招請講演 1

MDR *Acinetobacter*, *Pseudomonas* and *Klebsiella*: The Big Three!

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The treatment of multidrug resistant (MDR) pathogens presents serious challenges to the clinician. At the present time, three pathogens pose the most significant challenge: MDR *Acinetobacter baumannii*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* ("the big three"). Each of these MDR pathogens harbors unique resistance mechanisms. Although they are lactose non fermentors, *A. baumannii* and *P. aeruginosa* convey the MDR phenotype by a series of different mechanisms. In *A. baumannii* a series of genetic traits are distinguished by the presence of a large resistance island (RI). There are presently up to ten different RIs. Secondly, genetic elements exist that convey resistance to β-lactams (OXA genes, metallo-β-lactamases, AmpC) quinolones, aminoglycosides (modifying enzymes and ribosomal methyl transferases), and efflux pumps. Unfortunately, resistance to colistin, a “last resort” antibiotic, emerges. Colistin resistance can arise while on therapy. There are two mechanisms responsible for resistance to colistin in *A. baumannii*.
The main resistance mechanism in *P. aeruginosa* involves the hyperproduction of AmpC, the loss of porin channels and resistance to quinolones modulated by changes in DNA gyrase and efflux pumps. In *P. aeruginosa*, the presence of many efflux pumps complicates the evaluation of resistance.

In *K. pneumonia*, resistance is mediated by extended spectrum β-lactamases and carbapenemases. KPC is encoded on a mobile transposon. ESBLs are usually carried by large resistance plasmids.

Novel combination therapies based upon an understanding of these basic mechanisms can help in select instances. There has been renewed interest in colistin despite its toxicity. Physicians have also tried tigecycline, but reports are published questioning the safety of tigecycline. Combination chemotherapy may be the best approach, especially against MDR *K. pneumoniae*.