

THE TREASURE CALLED ANTIBIOTICS

Prior to the beginning of the 20th Century, infectious diseases accounted for high morbidity and mortality worldwide. The average life expectancy at birth was 47 years (46 and 48 years for men and women respectively) even in the industrialized world. Infectious diseases such as smallpox, cholera, diphtheria, pneumonia, typhoid fever, plague, tuberculosis, typhus, syphilis, etc. were rampant.¹

The discovery of penicillin in 1928 by Sir Alexander Fleming (1881-1955) marked the beginning of the antibiotic revolution.² Ernst Chain and Howard Florey purified the first penicillin, penicillin G, in 1942 but became widely available outside the Allied military in 1945.³ This marked the beginning of the antibiotic era. This antibiotic era witnessed the discovery of many new antibiotics, and the period between the 1950s and 1970s was named the golden era of discovery of novel antibiotics, and no new classes of antibiotics have been discovered since then. After that, the approach to discovery of new drugs was the modification of existing antibiotics.⁴

The antibiotic era revolutionized the treatment of infectious diseases worldwide, although with much success in developed countries. In the US for example, the leading causes of death changed from communicable diseases to non-communicable diseases (cardiovascular disease, cancer, and stroke), the average life expectancy at birth rose to 78.8 years, and older population changed from 4% to 13% of the entire US population.¹ And infectious diseases now become the problem of elderly, cancer patients, transplant patients, surgical patients, patients on immunosuppressive drugs and other at-risk groups in developed countries.⁵ Although the developing countries also recorded a lot of improvement in the morbidity and mortality rate, infectious diseases still disproportionately affect all age group in these parts of the world.^{5,6} This is due to a combination of other factors like poverty, inadequate public health measures, poor sanitation, poor vaccination coverage, etc.

A significant threat to the achievements of the antibiotic era is the antibiotic resistance, which is the ability of the bacteria to resist the effect of antibiotic for which they were initially sensitive to. Resistance results from natural resistance in certain types of bacteria (present even before antibiotics were discovered), genetic mutations in microbes, by one species acquiring resistance from another and selection pressure from antibiotic use that provides a competitive advantage for mutated strains. Suboptimal antibiotic doses,

especially from misuse of antibiotics, help in the stepwise selection of resistance.^{6,7} Examples of significant resistant pathogens in the world are Penicillin-Resistant *Streptococcus pneumoniae* (PRSP), Methicillin-Resistant *Staphylococcus aureus* (MRSA), Vancomycin-Resistant Enterococci (VRE) and Multiple-Drug-Resistant Gram-Negative Bacilli (MDRGNB).⁵

Resistant organisms are difficult to treat, requiring higher doses or alternative drugs, which are possibly more toxic and expensive. According to the Centers for Diseases Control and Prevention (CDC), at least 2 million people become infected with antibiotic-resistant bacteria and more than 23,000 people die annually as a consequence of these infections.⁸ This is expected to be more in developing countries where communicable diseases remain the leading causes of death. To worsen the situations are the emerging and re-emerging infectious diseases, lack of development of new classes of antibiotics and continuing increasing antibiotic resistance, including superbugs (bacteria with accumulated resistance to almost all available antibiotics), at alarming and dangerous levels worldwide.

Natural antibiotic resistance in bacteria may predate the discovery of some antibiotics, and it may be difficult to control since this is one of the natural coping mechanisms for their survival. However, the majority of the acquired antibiotic resistances are promoted by the socioeconomic and behavioural factors, especially in the developing countries. Some of these factors include misuse of antibiotics by health professionals, misuse and inappropriate antibiotics use by unskilled practitioners and laypersons. Other factors are poor quality medicines, dissemination of resistant organisms through overcrowding and unhygienic condition, inadequate hospital infection control practices, inadequate surveillance, poverty, lack of resources to implement strategies against antibiotic resistance and lack of political will.⁹

To halt this dangerous, vicious cycle, there is a need for the effective prevention and control of antibiotic resistance. The Program/Committee on the Global Action Plan on Antimicrobial Resistance by the World Health Organization (WHO) was launched with the primary aim of stemming the tide of antimicrobial drug resistance. The five strategic objectives of the global plan include: to improve awareness and understanding of antimicrobial resistance; to strengthen surveillance and research; to reduce the incidence of infection; to optimize the use of antimicrobial

medicines and to ensure sustainable investment in countering antimicrobial resistance.¹⁰

There is a need for the education of the patients and general community on the appropriate use of antibiotics, importance of infection preventive measures (e.g. personal hygiene, food hygiene, environmental health, bed nets, immunization, etc.) and proper and informed health care seeking behaviour. They should be educated on alternatives to antibiotics for the relief of symptoms and avoidance of antibiotic self-medication. Also essential is the continuing medical education for prescribers and dispensers on the rational use of antibiotics, containment of antibiotic resistance, disease prevention and infection control, the need to educate patients and the general public on antibiotics use and the importance of adherence to prescribed treatments. In the hospital, management should ensure the establishment and strengthening of infection control programme, with the responsibility of effective antibiotic resistance control; the hospital drug and therapeutics committees should be duly constituted to oversee uses of antibiotics in the hospital. The committee should also develop and regularly update antibiotics treatment and prevention guidelines, and hospital antibiotics formularies.¹⁰

Furthermore, the policy makers should: ensure a robust national action plan to tackle antibiotic resistance; improve surveillance of antibiotic-resistant infections and strengthen policies, programmes, and implementation of infection prevention and control measures. They should regulate and promote the appropriate use and disposal of quality medicines, and make information available on the impact of antibiotic resistance. The healthcare industry should invest in research and development of new antibiotics, vaccines, diagnostic and other tools. And Government at all levels should fund research in the Universities and research institutes aiming at the discovery of new classes of antibiotics from the abundance plants in the developing countries.¹⁰

The inappropriate use of antibiotics in the agricultural sector must be regulated. Antibiotics must be given to animals under veterinary supervision and avoided for growth promotion or to prevent diseases. There is the need for immunization of animals to reduce the need for antibiotics, and using alternatives to antibiotics whenever available. There should be promotion and application of good practices at all steps of production and processing of foods from animal and plant sources. Farmers must improve biosecurity on farms, and prevent infections through improved hygiene and animal welfare.¹⁰

The threat of antibiotic resistance is real. Therefore, all the stakeholders must employ strategies to prevent and control antibiotic resistance in order to prevent an imminent post-antibiotic era, a condition that may be worse than pre-antibiotic era.

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