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LETTER TO THE EDITOR

Increasing Trends in *mcr-1* Prevalence among Extended-Spectrum-β-Lactamase-Producing *Escherichia coli* Isolates from French Calves despite Decreasing Exposure to Colistin

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Since the first description of the plasmid-mediated colistin resistance gene (*mcr-1*), over 30 follow-up reports have proved the worldwide geographical distribution of this gene (1, 2). The overall picture indicates a very low prevalence in animals, human beings, and retail food, with two exceptions, the first in China, where *mcr-1* carriage was observed in 21% and 15% of the animals and raw meat samples, and the second in France, where 21% of the extended-spectrum-β-lactamase (ESBL)-producing *Escherichia coli* isolates from calves were *mcr-1* positive (1, 3).

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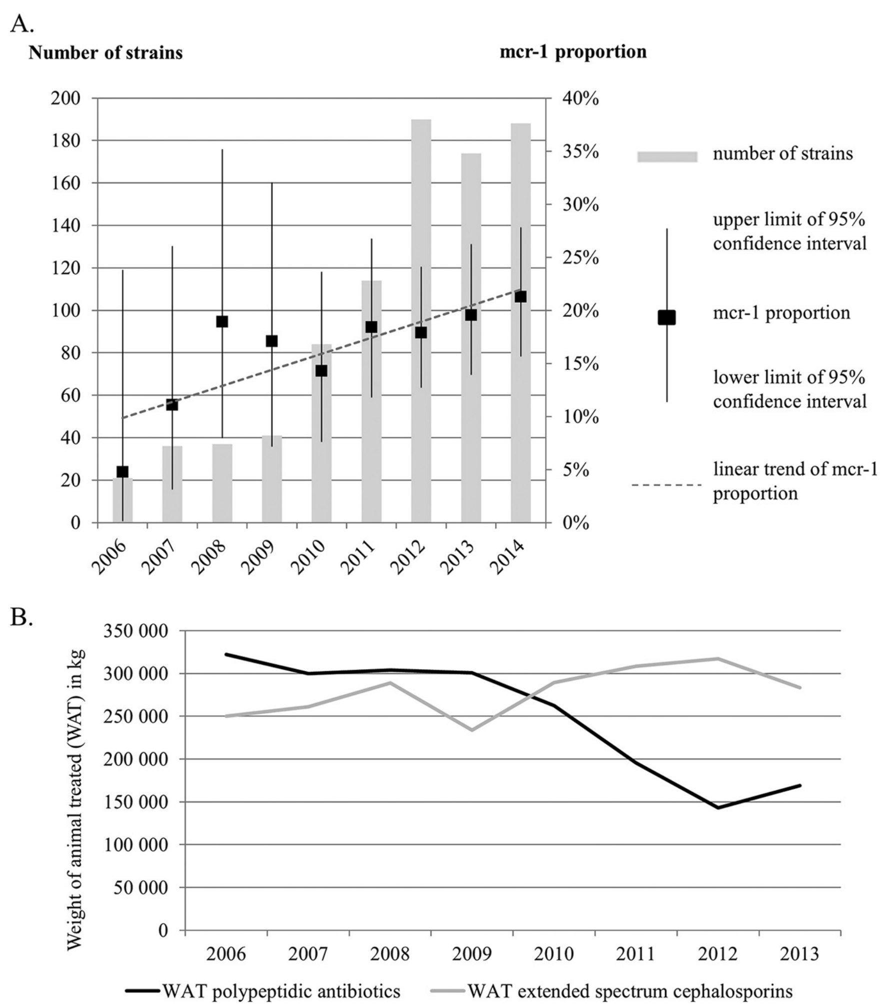

FIG 1 (A) Proportion of *mcr-1*-positive *E. coli* strains among ESBL-producing *E. coli* isolates from French calves and linear trend of the evolution between 2006 and 2014. Upper and lower limits of confidence intervals at 95% of the *mcr-1* proportion are shown. (B) Trends in weights of animals treated (WAT) (bovines) with polypeptidic antibiotics (almost exclusively represented by colistin) or extended-spectrum cephalosporins.

