

Growing Antibiotics Resistance and the Need for New Antibiotics

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Emerging and increasing resistance to antibiotics has become a threat to public health globally. Only 70 years after their introduction, we are now facing the possibility of a future without effective antibiotics. On the other hand, there is lack of concerted efforts to unearth new groups of antibiotics to take on the menace of antimicrobial resistance.

STATUS OF ANTIBIOTICS RESISTANCE: GLOBAL AND INDIAN SCENARIO

Growing antibiotic resistance is a global phenomenon in both developed and developing countries. Methicillin-resistant *Staphylococcus aureus* (MRSA) alone infects more than 94 000 people and kills nearly 19,000 in the US every year, more deaths than are caused by HIV/AIDS, Parkinson's disease, emphysema, and homicide combined(1). Penicillin-resistant *streptococcal pneumonia* and vancomycin resistant enterococci (VRE) are more frequently incriminated from many industrialized countries forcing frequent changes of recommendations of management of diseases caused by these bugs. Despite a few hopeful trends (e.g., declining penicillin resistance among pneumococci in the UK), established resistance is proving hard to displace; moreover, new resistance continues to emerge and to proliferate at new sites. Consequently there remains a strong need for new antibiotics, particularly those directed against multi-drug resistant (MDR) Gram-negative bacteria in hospitals. Already some non-fermenters of the genera *Acinetobacter* and *Pseudomonas* are resistant to all good antibiotics and many Enterobacteriaceae are resistant to all except carbapenems. Health care associated infections due

to resistant gram negative bacteria are the most threatening development all over the world.

In the absence of a central monitoring agency, the National scene in India with regard to antimicrobial resistance is not known. The two probable exceptions are *M. tuberculosis* and *Leishmania donovani*. However, the available sporadic reports point to growing resistance of gram-negative bacteria responsible for UTI, diarrhea, dysentery, enteric fever, and sepsis. Fortunately, penicillin resistance to *Streptococcus pneumoniae* is still not a big problem. MRSA and VRE are reported from many centers across the country. However, the greatest threat is posed by gram negative organisms responsible for nosocomial sepsis in neonatal and pediatric ICUs. Astonishingly, some members of *Acinetobacter* spp. have shown a high prevalence of resistance to even a most recently introduced antibiotic, tigecycline. And to compound the situation, the only drugs showing good coverage are older antibiotics like polymyxin-B and colistin having questionable efficacy and safety.

WHY ARE MICRO-ORGANISMS DEVELOPING RESISTANCE?

Rampant, unrestricted and often inappropriate use of most antibiotics is the main reason why antibiotics are rapidly losing their efficacy. There is a need to review the antibiotic prescription practices of the clinicians. Unfortunately, majority of the prescriptions are irrational as they are based by the information gathered from representatives of pharmaceutical companies, especially for the newer antibiotics.

The Indian scene is particularly grim due to

various factors. Generally, there is little control on the use of antibiotics. Community awareness of the issues involved in antibiotic therapy is poor and this is compounded by over-the-counter availability. Coupled with primitive infection control in hospitals and weak or deficient sanitation, the conditions are suited for transmission and acquisition of antibiotic resistance. Apart from the medical consequences of antibiotic resistance, there is also a direct cost to society. Unfortunately, the economic burden of antimicrobial resistant organisms on health care expenditure in India is not known.

STATUS OF DEVELOPMENT OF NEW ANTIBIOTICS

The 1990s saw only one new antibiotic class viz the oxazolidinones joining the approved list. All other introductions have been variants of existing classes. Only a few new antibacterial agents have received approval by the US Food and Drug Administration in the last 10 years, including linezolid in 2001, cefditoren pivoxil and ertapenem in 2002, gemifloxacin and daptomycin in 2003, telithromycin in 2004, and tigecycline in 2005(2). Only a single new antibacterial—doripenem—has been approved in the USA since 2006(1). Many of these agents are improved derivatives from established classes of antibiotics, and several are directed primarily at resistant Gram-positive bacteria (e.g., linezolid and daptomycin). These modified agents suffer from the disadvantages of the parent molecules. In view of the crossover of resistance across related compounds, the future may see sharply depleting antibiotic resources.

NEED OF THE HOUR

There is a strong case for continued surveillance for antibiotic resistance at all levels, the hospital, city/region, country, and supra-national levels. It is only then the ramifications of problem can be learnt. Such mechanisms are in position in the industrialized countries but the developing world (including India) is yet to invest in building them.

There is a need to keep a check and control the

prescription of any newly introduced broad-spectrum antibiotics or those targeting highly resistant organism, both in indoor and outdoor practices. There should be active surveillance of antibiotic use and resistance rates, and all attempts should be made to optimize antibiotic use with treatment guidelines along with education of professionals and the public. Prevention of acquiring new resistance can be achieved with infection control measures and immunization. Industry should also revise its antibiotic development policy and international health agencies, national governments and NGOs should support them in financial resource mobilization and slackening of regulatory issues. There should be refined regulation of antibiotic registration for use with central prescribing and advertising restrictions.

The microbial world has demonstrated remarkable resilience and the emergence of resistance is practically invariable upon the introduction of an antibiotic into the environment. The relentless build-up of resistance may make the valuable antibiotic assets useless and a 'post-antibiotic scenario' may emerge. A global strategy is urgently needed to create a stable research infrastructure for antimicrobial development. Unless antibacterial development is re-energized, there is a serious risk that a growing proportion of infections, especially in hospitals, will become effectively untreatable. Given that it takes more than 10 years to establish the efficacy and safety of new compounds, there is a dire need to restock the antibiotic pipeline.

Funding: None.

Competing interests: None stated.

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