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Eugenie Bergogne-Berezin

Centre Hospitalo-Universitaire Bichat-Claude Bernard, France

Rationale approach to combat resistance

After 60 years of use of antibiotics, the world experienced antibiotic resistance. Dissemination of genes of resistance in hospitals, in population has imposed to experts to look for measures to combat resistance, major challenges in developed countries. Combat antibiotic resistance includes knowledge of resistance mechanisms, role of genes associated to gene cassettes, multidrug resistance with transmissible plasmids, efflux mode of resistance, role of integrons in acquisition of resistance genes. Among pharmacologic factors, antibiotic distribution in body at site of infection, low serum concentrations (sub-MICs) are factors for emergence of resistance; intracellular concentrations of macrolides, fluoroquinolones are needed to eradicate intracellular *Legionella*, chlamydia. Pharmacokinetic parameters are factors for proper use of antibiotics to combat resistance. Research for new antibiotics is developing in Biotech companies: Rehabilitation of antibiotic classes (glycopeptides, ketolides, oxazolidinones) to overcome resistant Gram positive bacteria; a renovated cyclic peptide colistin (polymyxin) active against "super-bug" *Acinetobacter baumannii*. β-lactamase inhibitors clavulanate, sulbactam, tazobactam did not solve resistance related to β-lactamases C, D, carbapenemases: New β-lactamase inhibitors NXL-104, MK-7655 restore activities to imipenem, 3d generation cephalospsorins. Newer drugs based on integrated new tools, combinatory chemistry, high speed parallel synthesis, genomics and proteomics, able to lead to new bacterial targets: DNA replication, target genes, cellular division, secretion of efflux pumps. Inhibition of virulence of bacterial communication systems, immunomodulatory systems are leading to new molecules: Artilysins as cell wall targets, Torezolid, active on MRSA, Iclaprim (a diaminopyridine-dihydrofolate reductase) inhibits VRSA. The current clinical development estimated in March 2015 the number of new antibiotics to 36 molecules in clinical development in the US.

Biography

Eugenie Bergogne-Berezin is a Professor of Clinical Microbiology at University Diderot, Paris. She has studied MD in Medicine and PhD in Sciences in the early 1970s. She is a Chief of Department of Clinical Microbiology and research group, University Bichat Claude-Bernard and developed research on *Acinetobacter* spp., (nosocomial pathogen, pathogenicity, resistance), pharmacology of antibiotics, tissue distribution (lungs, brain, bronchi), research on intestinal ecology, jejunal flora and bacterial adhesion. She is an Adviser to pharmaceutical companies, expert in pharmacology-toxicology for the Ministry of Health, expert for international journals. She has developed a journal *Antibiotics*, (Elsevier). She has published 6 medical books, many chapters in international infectious diseases books, 200 articles in scientific journals.

eugenieberezin@gmail.com

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