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To date, only one study from China has provided dynamic information on the prevalence of the *mcr-1* gene (4). The earliest *mcr-1*-positive *E. coli* isolate from chickens was identified in the 1980s, and a dramatic rise in *mcr-1* prevalence was highlighted over the past 6 years (from 5.2% in 2009 to 30% in 2014) (4). Here, we provide annual figures of the proportion of *mcr-1* among ESBL-producing *E. coli* isolates from French calves from 2006 to 2014. Using the recently published *mcr-1*-specific primers (1), we retrospectively screened our collection of 885 nonduplicate ESBL-producing *E. coli* isolates collected through the long-term French monitoring program Resapath (www.resapath.anses.fr). All isolates were obtained from different individuals and farms and mostly presented differing pulsed-field gel electrophoresis profiles.

As shown in Fig. 1A, the proportion of *mcr-1*-positive *E. coli* strains among ESBL-producing *E. coli* isolates increased from 4.76% in 2006 to 21.28% in 2014. This corresponded to an increase from 1 *mcr-1*-positive strain recovered in 2006 to 37 in 2014. The proportion of *mcr-1*-positive strains increased until 2014, with an estimated rise of 1.28% per year (chi-square test for linear trend, $P = 0.038$). The number of strains tested from 2006 to 2009 was low due to the still limited number of ESBL-producing *E. coli* strains in bovines. Therefore, the confidence intervals of the proportions of *mcr-1*-positive *E. coli* strains among ESBL-producing *E. coli* isolates are wide, but the results of tests for linear trend, which take such variability into account, are statistically significant. Interestingly enough, the 2006–2007 period, which was seemingly a starting point of this rising trend, came shortly after the first reports of ESBL-producing *E. coli* in bovines in France (5). Taking the data together, the increasing *mcr-1* prevalence among ESBL-producing *E. coli* strains clearly differs from the low *mcr-1* prevalences in non-ESBL-producing *E. coli* strains, which stand at around 1.0% in healthy calves (M. Haenni, unpublished data), 0.5% in pigs, 1.8% in broilers, and 5.9% in turkeys (6). This suggests that the use of extended-spectrum cephalosporins may have simultaneously favored the spread of *mcr-1*. This hypothesis is also supported by previous data demonstrating the colocalization in *E. coli* of *mcr-1* and bla_{ESBL} genes on a unique IncHI2/ST4 plasmid in French calves (3, 7).

In terms of usage, it was not possible to retrospectively trace the individual treatments, either with colistin or cephalosporins, of the *mcr-1*-positive calves, and this is a limitation of the study. However, as reported in the 2013 sales survey of veterinary medicinal products containing antimicrobials in France (https://www.anses.fr/en/content/monitoring-sales-veterinary-antimicrobials), the global exposure of bovines to polypeptidic antibiotics (almost exclusively represented by calves orally treated with colistin) decreased by 52.4% between 2005 and 2013 (Fig. 1B). In contrast, during the same period, the global exposure of bovines to extended-spectrum cephalosporins was constantly high (Fig. 1B) (https://www.anses.fr/en/content/monitoring-sales-veterinary-antimicrobials), with the main ESBL reservoir in bovines being found also in calves, as previously reported (8).

Shen et al. attributed the rise in *mcr-1* prevalence in China to a parallel increased use of colistin in food animals (4). In line with recent data on *mcr-1* in Brazilian poultry not exposed to polymyxins (9), our data strongly indicate driving forces for the spread of *mcr-1* other than the use of colistin only, notably operating through the use of extended-spectrum cephalosporins. This reinforces the idea of the need for global intervention programs on the prudent use of all antibiotics in the Agri-Food sector worldwide, beyond the very recent advice of the European Medicine Agency focused on colistin use in food animals (10).

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We declare that we have no conflicts of interest.

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