Editorial

Antibiotics: Uses, Underuses, Misuses & Abuses

Now medical science can not think a day without antibiotics. These antimicrobial medicinal products are most commonly used drugs world-wide. These are used for therapeutic and prophylactic purposes to get cure from frank infections and to prevent the development fresh infections respectively. They need to be used in adequate doses for sufficient length of time, keeping in mind the age, the body weight, the liver and kidney functions, the immune status and other parameters of the patient plus the pharmacokinetic and the pharmacodynamic properties of the said drug or drugs. They are used either singly or in combination to attack the offending organisms from multiple directions or to cover a wide spectrum of presumed offenders on empirical basis. However, antibiotics are best chosen by culture and sensitivity studies. Underuses, misuses and abuses of antibiotics, like many other drugs impose a huge unnecessary expenditure upon the patients or their guardians or the local, regional and national health authorities. In addition, underuse, misuses and abuses of antibiotics lead to the development of resistant superbugs imposing much more cost and substantially increasing the morbidities and mortalities of the patients. Now over hundreds of antibiotics are in use all over the world. The history of logical, rational and scientific use of antibiotics is less than a hundred year. The sense of antibiosis or fighting microbial offenders was there amongst humans in the prehistoric period. The crude forms of antimicrobials were used then to treat and prevent infections, though the people probably did not know what infections were. The antimicrobial properties of topical molds, moldy breads and other plants were then known to the Greeks and the Indians. Beer soup, turtle shells and snake skins were used as antimicrobials by the Russians, mixture of frog bile and sour milk by the Babylonians, the oil-cake (sweetmeat) by the Sri-Lankans. Moreover, nectar, honey, garlic and several other known and unknown matters, plants, plant extracts, leaves, leaf-extracts were used by humans in different times in different regions of the world till the end of nineteenth century. That is to say that before the early 20th century, infections were treated primarily and mostly on basis on medicinal folklore. Mixtures having antimicrobial powers were documented over 2000 years ago. Earlier observations in this modern era led to the discovery of natural antibiotics produced by microorganisms. The description of pasteurization in 1665 by French Lois Pasteur, the invention of microscope in 1675 and the discovery of microbe in 1676 by Dutch AV Leewenhoek, the explanation of Koch Postulate describing the microbial etiology of diseases in 1884 by German Robert Koch and the practical application aseptic and antiseptic surgery using carbolic acid by British surgeon Joseph Lister between 1887 to 1997 revolutionized a dramatic upgradation in understanding the prevention and the treatment of microbial infections. Further revolution in our understanding the molecular and ultra-structural biology plus microbial and molecular etiology, diagnosis and treatment of diseases followed the invention the electron microscope by German Physicist Ernst Ruska and Max Knoll in 1931. The old definition of antibiotics proposed by Selman Waksman in 1942 is no longer in vogue. He defined antibiotics as natural substances produced by some microbes which prevent the growth of some other microbes. Now a days, antibiotics are defined as natural, semi-synthetic and synthetic chemicals that are processed in oral, parenteral, rectal, aerosolized and topical forms to prevent and treat various infections. Most antimocrobial compounds are relatively small molecules with a molecular weight of less than 2000 atomic mass units, which are chemically semisynthetic modifications of various natural compounds. For example, the beta-lactam antibacterials, which include the penicillins, the cephalosporins and the carbapenems. The antimicrobials that are still isolated from living microbes are the aminoglycosides, whereas other antibacterials, for example, the sulfonamides, the quinolones, and the oxazolidinones are produced solely by chemical synthesis. Accordingly, many antibacterial compounds are categorized on the basis of chemical/biosynthetic origin into natural, semisynthetic, and synthetic. Another classification system is based on biological activity; where antibacterials are divided into two broad groups according to their biological effect on microorganisms: bactericidal agents (that kill bacteria) and bacteriostatic agents (that slow down or inhibit bacterial growth of bacteria). Penicillin is the first natural antibiotic discovered by Alexander Fleming in 1928 from Penicillium fungus for which he won the Nobel prize in medicine in 1945.

