



An obituary- On the Death of antibiotics!

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Homosapiens is an alien species on earth. This planet belongs to bacteria. There are more bacteria on earth than all other living organisms. The human body contains more number of bacteria than human cells themselves. We lived with arrogant optimism that we had conquered infections, at least the bacterial infections, if not the viruses. How wrong we were! Bacteria have finally reclaimed their premier status and superiority and won the war against humans. They are literally mocking our intellect, knowledge and antibiotic weaponry.

Indian Health care professionals involved in the treatment of patients with severe infections especially healthcare associated infections will agree that it is commonplace to come across pan-resistant Gram negative bacterial infections where we do not have a single effective antibiotic option. We are, therefore, forced to use a cocktail of antibiotics to which the bacteria is resistant with the infinitesimally small hope of a synergistic effect. Immunocompromised patients especially transplant and cancer chemotherapy patients, who develop infections, are known to have high mortality rates. Until a few years ago we could at least try our powerful antibiotics against these infections. With increasing pan resistant bacteria, we will be forced to stop organ transplantation, bone marrow transplantation and cancer chemotherapy. We are going to face this catastrophic situation in the near future - not in a decade or so but within a few years time. May I encourage the readers to examine the excellent article "Antibiotic-Resistant Bugs in the 21st Century —A Clinical Super-Challenge" by Cesar A Arias, in one of the recent issues of NEJM.¹

The easiest way of tackling the superbug problem is to use the notorious ostrich strategy which denies the existence of the problem: stop looking for these bugs, stop looking for the hidden resistance mechanisms and closing your eyes even if you find them. A National Resistance Alert from UK, issued in January 2009,² warned of an increasing number of carbapenem-resistant strains of Enterobacteriaceae being identified in UK hospital patients, a significant proportion of whom had received medical treatment in India and Pakistan. This new resistance mechanism is named as "New Delhi Metallo-1" (NDM-1). At the time of the publication of the UK HPA warning, the Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL), UK identified a total 22 isolates of NDM-1.

We have now data from one of our own hospitals. Deshpande P and team from Hinduja National hospital, Mumbai have isolated 22 NDM-1 producing Enterobacteriaceae, from span of just 3 months and a single hospital.³ This is the first Indian study on NDM-1 and an eye opener on how deep a trouble we are in. If a single hospital can isolate such a significant number of bacteria with a new resistance gene in a short period of time; the data from all the Indian hospitals, if available would potentially be more interesting and shocking than the human genome project data, which is considered as a discovery more important than the moon landing itself. I congratulate the

authors and their departments for doing such an important study, especially considering the fact that majority of Indian hospitals are struggling to hide their resistance statistics.

We come across MDR or even pan resistant Gram negative bugs quite often and such bugs are reported in almost all major centers in India and most of international centers though to a lesser extent than India. We Indians are the leaders in antibiotic resistance. Many of MDR superbugs are from bacterial cultures taken at the time of admission to the hospital. By the time a patient is being admitted to a tertiary care centre, that patient has already visited many other hospitals and doctors and has received multiple courses of different antibiotics. These patients are literally walking culture plates of superbugs and you don't have to be Nostradamus to predict their clinical outcome

When we are called to manage patients with severe infections due to pan resistant bugs, we do really wonder whether we are living in pre-Alexander Fleming years without antibiotics and then with a shock, but no surprise, realise that we have reached the end of antibiotic era. Still, the Indian medical community remains in a state of denial. We have not yet taken the issue of antibiotic resistance seriously. We believe that Dr. Fleming has discovered penicillin only early this morning and consider antibiotic resistance a problem of next century where in fact antibiotics are dead and the foul smell of decay is already around us. You may call me a pessimist, but I sincerely believe that it is too late to save antibiotics; unless you have divine powers to bring the dead back to the life.

There is no restriction on the usage of higher end antibiotics in India. Indian doctors need not justify their prescription. Any doctor can prescribe and in some cases even pharmacists can dispense without prescription meropenem in a situation where ampicillin would have been adequate and at the same time prescribing ampicillin in a case where meropenem would have been the right choice. Under usage of antibiotics is as dangerous as overusing them. Choosing the right antibiotic is critical and requires adequate knowledge on the spectrum of antibiotics. Unfortunately a good percentage of our medical community lack that knowledge. India is a country where infectious diseases are rampant and we manage plenty of these cases every day. This experience gave us a false sense of confidence on antibiotic usage. We consider ourselves masters of the encyclopedic knowledge of antibiotics where in fact some of us do not even think about the spectrum of an antibiotic and others do not even consider the need of an antibiotic before giving a prescription. The Indian medical curriculum lacks importance on the teaching of infectious diseases to undergraduate and post graduate students. An MD General Medicine candidate can clear his or her examination without reading the chapter on infectious diseases and antibiotic usage. Our curriculum is still revolving around the colonial concepts. When are we going to teach our students the difference between cefotaxime and meropenem rather than spoon feeding them with the dynamics of opening snap, release reflexes and tidal percussion?

