continuously reviewed. To be an effective tool guidelines should be widely disseminated to the prescribers who should be also accept and help implement them.

Patient education, ensuring compliance with the prescribed regimens and avoidance of self medication are important patient factors for rational use of antibiotics.

Formulary restriction will control which drugs get placed on the hospital formulary. This is a direct method of influencing antibiotic utilization and curtailing drug costs. An ideal hospital formulary should be dynamic and respond to changes in local pathogens and susceptibility patterns. It should consider new drugs that become available and other pertinent information in making decisions about formulary inclusions ad deletions. The formulary should make recommendations for therapy of common infectious diseases seen at the institution. While it will have restriction policies for use of certain drugs and thus

limit the number of antibiotics available to prescribers, it will not restrict the overuse of broad-spectrum antibiotics. The success of formulary restrictions in controlling antibiotic use is closely related to prescriber accountability. All these are labour, time and resource intense and hospital formularies are therefore not very attractive to many hospitals.

The success of any intervention to improve rational prescribing of antibiotics is dependent on an effective regulatory system that has policies in place to maintain the quality of antibiotics available and to ensure an uninterrupted supply. The regulations that are prepared needs regular monitoring to ensure adherence to them.

Conclusion
Resistance of bacteria to available antibiotics is a global pandemic which needs immediate measures. As there are no new antibiotics being developed and the availability of antibiotics is thus limited, immediate measure need to be taken to reduce emergence of resistant bacteria and to optimise and extend the effectiveness of currently available agents. Countries and institutions should select the most appropriate measures suitable for them to ensure rational use of antibiotics.

References

1. WHO : Antimicrobial resistance: global report on surveillance 2014

2. ARSP Working Group, The Sri Lanka College of Microbiologists. A multi centre laboratory study of Gram negative bacterial blood stream. infections in Sri Lanka Ceylon Medical Journal 2013; 58: 56-61

3. National Surveillance of Antimicrobial Resistance: SLCM Report to MOH 2014

4. Slama TG, Amin A, Brunton SA et al. A clinician's guide to the appropriate and accurate use of antibiotics: the Council for Appropriate and Rational Antibiotic Therapy (CARAT) criteria. The American Journal of Medicine 2005; 118 : 1S-6S

5. Fishman N. Antimicrobial stewardship. American Journal of Infection Control 2006;34:S55-63

Dr Chandanie Wanigatunge MBBS, MD, FCCP
Consultant Physician and Clinical Pharmacologist
Senior Lecturer in Pharmacology
Faculty of Medical Sciences, University of Sri Jayewardenepura
Phone: 0777 616 752 | 0112 733 170
E-mail: chandanie.wanigatunga@gmail.com