

Dissemination of the mcr-1 colistin resistance gene

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Plasmid-mediated transferable colistin resistance encoded by the *mcr-1* gene was described in *Escherichia coli* and *Klebsiella pneumoniae* isolates from pigs and chicken at a prevalence of around 20%, and in clinical isolates from human beings at a prevalence of around 1% in China.¹ The prevalence of the *mcr-1* gene in Enterobacteriaceae in other countries and in the community is unknown.

We did a prospective study of acquisition of fecal colonisation and carriage with extended-spectrum β -lactamase (ESBL)-producing Enterobacteriaceae in 2001 Dutch travellers (the COMBAT study),² from November, 2012, to November, 2013. Acquisition was defined as the absence of ESBL-producing Enterobacteriaceae in a fecal swab sample taken immediately before travel and detection of ESBL-producing Enterobacteriaceae in a sample taken within 1–2 weeks after return to the Netherlands. Of 1847 travellers at risk, 633 (34%) acquired ESBL-producing Enterobacteriaceae. Nine of these 633 travellers acquired ESBL-producing *Escherichia coli* with a colistin minimum inhibitory concentration of 4–8 mg/L (EUCAST clinical breakpoint for resistance >2 mg/L) as detected using Vitek-2 and confirmed by E-test. After publication of the report by Yi-Yun Liu and colleagues,¹ these nine isolates were tested by PCR¹ for the presence of the *mcr-1* gene. The gene was detected in six of nine isolates and sequencing of the amplicons showed a 100% homology over the length of the fragments with the published sequence.¹ Three ESBL-producing *E. coli* were *mcr-1* PCR negative, suggesting colistin resistance due to other mechanisms.³ Analysis of ESBL genes by microarray,⁴ PCR, and sequencing showed that the *mcr-1* positive ESBL-producing *E. coli* carried ESBL genes belonging to multiple groups (table).

Of the six travellers who acquired ESBL-producing *E. coli* carrying the *mcr-1* gene, two unrelated travellers visited Peru and Bolivia, two unrelated travellers visited China, one visited Tunisia, and one visited multiple countries in southeast Asia (Thailand, Vietnam, Laos, and Cambodia). The duration of travel ranged between 8 and 40 days (mean 21.3 days). None of the travellers had accessed medical care and none had used antimicrobial drugs during travel, while five had experienced traveller's diarrhoea. Analysis of subsequent fecal samples collected at 1, 3, 6, and 12 months after return to the Netherlands did not show ESBL-producing *E. coli*, suggesting short-term colonisation with colistin resistant ESBL-producing *E. coli* or loss of plasmids carrying ESBL and potentially *mcr-1* genes.

Colistin is used as an ultimate refuge antimicrobial drug in the treatment of infections caused by multidrug resistant Gram-negative microorganisms.⁵ Our data suggest a worrisome spread of the *mcr-1* gene in *E. coli* in the community across at least three continents. The diversity of ESBL genes present in *mcr-1* positive isolates suggests that the *mcr-1* gene might be carried on multiple plasmid backbones.

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Table. Characteristics of travellers and acquired fecal *Escherichia coli* isolates carrying the *mcr-1* gene

	Traveller with isolate 1	Traveller with isolate 2	Traveller with isolate 3	Traveller with isolate 4	Traveller with isolate 5	Traveller with isolate 6
Travel destination	Thailand, Vietnam, Cambodia, Laos	Tunisia	Peru, Bolivia, Colombia	China	China	Peru, Bolivia
Travel duration (days)	21	8	40	14	23	22
Age (years)	56	55	25	54	62	26
Sex	Female	Female	Female	Male	Female	Male
ESBL gene (ESBL group)	CTX-M-14 (CTX-M group 9)	CTX-M-1 (CTX-M group 1)	CTX-M-15 (CTX-M group 1)	CTX-M-65 (CTX-M group 9)	CTX-M-55 (CTX-M group 1)	CTX-M-55 (CTX-M group 1)
Minimum inhibitory concentration of antimicrobial drug (mg/L)*						
Amoxicillin-clavulanic acid	16	8	>16	16	8	4
Piperacillin-tazobactam	8	≤4	8	≤4	≤4	≤4
Cefotaxime	16	8	32	16	>32	>32
Cefoxitin	16	≤4	8	≤4	≤4	≤4
Ceftazidime	≤1	≤1	16	≤1	4	4
Cefepime	2	2	2	≤1	2	2
Imipenem	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25
Meropenem	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25
Gentamicin	>8	≤1	>8	≤1	>8	≤1
Tobramycin	8	≤1	>8	8	8	≤1
Nitrofurantoin	256	≤16	128	32	64	≤16
Co-trimoxazole	>8	>8	>8	≤1	>8	>8
Norfloxacin	>8	8	>8	2	>8	>8
Ciprofloxacin	>2	>2	>2	1	>2	>2
Colistin	4	4	4	4	4	8

ESBL=extended-spectrum β -lactamase. *Determined using Vitek-2, except for colistin for which E-test results are provided.

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