The first sulfonamide and first commercially available antibacterial antibiotic, Prontosil was developed by a research team led by Gerhard Domagk in 1932 at the Bayer Laboratories of the IG Farben conglomerate in Germany. Domagk received the 1939 Nobel Prize for Medicine for his efforts. Now the main classes of antibiotics are (1) Penicillins, (2) Cephalosporins, (3) Macrolides, (4) Quinolones, (5) Sulfonamides, (6) Tetracyclines, (7) Aminoglycosides, (8) Polymixins, (9) Carbapenems, (9) Special group of anti-TB drugs, (10) Imidazles, (11) Oxazolidones and streptogramins, (12) Cyclic lipopeptides, (13) glycylcyclines, (14) Miscellaneous group like vancomycin, chloramphenicol, clindamycin etc. A penicillin allergy precludess a physician from prescribing amoxicillin and similar other antibiotics that has cross sensitivity/cross allergy. Microbial cultures and antibiotic sensitivity tests are very often ideally and classically performed for prescribing the appropriate antibiotic. Because of nephrotoxic, hepatotoxic and haematotoxic adverse effects, sulfonamides and tetracyclines are not now the systemic antibiotic of preferential choice. Cephalosporins are relatively hepatotoxic when compared with penicillins. Macrolides (erythromycin, azithromycin, clarithromycin) are not much effective against staphylococcus aureus.

