Screening of plasmid-mediated MCR-1 colistin-resistance from bacteremia

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To the Editor,

Recently, the very first plasmid-mediated colistin resistance (MCR-1) mechanism of resistance in *Enterobacteriaceae* was reported from animals, food and patients from China [1]. Then, it was reported worldwide, mostly in *Escherichia coli*. This finding is important since polymyxins are considered as last resort antibiotics for treating infections due to multidrug resistant bacteria.

Several pieces of evidence suggest that the reservoir of the *mcr-1* gene might be related to animals, taking into account the heavy usage of polymyxins in veterinary medicine, and the fact that this gene was mostly identified from veterinary isolates worldwide. We have reported several human cases of infections due to *mcr-1*-positive *E. coli* from community and hospital settings in Switzerland (Geneva and Neuchâtel regions) in 2015 and 2016 [2, 3]. When used in human medicine, polymyxins are mostly prescribed in hospital settings and the extent of diffusion of the *mcr-1* gene in human pathogens remain mostly unknown.

Therefore, a retrospective study was conducted to evaluate the spread of polymyxin resistance and MCR-1 positivity among enterobacterial isolates that had been isolated from clinically-significant specimens, i.e. blood cultures, at the University Hospital of Lausanne (1,200 beds), Switzerland, in 2015. This study was performed in the same French-speaking region of Switzerland as Geneva and Neuchâtel where *mcr-1* positive *E. coli* isolates had been identified.

A total of 257 non-duplicated enterobacterial isolates was screened that included *E. coli* ($n = 164$), *Klebsiella pneumoniae* ($n = 41$), *Enterobacter cloacae* ($n = 16$), *Klebsiella oxytoca* ($n = 14$), *Enterobacter aerogenes* ($n = 6$), *Citrobacter koseri* ($n = 5$), *Citrobacter freundii* ($n = 5$), *Hafnia alvei* ($n = 3$) *Kluyvera ascorbata* ($n = 1$), and *Salmonella* serovar *enteritidis* ($n = 2$) isolates. The predominance of *E. coli* isolates in that collection is in accordance with the known enterobacterial distribution in bacteremia. The strains were screened first by using the recently-developed Rapid Polymyxin NP test that is more reliable and rapid to detect colistin resistance than disk diffusion, E-test and automated systems [4, 5]. Then, all strains were screened for the *mcr-1* gene by using regular and real-time PCR techniques [3, 6]. Four isolates (three *H. alvei* and a single *E. cloacae*) were selected as resistant to colistin (prevalence rate, 1.17 %) according to the Rapid Polymyxin test. MIC determination confirmed that those four strains were indeed resistant to colistin (MIC > 2 mg/L) [7], the *E. cloacae* strain showing an heteroresistance phenotype as known [8]. In fact, *H. alvei* might correspond to an enterobacterial subspecies being naturally resistant to polymyxins (P. Nordmann, personal communication). All the strains tested negative for the *mcr-1* gene.

This study indicated that the extent of diffusion of the *mcr-1* gene is limited at least in this western part Europe. Very rarely reported in *K. pneumoniae*, the *mcr-1* gene was accordingly not identified here in that species, which is an important nosocomial gram-negative pathogen. This finding may be good news for medical specialities that rely on broad-spectrum antibiotics such as intensive care, heavy surgery and transplantation units. However, regular screening of

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plasmid-mediated colistin resistance is mandatory to detect the early occurrence of those polymyxin-resistant isolates and prevent their further spread.

Compliance with ethical standards

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