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Early emergence of *mcr-1* in *Escherichia coli* from food-producing animals

Our research group and collaborators reported the transferable colistin resistance mechanism caused by the *mcr-1* gene in Enterobacteriaceae.[1] Shortly after, researchers from different regions of the world showed that the *mcr-1* gene has been disseminated to many countries of at least four continents.[2–5] Colistin has long been used in animals as a therapeutic drug or feed additive. Evidence suggests that the spread of *mcr-1* is from animals to human beings.[1,5] Thus, we did a retrospective study to examine the approximate time of emergence of the *mcr-1* gene in food-producing animals.

Our laboratory has 1611 *Escherichia coli* isolates of chicken origin, derived from farms located in eight provinces of China and distributed from the early 1970s to 2014 (figure). All the isolates were tested for the presence of *mcr-1* by PCR and sequencing. The *mcr-1* gene was detected in 104 isolates and all amplicons showed 100% homology to the recent published sequence.[1] Surprisingly, the *mcr-1* gene was detected in three *E coli* isolates derived from the 1980s, when colisitin first started to be used in food-producing animals in China. However, we did not observe the presence of *mcr-1* for almost two decades after that time. Later, we noticed the sporadic occurrence of *mcr-1* in 2004 and 2006 (figure). The outbreak of *mcr-1*-containing *E coli* of chicken origin started in 2009. The proportion of *mcr-1*-positive *E coli* increased from 5·2% (6/115) in 2009, to 5·9% (4/68) in 2010, 11·9% (15/126) in 2011, 20·9% (24/115) in 2012, 25·4% (29/114) in 2013, and 30·0 % (15/50) in 2014 (figure). The increased colistin resistance corresponds with to the presence of *mcr-1* in *E coli* (figure).The annual use of colistin, ranging from 2470 to 2875 metric tons in food-producing animals in the past 5 years, might contribute to the rapid spread of *mcr-1* in *E coli* of chicken origin in China.

Our results suggest that the emergence of *mcr-1* is much earlier than previously thought. Further analysis of the genetic environment of the *mcr-1*-positive isolates would help us to understand the origin and the dissemination of this gene. We agreed that the worldwide distribution of *mcr-1* might be underestimated. Considering the continuously rising trend, and now the high positive rate of *mcr-1* in bacteria of animal origin, the use of colistin in veterinary practice should be urgently reconsidered.

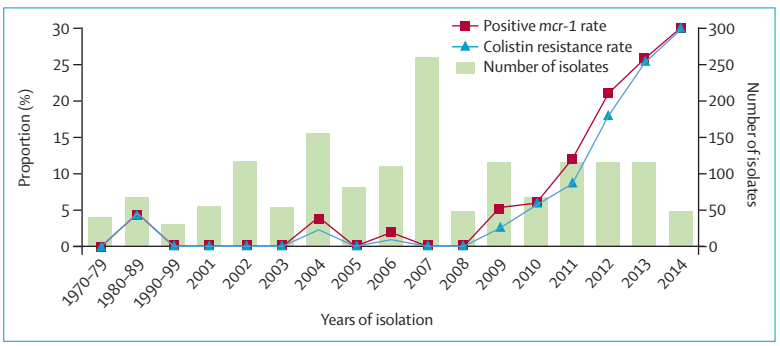

Figure: **Presence of *mcr-1* and colistin resistance in *Escherichia coli* of chicken origin during 1970–2014**
Susceptibility testing of colistin was done by agar dilution and interpreted according to European Committee on Antimicrobial Susceptibility Testing clinical breakpoints (version 6.0). Strains with a minimum inhibitory concentrations >2 mg/L are reported as resistant *E coli*.

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