COMMENTARY – Pathogens & Pathogenicity

Antibiotic resistance: the emergence of plasmid-mediated colistin resistance enhances the need of a proactive one-health approach

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One sentence summary: The recent emergence in Gram-negative bacteria of a transferable gene encoding resistance to colistin, a last resort antibiotic, emphasises the need of a holistic approach to fight antimicrobial resistance.

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For some years now, multi-resistant Gram-negative bacteria such as Escherichia coli or Klebsiella pneumoniae have been spreading globally, causing increasing difficulty in treating infectious diseases both in hospitals and the community at large. Of particular concern are carbapenemase-producing Enterobacteriaceae which are frequently resistant to nearly all antimicrobial drugs available.

Up to now, both colistin (an antibiotic of the family of polymyxins), and tigecycline (a glycyclcline), have been regarded as a last resort drug. And although colistin-resistant Enterobacteriaceae have been isolated, such resistance to date has been chromosomally mediated, and hence less prone to be efficiently transferred by horizontal gene transfer.

This situation, however, has suddenly significantly worsened, as reported in 'Lancet Infectious Diseases' in November last year. Liu et al. (2016) described in China the isolation from a pig of a resistant non-pathogenic E. coli strain whose resistance determinant (gene mcr-1) is encoded by a plasmid. This genetic element is transmissible, not only at rather high frequency by conjugation to E. coli, but also by transformation to both K. pneumoniae and Salmonella spp. originating from Asia, North and South America, Africa and Europe, including Denmark, UK, France, Netherlands, Belgium, Germany and Switzerland (Godbøl, Woodford and Larkin 2015; Hasman et al. 2015; Poirel et al. 2015; Arcilla et al. 2016; Földinghauer et al. 2016; Malhotra-Kumar et al. 2016; Webb et al. 2016). From these reports, it appears that the mcr-1 gene is more prevalent in bacterial strains from animals (mainly from pigs and poultry) than in those from humans, which suggests that the agricultural and veterinary sectors constitute an important reservoir where the plasmid-mediated colistin resistance has emerged. Indeed, the decades-long worldwide use of polymyxins in the treatment and prevention of livestock diseases could feasibly provide efficient selection pressure for resistance evolution. In 19 European countries, data available for 2010 show that polymyxins were the 5th most sold group of antimicrobials in veterinary medicine (European Medicines Agency 2013).

In addition to its potential dramatic implications for human health, the 'Lancet Infectious Diseases' report represents one of several examples highlighting how most resistance mechanisms involving enzymatic modification of either the target, as for mcr-1 (Liu et al. 2016), or of the antibiotic, as for the ill-famed New Delhi metallo-β-lactamase-1 (Yong, Toleman and...
Giske 2009), will eventually hop into mobile elements. It also stresses that the antibiotic resistance issue must be addressed in a holistic way, involving, in addition to human medicine, also veterinary medicine, agriculture and environment. This approach, currently identified as the One-Health approach, is now considered essential in the implementation plans to fight antibiotic resistance that are being established by an increasing number of countries.

**Box 1: The resistome and the One-Health approach**

The ‘resistome’ constitutes the collective genomic elements that include all sequences encoding resistance to antimicrobials, expressed or silent, present in bacteria, including both pathogenic and commensal bacteria that are hosted by animals and humans, as well as those present in the environment. Since these sequences are potentially transmissible by mobile genetic elements such as plasmids, transposable elements, and bacteriophages, they contribute significantly to the emergence and diffusion of antimicrobial resistance in strains isolated from both animals and humans, and most worryingly, in clinical isolates. The One-Health concept is currently being developed, recognizing linkages between humans, animals and their environments in the context of human health. Since the resistance genes are mobile within all these compartments, the issue of antimicrobial resistance needs to be addressed holistically by adopting the One-Health concept.

**Box 2: FEMS Endorses One Health**

The Federation of European Microbiological Societies (FEMS) strongly supports the One Health Initiative (OHI) and the call for increased collaboration between the human, veterinary and environmental communities. Many of our members look forward to seeing more interactions and partnerships between physicians, veterinarians and scientific researchers. Such collaboration could help find responses to serious societal challenges, such as emerging infectious diseases, pandemics and the transmission of antimicrobial resistance. Also, it is crucial for our health and the health of the planet to build a better understanding around the role and fate of microbes and viruses in the biotic and abiotic environment. OHI can show the way to a healthy future!

**Conflict of interest.** None declared.

**REFERENCES**


