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Various kinds of multigrug-resistant Gram-negative microbes including NDM-1-producing microbes belonging to the family *Enterobacteriaceae* and multigrug-resistant *Acinetobacter baumannii* have been emerged and spreading worldwide. Rapid global disseminations of CTX-M, KPC, and OXA-48-producing *Escherichia coli* and/or *Klebsiella pneumoniae* are becoming a general concern especially among medical staffs. Moreover, new molecular mechanisms responsible for acquisition of multidrug resistance such as plasmid-mediated quinolone resistance including Qnr peptides, AAC(6')-Ib-cr, and QepA efflux pumps, as well as 16S rRNA methyltransferases have been found among pathogenic Gram-negative bacteria. More worrisome problem is that these pan-resistant pathogens have already armed with combination of multiple antimicrobial resistance mechanisms as observed in NDM-1-producing bacteria that also harbor plasmid-mediated genes for CMY-type cephalosporinases, CTX-M-type ESBLs and 16S rRNA methylases such as RmtB, RmtC and ArmA. Furthermore, various sets of multifarious antimicrobial resistance genetic determinants have been highly organized and often mediated by diverse mobile genetic elements and integrons embedded usually into a variety of transferable large plasmids, predicting further continuous global proliferation of such stubborn microorganisms. Therefore, we should confront the stern realities and devote our utmost knowledge and skill to cope with such threatening superbugs.

