

**61.001****Extreme Drug Resistance (XDR) in Nosocomial Pathogens**

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The implacable increase in the prevalence of antimicrobial resistance among gram negative bacilli (BGN) is of great concern. Several highly resistant gram-negative pathogens, namely *Acinetobacter*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* sensitive to a small number of drugs, if not any, are emerging as significant pathogens. The mechanisms of this resistance are often complex but include outer-membrane impermeability, up-regulated efflux pumps, target-site mutation and, not surprisingly, the production of carbapenemases, in addition to several enzymes. Given the frequency of worldwide reports now describing infection with carbapenemase-producing BGN, in addition to the intercontinental spread of hyper-epidemic clones, such as KPC-3-possessing *K. pneumoniae* ST258, it is possible that any institution on the globe could be beset by multi-resistant BGNs. Proficient methods are needed for early detection and confirmation in clinical microbiology laboratories of multidrug resistant bacteria, specially those producing carbapenemases, in any attempt aimed for targeting optimal antimicrobial therapy and controlling their spread. Therapeutic options for these pathogens are so extremely limited. Even now, resistance to new "salvage" therapy, such as tigecycline and colistin is being observed. Several new terms definitions have been introduced in the medical literature to describe this complex scenario: pan-resistance, extreme-resistance, extensively-resistant.

Although there is no international harmonization of this terminology, their adequately capture the public awareness for the desperate need for attention to this problem. As expected, mortality rates among patients with infections due to these organisms are significantly higher than those caused by sensitive germs. The urgency of the problem is compounded by the recognition that fewer new antimicrobial agents are introduced each year. Thus, clinicians are forced to use older drugs for which there is a lack of robust data about their effectiveness. The complex nature of this scenario requires the coordinated efforts of all sectors involved, in any attempt to curb antimicrobial resistance.

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**61.002****Basic Principles of Implementing an Antibiotic Optimization Program**

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Antimicrobial stewardship is an important and evolving aspect of patient care and safety programs in hospitals around the world. A team of involved specialists, including infectious diseases physicians, clinical microbiologists, hospital epidemiologists and others, is needed to address this complex problem. In United States a clinical pharmacist has been also claimed to collaborate in this kind of program,

but in Latin America and other limited-resources areas, lack of appropriate personnel are part of the limitations to implementation. Two strategies, not to be exclusively applied, are proposed. Prospective audit with intervention and feedback is an option, while the use of formulary restriction and pre-authorization might be also used. The first strategy might be time consuming and requires a series of tools to succeed. The implementation of the program requires administrative and economic support and the use of education, development of guidelines, antimicrobial order forms, de-escalation therapy (which requires an active participation of the microbiology laboratory), dose optimization, and switch to oral therapy. Effective use of antimicrobials but also prevention of resistance are the goals to achieve in the individualised care of patients and new targets are being currently defined (pharmacodynamic objectives). Up to the moment more research is required to find the best ways to achieve these goals.

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**61.003****Infection Control Program as an Additional Tool to Control Bacterial Resistance**

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The combination of effective antimicrobial stewardship with a comprehensive infection control program has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria, reducing health care costs.

There are multiple mechanisms postulated by which antimicrobial resistance may appear and disseminate within hospital organisms:

- 1) Introduction of a resistant organism to a previously susceptible population;
- 2) Acquisition of resistance by a susceptible strain: spontaneous mutation or genetic transfer;
- 3) Expression of regulated resistance already present in the population;
- 4) Selection of resistant subpopulations; and,
- 5) Dissemination or spread of resistant organisms

There have been proposed five strategic goals to optimize antimicrobial use: 1) Optimize antimicrobial prophylaxis for surgery 2) Optimize choice and duration of empirical therapy; 3) Improve prescribing by education; 4) Monitor and feedback information on antimicrobial resistance rates, and, 5) Produce protocols for antibiotic usage. Also the strategies must include optimal selection, dose, and duration of treatment, as well as control of antibiotic use, for prevention or slowing the emergence of resistant among microorganisms.

An effective Antimicrobial Control Program Infection must prevent or reduce antimicrobial resistance. Specific goals related to this program are:

- 1) A determination of who will be responsible for maintaining control.
- 2) A determination of which antimicrobial(s) to control.
- 3) Precise definitions of antimicrobial resistance for antimicrobials and organisms.
- 4) A system for monitoring the frequency of resistance (clinical and environmental).
- 4) Education. It is an essential element to influence prescribing behavior.
- 5) A method to determine antimicrobial use per geographic area per unit time.
- 6) Ability to distinguish community from nosocomial isolates.
- 7) A method to assure