

## Antibiotic Resistance: Preparation for Post-Antibiotic Era

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*“But I would like to sound one note of warning.... It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body.”*

**(Alexander Fleming)**

Counting from the first clinical use of penicillin on the soldiers of World War II, antibiotic resistance has now been 75 years old global issue. During this period numerous antibiotics have been developed, and the bacterial pathogens have acquired resistance against several antimicrobials in almost all the known classes of antibiotics. It was a 12 years gap from the penicillin discovery [1] to its extraction in pure form, [2] whereas the *Staphylococcus aureus* (*S. aureus*) amazingly developed resistance to penicillin in just 12 months [3-5]. On the development of methicillin for penicillin resistant bacteria, it was believed to be the end of the drug resistant bacteria [6]. The 20 years distance from first report of penicillinase-producing *S. aureus* [3-5] to the first entry of methicillin in market was spoiled again in just 1 year with the appearance of methicillin resistant *S. aureus* (MRSA) in 1961 [7-10].

Vancomycin is the potential glycopeptides drug, discovered in 1953, that can reliably treat MRSA infections [11]. However, the massive use of vancomycin for treating MRSA infections has caused the emergence of vancomycin resistant *S. aureus* (VRSA) and vancomycin intermediate *S. aureus* (VISA) cases [12]. The first strain of *S. aureus* with reduced susceptibility to vancomycin was isolated in 1996 from a Japanese patient [13]. The first clinical isolate of VRSA was reported from United States in 2002 [14]. Emergence of VISA and VRSA has now become a global issue [15-21].

The therapeutic and life-saving option for VRSA and VISA infections remains linezolid, first antimicrobial of oxazolidinone group available since 2000. The first case of linezolid-resistant staphylococci appeared within 1 year after linezolid was approved for therapeutic use [22]. Although linezolid resistance in *S. aureus* is uncommon, emergence has been shown from some parts of the world [23]. First time from India, two linezolid resistant *S. aureus* isolates were recovered in March 2011 from a tribal region of central India [24-26].

The fast increase in resistance to even newer antimicrobial agents is alarming to our entry into post-antibiotic era [27,28]. No doubt, the discovery of a plethora of antibiotics have contributed a lot to save the lives of human, but it is the time to save the life of antibiotics. The microorganisms are ubiquitous and residing together in a vast ecological niche. Fossil evidence shows their existence 3.5 billion years ago. In this huge period, it seems surprising that the penicillin resistance was controlled by the nature, and the antibiotic evidently worked against bacteria after the discovery of penicillin as magic bullet, although the resistance problem emerged within one year after the discovery. It seems quite easier, as evident from the historical milestones in the antibiotic resistance, for microorganisms to develop resistance to a pure antibiotic than to the one with the combination of certain unknown molecules in the crude extract of antibiotic. One of the antibiotic resistance mechanisms is by the over-expression of efflux pump by the bacterial cell [29]. The experimental evidences show that the organisms become sensitive to the resistant or less susceptible antibiotics, if the pump hyperactivity is blocked using efflux pump inhibitors [30]. The studies can be carried out to see the effect of regulator (or inhibitor)-supplemented antibiotics on the spread or development of resistant strains.

The antibiotic stewardship programs and strategies should be strictly abided by geographical regions or countries to limit the misuse and overuse of the antimicrobials. Recordkeeping of the consumption of the total amount of antibiotics on a mass level may help decide the concerned authority, organization or ministry to stop the commercial launch of overused antibiotics periodically. It is suggestive to the authors of the text books of medicine, and related health sciences to strictly avoid writing the antibiotic-of-choice in the relevant chapters, and rather it will be fruitful to encourage for the correct treatment based on the result of antimicrobial susceptibility testing. The periodic screening of antibiotic susceptibility of the bacterial pathogens with a sufficiently large sample size may decide the correct empirical antibiotics for the treatment startup, but the empirical drugs must immediately be replaced with the correct antibiotics according to the susceptibility test results from the microbiology laboratory. I conclude to encourage the researchers to screen for certain regulatory molecules or compounds which could stop or regulate the expression of antibiotic resistance in the organisms.

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