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Conceptual Paper

Antibiotic Resistance

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"The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug, make them resistant", said Alexander Fleming, speaking in his Nobel Prize acceptance speech in 1945.

As the pioneer of antibiotics predicted it almost 73 years ago, drug resistance is actually upon us. Antibiotics are substances, actually secondary metabolites, produced by one microorganism that selectively inhibits the growth of another (especially bacteria). Antibiotic came into use as boon for the mankind and have been serving the purpose quite well since then .But in recent times there had been problems arising due to the usage of antibiotics. This is due to many reasons. Use of antibiotics create a biological stress for the bacteria and this promotes the development of such systems which would protect bacteria and aid their survival.

Antibiotics, when needed, should always be used to prevent or treat diseases. But research has shown that approximately 50% of the times, antibiotics are prescribed when they are not required or they are misused. This inappropriate use of antibiotics unnecessarily promotes antibiotic resistance. The misuse of antibiotics covers a wide range of usage patterns. This may include wrong prescription, over or under dose of drugs or sometimes incomplete regimen or drug follow up.

Talking from microbiological point of view, the bacteria had developed various mechanisms to deal with the antibiotics. The aim of the survival strategies of bacteria is either to stop the antibiotic from reaching the target or to modify the target.

Before proceeding further, it is important to consider a few points. Since antibiotics' usage for clinical purposes is an exploitation of the natural phenomenon or part of the metabolism of certain microorganisms, it is quite obvious that they produce it in their natural environment also. Therefore, other microorganisms (bacteria) might be previously exposed to some types of antibiotics although in lower or non-target amounts. Thus it would be totally justified to come across certain bacterial species which might be "intrinsically" resistant to some antibiotics. But these microorganisms are not the main focus. We are more concerned about the "acquired resistance" among bacterial species. The other main point is to understand the complexity of this resistance mechanism.

Bacteria have a remarkable genetic make-up that allows them to respond to various environmental threats or stimuli including exposure to antibiotics. Most commonly, mutations are the major force that drives the resistance mechanisms. The antibiotic action is neutralised by one of the following strategies:

1. Alteration of the target molecules upon which antibiotics act
2. Reduction in the amount of drug uptake
3. Efflux mechanism to expel out the harmful molecules
4. Modifications in important metabolic pathways

Another important factor is Horizontal Gene Transfer. It is one of the most important drivers of evolution in bacteria and is also of considerable importance when related to development of antibiotic resistance. According to HGT, genetic exchange has been known to occur among bacteria. Due to this there are fairly large chances that, at times, such genes might get transferred from resistant bacteria to non-resistant ones, which will provide resistance against antibiotics. Not only this, but there can also become combinations of such resistance genes, providing resistance against a broader range of drugs (MULTI-DRUG RESISTANCE).

The danger of antibiotic resistance can be estimated by briefly considering two examples-MRSA (Methicillin Resistant *Staphylococcus aureus*) and XDR (Extensively Drug Resistance *Mycobacterium tuberculosis*). MRSA is a genetically different strain of *Staphylococcus aureus* which is resistant to β-lactam antibiotics like penicillin, methicillin, cephalosporin etc. Thus it is harder to deal with during infection and will require stronger antibiotics to be inactivated or killed. Similarly, XDR strain of tuberculosis pathogen is also resistant to normally used antibiotics (Rifampicin, Isoniazid etc). So, other antibiotics are required which have their own side effects.

Antibiotic resistance, due to its major influence in diseases and recovery from diseases, is really important to be communicated to individuals because awareness will definitely be the first step towards controlling the problem. As microbiological aspect is difficult to be explained to everyone, simple language and easily understandable methodology should be adopted. Scientific community and medical community (doctors, chemists etc.) should play their roles with more responsibility.