The pharmaceutical industry, both international and Indian

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generic, has made its own contribution to this resistance saga. The lack of restriction on the usage of newer antibiotics with specialist spectrum has given fertile ground for companies to exert their excessive pressure on doctors to increase prescription of antibiotics. The aim of any industry is to make profit. So let us not blame the industry, let us blame ourselves. We are the individuals making prescriptions, not the medical representatives. Indian doctors should update their awareness on antibiotics and antibiotic resistance. That should not be through the pamphlets issued by companies, but through unbiased medical information. The pharma companies should realise that indiscriminate usage of antibiotics in a situation where there is no good new antibiotics in the pipeline, is like killing a duck laying golden eggs.

Most of the Government hospitals in India are not worried about resistance. They are still struggling to get hold of life saving antibiotics. The private practitioners, private and corporate hospitals are the breeding grounds for resistance. There are very few hospitals in India with infectious diseases and infection control specialists. Only in a minority of Indian private hospitals are antibiotic policy and antibiotic stewardship implemented. The majority of private and corporate hospitals are in denial, either purposefully or due to ignorance. I have come across many hospital administrators in India claiming zero infection in their hospitals. It is sad to say that many of these hospitals do not have the necessary microbiology laboratory support or trained infection control specialists to look for resistance. The claim of zero infection is in fact an innocent advertisement of the lack of necessary infection control infrastructure in that hospital.

'Bad bugs, No drugs: No ESKAPE!' is an excellent article by the infectious disease society of America on the superbug problem.⁴ There is a dramatic increase in the prevalence of superbugs and there is an equally dramatic drop in the number of new antibiotics available. We need new antibiotics to treat difficult Gram negative infections. But for the time being we can only dream about these new molecules. The pipeline of antibiotic research and development is nearly dry. There are some good gram positive antibiotics in the pipeline, not even a single promising antibiotic in the advanced stage of development which is useful against resistant gram negative bacteria. Research and development of any antibiotic is a huge investment for any pharmaceutical company. Unlike anti-diabetics or anti-hypertensives, which do not become resistant with usage, antibiotics frequently lose their utility within a few years of coming to market. So antibiotic development is not a profitable option for pharmaceutical companies and that

is one of the reasons why the pipeline is getting drier. It is the responsibility of the medical community especially the Indian medical community to save the antibiotics which remain, by prudent and sensible use of these drugs.

Carbapenems are the most powerful tools against Gram negative bacteria. Due to the extensive misuse of these antibiotics, a good proportion of *Pseudomonas* and *Acinetobacters* species in Indian hospitals have developed carbapenem resistant mutations. Now even our *Enterobacteriaceae* are becoming resistant to carbapenem. I congratulate the authors for their excellent study and the result of this study is the final nail on the antibiotic coffin. It may be overconfidence however to believe that this study will open the eyes of Indian medical community.

The art of war is deception; that is deceiving the enemy. But in the war against microbes we have deceived ourselves by misusing, under using and overusing antibiotics. Our country, India, is the world leader in antibiotic resistance, in no other country antibiotics been misused to such an extent. Microbes are the ultimate warriors. They have sophisticated weapons and use ingenious methods of attacks. They have always been many steps ahead of us. Even in the twenty first century with all the developments in the modern medicine, when we face microbes, we feel helpless. Whatever weapons we had in the form of antibiotics, we ourselves have ruined them.

Indian medical community has to be ashamed of the NDM-1 ("New Delhi Metallo-1") gene. Even though we have not contributed to carbapenem development, we have contributed a resistance gene with a glamorous name. The overuse of antibiotics is embedded in our Indian gene. It is an Indian tradition. Why should we Indians worry? We can always depend on honey, yoghurt and cow's urine. At any rate within a few years, these products may be more useful than antibiotics!

References

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18th annual conference of MAPICON 2010 (Maharashtra association of physician of India) will be head on 8th ,9th& 10th October 2010 at Nashik. Please contact organizing secretary Dr. Narayan Deogaonkar on mobile number 09823031314 & email address : drnarayan_04@yahoo.co.in for further communication.