Aminoglycosides (e.g. gentamicin, amikacin) are nephrotoxic and ototoxic. Quinolones (e.g. Ciprofloxacin) like aminoglycosides are inactive against streptococci and anaerobes. Imidazoles (e.g. metronidazole, nitazoxanide, ornidazole) are effective against anaerobes and clostridia. Carbapenems (e.g. meropenem, imipenem) and vancomycins (Tricyclic glycopeptides) are extended spectrum anti-penicillinase antibiotics; but still resistant superbugs are emerging. Because of toxicities like hemolytic and aplastic anaemias and grey baby syndrome, Chloramphenicol (a potent broad spectrum antibiotic) has lost its systemic use. Because of mutagenic and carcinogenic adverse effects, nitrofurantoin (a potent antibiotic) was banned by the FDA. Quinolones are first oral antibiotic for use against aerobic gram negative bacilli. But now resistant strains have emerged due to underuse, misuse and abuse over the last three decades. It is still the preferable safe antibiotic for use in jaundiced patients provided its use is justified by culture and sensitivity tests. 'Prevention is better than cure' is a time-honored medical proverb. If proper preventive measures are undertaken, we can save lives of millions of people and reduce the morbidities, mortalities and treatment cost to a great unimaginable level. There are definite guidelines to prevent infection that include active and passive vaccination, neatness and cleanliness in health caring centers and hospitals, peri-operative prophylaxis, proper antenatal, perinatal and postnatal care and follow-up, classical trauma care strategies, ensuring utmost personal hygiene by physicians, paramedics, patients, their guardians and attendants. Frequent nationwide rational scientific surveillance and audits are essential to implement the preventive measures. There are many documented difficulties in antibiotic therapy. These include (1) difficulties in drug delivery (topical, oral, rectal, aerosolized, parenteral i.e. intramuscular, intravenous etc.), (2) drug accumulation problems (leading to increased adverse effects and requiring frequent monitoring for serum levels, searching for hepatic and renal functional status), (3) wrong dose of the antibiotic (underuse and overuse i.e. abuse), (4) selecting the ineffective wrong antibiotic (misuse), (5) adverse effects of antibiotic that include toxicities, anaphylactoid purpura, allergic reactions, anaphylactic shock, aggravating septic shock, development of resistance, cross resistance, multi-drug resistance, life-threatening infections by multi-drug resistant superbugs, opportunistic infections like pseudomembranous colitis, gastro-intestinal and vaginal candidiasis etc. (resulting in increased morbidities and mortalities, increased hospital stay and loss of working days, unusual higher treatment cost). These difficulties can be balanced and minimized by (1) choosing the right/appropriate specific antibiotic (possible narrow spectrum which is the sensitive 1st line antibiotic with least cost, least toxicities, greater availability; then the 2nd line antibiotic having a higher risk for adverse effects if unresponsive to the 1st line or relapse following use of the 1st line; lastly the third line antibiotic with the highest risk for adverse toxic effects if the 2nd line is resistant and the potential benefit of using it outweigh the risk), (2) preventing resistance by using only the necessary antibiotic singly or in combination at right doses for the right duration or rotational use of more than one antibiotics, (3) Eliminating the pathogens or preventing their growth by suitable bactericidal or bacteriostatic antibiotic and enhancing host response (chiropractice); combination of bacteriostatic antibiotic with a bactericidal antibiotic is considered incompatible and unjustified, (3) not underusing, misusing, overusing (abusing) the relevant antibiotic. It is to be noted that antibiotics do not work in most of the infections caused by viral, fungal and protozoal pathogens. Viral sore-throat, cold, flue, cough, bronchitis, bronchiolitis etc are not essentially cured always by commonly used antibiotics. They may need more specific antiviral, antifungal, antiprozoal drugs/antibiotics. Commonly used antibiotics rather can cause much harm in these cases. Infections cause well-documented enhanced morbidities and mortalities in the elderly people who have relatively reduced lean body weight and reduced renal functions, where renally excreted antibiotics need to be used mostly in reduced doses with longer dosing intervals as in younger patients. Duration of therapy in such cases should be conservative as underlying anatomic or functional predispositions to infections might complicate the treatment. In addition, presence of diabetes mellitus and/or age-related immunocompromised and nutritional status in elderly people require further judicious adjustment of doses. Empirically broader spectrum antibiotic therapy is usually advised for severe infections in the elderly people than the younger ones because the infecting bacteria tends to be more and polymicrobial in the former. Antibiotics like penicillins fall to the pregnancy category A and thence are said to be safe during pregnancy. Antibiotics of pregnancy categories B and C should be used during pregnancy if the potential benefits following use outweigh the potential risks if the causative organism is not sensitive to the antibiotics of pregnancy category A. Antibiotics of pregnancy category D are harmful to the fetus and their use is justified only if they are life saving. Antibiotics of pregnancy category E are notorious and embryocidal that they are totally contra-indicated during pregnancy. There are many antibiotics which were not categorized as regards to their safety in using during pregnancy. They fall to the pregnancy category X. Their use during pregnancy is controversial and they should not be used until and unless their safety is documented. Thus, before and during prescribing antibiotics, the physician must consider the following parameters of the patient; (1) age, (2) body weight, (3) liver functional status, (4) Kidney functional status, (5) pregnancy and breast-feeding status, (6) body resistance (immunological and nutritional status) etc. The definite indication and sensitivity need to be be ideally documented as far as practicable. Before getting the culture and sensitivity report, the physician should start a narrow spectrum 1st line antibiotic empirically, followed by switching over to the right one or ones in accordance to the report, if required. It has been found that the broader the spectrum of the antibiotic used, the more multi-drug resistant pathogen/pathogens will emerge. Antibiotics alone can not prevent, eradicate and treat infections. For a success in preventing, eradicating and treating infections, a team work comprising physicians, paramedics, hospital-local-regional-national health authorities, plus continued medical and surgical audits, follow-ups are mandatory to go ahead with better and better results in the upcoming days. Underuse, misuse and abuse of antibiotics must be forbidden.

Prof. ABM Moniruddin
Member of Editorial Board
Khwaja Yunus Ali Medical College
Enayetpur, Sirajgonj, Bangladesh.