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Letter to the Editor

Dramatic decrease in colistin resistance in *Escherichia coli* from a typical pig farm following restriction of colistin use in China

Sir,

Antimicrobial resistance is a serious threat to global public health and has attracted worldwide attention, especially since the discovery of a novel plasmid-mediated colistin resistance gene *mcr-1* [1]. Colistin is a last-resort antibiotic for the treatment of Gram-negative multidrug-resistant infections, particularly carbapenem-resistant infections. The rapid spread of plasmid-mediated colistin resistance could quickly lead to untreatable infections [2–4]. Colistin (polymyxin E) had been used as an antimicrobial growth promoter (AGP) for decades in Chinese livestock, and livestock in China may be the origin of the global spread of *mcr-1*. Importantly, colistin-resistant *Escherichia coli* may spread from livestock to humans through the food chain [5].

Chinese action on colistin use was comparatively swift, absolute and immediate. After our colleagues first discovered plasmid-mediated colistin resistance in November 2015, The Chinese Ministry of Agriculture formally announced a ban on the use of colistin as an AGP in 2016 (Announcement no. 2428). The announcement indicated that existing products could continue to be in circulation until 30 April 2017. Subsequently, China has issued a National Action Plan Against Antimicrobial Resistance in Animals (2017–2020). In the current study, we traced the trend in colistin resistance before and after the ban on colistin use in animals in China.

The studied farm was a semi-automated pig farm that sends 6000 finishing pigs to slaughter every year. Five employees, including one veterinarian, are employed on the farm, which is divided into the nursery area, delivery area, fattening area, office area and manure treatment area.

Data on the use of drugs, including antimicrobials, AGPs and healthcare drugs, on the farm was collected. Commonly used drugs were amoxicillin, doxycycline, florfenicol, tilmicosin and colistin. Detail medication plans and records are presented in Supplementary Tables S1 and S2. Before January 2017, colistin was used as an AGP on this farm, after which it was banned from AGPs. Samples were collected at six time points before and after the ban on colistin as an AGP in order to verify whether it effectively caused a dramatic decrease in colistin resistance in *E. coli* isolated from pigs.

A total of 324 *E. coli* strains were isolated through antibiotic-free medium from 380 rectal swab specimens commonly from healthy pigs including sows, piglets, nursery pigs and fatting pigs (Supplementary Table S3). Susceptibility to 10 antimicrobial agents was examined by the agar dilution method according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI). In addition, susceptibility to colistin was examined following the ISO 20776-1 standard broth microdilution method as recommended by the CLSI/European Committee on Antimicrobial Susceptibility Testing (EUCAST) Joint Polymyxin Breakpoints Working Group. A total of 138/324 (42.6%) of the *E. coli* isolates from pigs were resistant to colistin. PCR amplification of *mcr* genes (*mcr-1, mcr-2* and *mcr-3*) indicated that 44.1% (143/324) of *E. coli* harboured the *mcr-1* gene. No isolates positive for *mcr-2* or *mcr-3* were identified. Interestingly, five *E. coli* isolates harbouring *mcr-1* were susceptible to colistin, which could be due to the fact that *mcr-1* mediates low-level resistance [1]. Colistin-resistant *E. coli* isolates showed a significantly downward trend after colistin was banned as an AGP compared with other antimicrobial agents (Fig. 1; Supplementary Table S4). The *E. coli* isolates exhibited high resistance rates to tetracycline (99.1%), trimethoprim/sulfamethoxazole (96.0%), ampicillin (92.6%) and florfenicol (90.7%) but were susceptible to amikacin and imipenem (Supplementary Table S4).

Escherichia coli isolated from piglets and nursery pigs were more resistant to ciprofloxacin than those from sows and fatting pigs. Meanwhile, resistance to gentamicin was lower in *E. coli* isolated from fattening pig samples. The main reason may be that piglets and nursery pigs are liable to get sick and therefore more drugs are used to treat or prevent diseases. The amount of drug used in the finishing pig stage was relatively less. It was noteworthy that isolates from nursery and fatting pigs were more resistant to colistin than those from other pigs (Supplementary Table S5). Colistin was mainly used in piglets before and after weaning on this farm (Supplementary Table S2). It should be noted that most of the fatting pigs before June 2017 used colistin as an AGP when they were nursery pigs (unpublished data).

Of note, although colistin is still used in China for the treatment of intestinal infections caused by Gram-negative bacteria, such as diarrhoea, the proportion of colistin-resistant *E. coli* isolates declined rapidly within 18 months after colistin being banned as an AGP, from 71.1% to 11.3%. The rate of *mcr-1*-positive isolates also decreased synchronously. These results suggested that the ban was an effective way to reduce the prevalence of colistin-resistant *E. coli* strains through rational use of colistin.

Here we followed colistin resistance in livestock after the ban of colistin for AGPs in China. It is a good example of the One Health stewardship of colistin against *mcr-1* in China. These results indicate that plasmid-mediated colistin resistance has been effectively reduced on Chinese farms. International One Health stewardship of colistin must be national and international with multisectoral collaboration in order to reduce antimicrobial-resistant bacteria.

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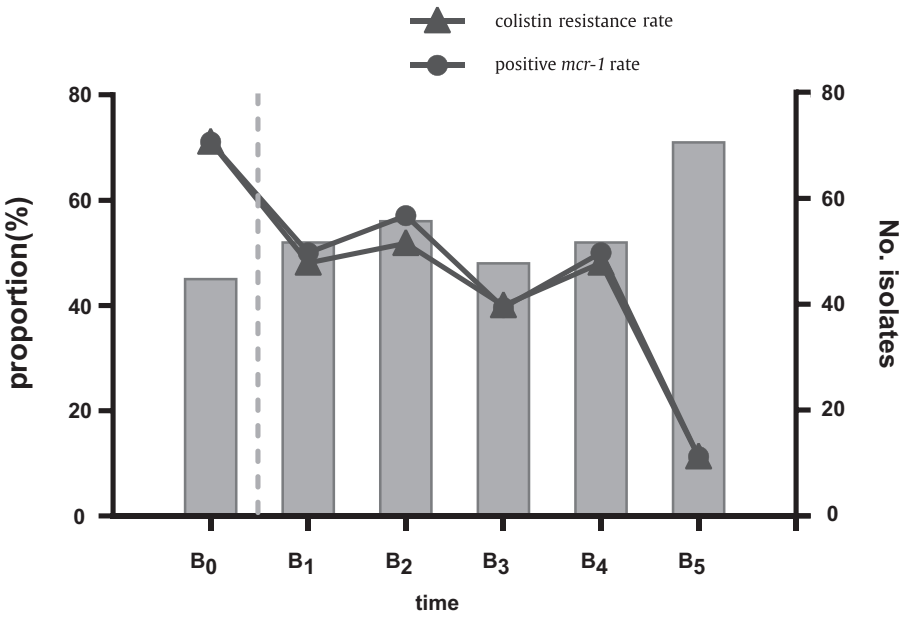

Fig. 1. Proportion of colistin resistance and *mcr-1*-positive rate in *Escherichia coli* from pigs in China.
B_0, 23 December 2016; B_1, 3 March 2017; B_2, 1 April 2017; B_3, 28 April 2017; B_4, 26 May 2017; and B_5, 24 May 2018.

Competing interests

None declared.

Ethical approval

Not required.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijantimicag.2019.03.021.

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