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SHORT REPORT
Antimicrobial resistance in *Campylobacter jejuni* from humans and broilers in Norway

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SUMMARY

In this study comprising isolates from 2001 to 2003, resistance was considerably more widespread among *Campylobacter jejuni* from humans infected abroad than infected within Norway. The discrepancy was particularly notable for fluoroquinolone resistance (67·4% *vs.* 6·5%). This is probably a reflection of a low resistance prevalence in Norwegian broiler isolates (1·2% fluoroquinolone resistant).

Fluoroquinolone-resistant *Campylobacter* spp. is recognized as an emerging public health problem [1]. Fluoroquinolone resistance in *Campylobacter* spp. is increasing in many countries throughout the world [2–5]. In several countries, an association between the usage of fluoroquinolones in food animals and the occurrence of fluoroquinolone-resistant *Campylobacter* from humans has been documented [2]. Fluoroquinolones are commonly used in poultry medicine both for therapeutic and prophylactic purposes. Poultry meat is considered as the most important risk factor for campylobacteriosis in humans [4, 6, 7]. Thus, an extended use of fluoroquinolones in poultry production thereby increases the risk of transmission of fluoroquinolone-resistant *Campylobacter* spp. to humans. Antimicrobial agents are normally not indicated for treatment of campylobacteriosis in humans. However, severe cases may require treatment. An increased resistance to fluoroquinolones reduces the possibilities to treat severe infections in humans, which can have fatal consequences [1, 8].

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Norway has a long tradition for a restrictive antimicrobial policy in animal husbandry, and fluoroquinolones were never licensed for use in poultry. In 2000, the Norwegian government established an action plan against antimicrobial resistance, which resulted in the establishment of monitoring programmes for antimicrobial-resistant bacteria from both humans (NORM) and animals and food (NORM-VET). There is close cooperation between these programmes and a joint report (NORM/NORM-VET) is published annually [9] to describe the current situation and to evaluate trends. Monitoring of antimicrobial resistance in zoonotic bacteria such as *Salmonella* spp. and *Campylobacter* spp. is included in both programmes.

Campylobacteriosis is currently the most frequently reported cause of bacterial gastroenteritis in Norway. Most cases are sporadic and close to half of the reported cases acquire the infection in Norway. Of the 2192 cases of human campylobacteriosis recorded in Norway in 2002 (incidence rate 48·5/100 000), 52% were reported as acquired abroad [10]. A case-control study conducted in Norway during 1999–2000 identified consumption of untreated drinking water, consumption of poultry meat purchased raw, consumption of barbecued meat, and professional

contact with animals as significant risk factors in regard to campylobacteriosis [11]. To reduce the human exposure to *Campylobacter* through Norwegian broiler meat products, an action plan against *Campylobacter* in Norwegian broilers was implemented in the spring of 2001 [9]. The present study assesses and compares the prevalence of resistance in *C. jejuni* isolates from imported and indigenous human cases and from Norwegian broilers using data from NORM/NORM-VET for the period 2001–2003.

The isolates of *C. jejuni* in broilers originate from the Norwegian action plan against *Campylobacter* in Norwegian broilers. All broiler flocks slaughtered before 50 days of age are tested for the presence of *Campylobacter* spp. and 100 samples of broiler meat products from retail level are tested monthly. Annually, one isolate per positive farm as well as one isolate from each batch of positive broiler meat products are submitted for susceptibility testing in NORM-VET. In the period 2001–2003, a total of 413 broiler isolates, 343 from cloacal samples and 70 from broiler meat products, were tested for antimicrobial susceptibility. The human isolates included were obtained from clinical specimens as part of the NORM programme. Each of the five regional NORM laboratories submit isolates from the first five patients with campylobacteriosis for susceptibility testing to the National Reference Laboratory for Enteropathogenic Bacteria at the Norwegian Institute of Public Health each month. In the present study, only isolates of *C. jejuni* where the source of infection was known (indigenous or abroad) were included. This resulted in 567 human isolates, 184 from patients infected in Norway and 383 from patients infected abroad. This skewed sample, twice as many isolates from imported cases from as indigenous cases, can be explained by the sampling strategy since indigenous campylobacteriosis is subject to seasonal fluctuation with an increased number of cases during the summer season and only few infections during the rest of the year [12].

Broiler isolates were isolated and identified according to the Nordic Committee on Food Analyses (NMKL) method number 119 with minor modifications, and human isolates according to conventional methods described in standard reference literature. Broiler isolates were tested at the National Veterinary Institute. Minimum inhibitory concentration (MIC) values for ampicillin, erythromycin, gentamicin, nalidixic acid and enrofloxacin were obtained using the VetMIC^{TM} panels produced at Department of Antibiotics, National Veterinary Institute, Sweden. This is a broth dilution method which is based upon standard methods described by NCCLS and adapted for *Campylobacter* spp. MIC was recorded as the lowest concentration of the antimicrobial that inhibits bacterial growth. Human isolates were tested for susceptibility to doxycycline, erythromycin, gentamicin, nalidixic acid and enrofloxacin using *E* tests (AB Biodisk, Solna, Sweden). At the present stage, there are no internationally accepted criteria for interpretation of susceptibility in *Campylobacter* spp. and subsequently no break-points. The isolates were classified as resistant or susceptible applying microbiological cut-off values. Microbiological cut-off values are determined on the basis of the distribution of MICs for each antimicrobial and bacterial species. The population that clearly departs from the normal genetically unchanged population ('wild-type') are defined as resistant ('non-wild-type').

Data were analysed using a program developed by the World Health Organization for analysis of antimicrobial resistance data [13]. The results revealed that the prevalence of resistance among *C. jejuni* isolates from Norwegian broilers is low (Table). There was no significant difference in resistance prevalences between the isolates from broiler meat products and cloacal samples. A total of 91·2% of the isolates from broilers were susceptible to all antimicrobials included in the test panel. None of the isolates were resistant to more than two antimicrobials, and only 1·2% of were fluoroquinolone resistant. Compared to the prevalence of resistance among poultry in other countries this figure 1 is low [14]. The low prevalence of fluoroquinolone resistance in isolates from broilers most probably reflects the restrictive use of antimicrobials in Norwegian broiler production. Antimicrobials (except coccidiostats) are rarely used, and only for therapeutic purposes. If used, amoxicillin and tetracycline are the drugs of choice. No quinolone preparations are licensed for use in broilers in Norway. However, several fluoroquinolones are approved for use in broilers in the EU and may, therefore, also be used in broiler production in Norway if specifically applied for. The resistance situation among *Campylobacter* spp. from Norwegian broilers probably reflects the resistance situation among *Campylobacter* spp. in the Norwegian environment [10, 11] as broilers typically are infected from environmental sources, including untreated surface water.

The data show that resistance was significantly more prevalent among the *C. jejuni* isolates derived

Table. *Percentage of isolates of* Campylobacter jejuni *from various sources and years classified as resistant to various antimicrobials*

Substance	Cut-off value* (mg/l)	Norwegian broilers			Humans infected in Norway			Humans infected abroad		
		2001 ($n=113$)	2002 ($n=161$)	2003 ($n=139$)	2001 ($n=84$)	2002 ($n=37$)	2003 ($n=63$)	2001 ($n=129$)	2002 ($n=110$)	2003 ($n=144$)
Doxycycline†	>2	0·9	0·0	2·2	9·5	2·7	9·5	43·4	54·5	62·5
Erythromycin	>2	0·0	1·0	0·0	4·8	2·7	4·8	3·1	6·4	5·6
Gentamicin	>4	0·0	0·0	0·0	0·0	0·0	0·0	0·8	1·8	3·5
Nalidixic acid	>16	2·7	1·9	1·4	8·3	8·1	11·1	59·7	71·8	72·9
Ciprofloxacin‡	>2	2·7	0·6	1·4	7·1	2·7	7·9	59·7	71·8	70·8

* Values above the cut-off value indicate resistance.
† Oxytetracycline for broilers.
‡ Enrofloxacin for broilers in 2002 and 2003.

from patients infected abroad (23·0% susceptible to all antimicrobials included) than patients infected in Norway (85·3% susceptible to all antimicrobials included). These discrepancies are explained by the widespread prevalence among isolates acquired abroad of resistance to ciprofloxacin/nalidixic acid (67·4/68·1% *vs.* 6·5/9·2%) and to tetracycline (53·8% *vs.* 8·2%). The resistance prevalences for domestically acquired human cases correlate quite well with the data for Norwegian broilers, although resistance to quinolones, particularly nalidixic acid, was more prevalent among the human isolates. The discrepancy between broiler isolates and indigenous human isolates might be explained by sporadic cases of secondary human infection with imported *Campylobacter* strains and infection with *Campylobacter* spp. from imported poultry. The official import of chicken is relatively limited, but there is some import of other types of poultry products such as ducks or pheasants from the EU (data provided from The Norwegian Food Safety Authority).

The resistance prevalences were stable and low throughout the study period both for isolates from humans infected in Norway as well as for isolates from broilers, whereas the resistance prevalences in isolates from humans infected abroad increased slightly. This is illustrated by the trend for fluoroquinolone resistance during the same period (Fig.). In a study from Northern Ireland, isolates from human cases showed a greater similarity with indigenous broiler isolates than with isolates from imported chicken [14]. However, the source of infection for the human cases was not presented.

In many countries, *Campylobacter* spp. has become the most frequently reported cause of bacterial

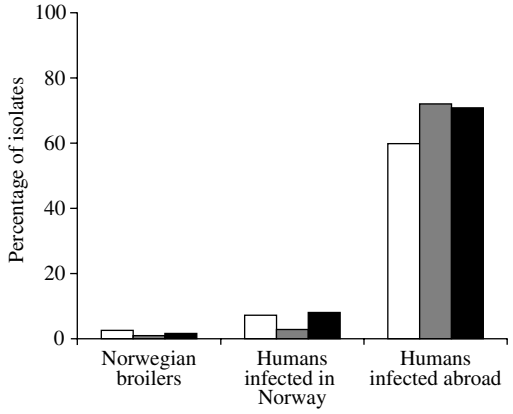

Fig. Proportion (%) of isolates of *Campylobacter jejuni* from various sources and years resistant to fluoroquinolones. □, 2001; ▩, 2002; ■, 2003.

gastrointestinal illness [6, 7, 15]. Some countries report that many cases of campylobacteriosis are associated with foreign travel [15]. The humans infected abroad in this study had to a large extent been visiting Southern European countries and Asia. Recent studies have shown that the prevalence of fluoroquinolone resistance among isolates of *C. jejuni* from humans infected when travelling to Southern European countries is high [2]. The prevalence of fluoroquinolone resistance in *Campylobacter* is also high in Thailand [16, 17].

The present study documents that a limited use of fluoroquinolones in food animal production within a country is associated with a low prevalence of fluoroquinolone resistance in indigenous human *C. jejuni* isolates. Thus, the restricted use of fluoroquinolones in food-producing animals is recommended in order

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to keep such antimicrobials efficient for the treatment of severe cases of campylobacteriosis in humans.

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