Campylobacter spp. in Human, Chickens, Pigs and Their Antimicrobial Resistance

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ABSTRACT. Campylobacter spp. have been identified as etiologic agents in outbreaks and sporadic cases of gastroenteritis in developed countries. In developing countries, most reported Campylobacter infections are in children. Previously reported prevalences of Campylobacter spp. in children in Southeast Asia range from 2.9% to 15%. The frequency and pattern of occurrence of Campylobacter spp. differ between developed and developing countries, especially in the number of cases reported in adults and the presence of any seasonal patterns in occurrence. Although the severity of Campylobacter infection in adults was different between developed and developing countries, the clinical symptoms of infection in adults resulting from infection in developing countries was similar to those in developed countries. Many different animal species maintain Campylobacter spp. with no clinical signs. There do not appear to be significantly different colonization rates of Campylobacter in food animals between developed and developing countries. The role of C. jejuni as a primary pathogen in farm animals is uncertain. C. jejuni can be found in feces of diarrheic and healthy calves and piglets. Campylobacter with resistance to antimicrobial agents have been reported in both developed and developing countries, and the situation seems to deteriorate more rapidly in developing countries, where there is widespread and uncontrolled use of antibiotics resistance was observed at high levels in food animals in both developed and developing countries. Studies suggested an association between antimicrobial use in food animals and the development of resistance in human isolates in developed countries.

KEY WORDS: antimicrobial resistance, Campylobacter spp., food animal, human.

PREVALENCE AND INCIDENCE OF CAMPYLOBACTER SPP.

Campylobacter in humans: Of all Campylobacter spp., C. jejuni is the species most frequently isolated in cases of human infection [108]. In developing countries, most reported Campylobacter infections are in children. Peaks in Campylobacter infection rates have been reported in children less than one year of age [33], and children less than 5 years old in Southeast Asia [72]. Previously reported prevalences of Campylobacter spp. in children in Southeast Asia range from 2.9% to 15% [79, 87, 109, 115]. In children in Thailand, Campylobacter spp. and Salmonella are common causes of diarrhea [87, 115], and co-infection with Campylobacter and E. coli, Salmonella or Shigella is common [82]. This exposure to Campylobacter spp. early in life, and reports of levels of Campylobacter-specific antibodies increasing with age [109], may result in less severe clinical symptoms in adults, which makes detection and reporting of cases rare. Since Campylobacter is commonly isolated with other enteric pathogenic bacteria in developing countries, reports of Campylobacter cases may be largely underestimated. There have been no reports of seasonal patterns in the occurrence of human Campylobacter infection in developing countries.

In developed countries, Campylobacter spp. have been identified as etiologic agents in outbreaks and sporadic cases of gastroenteritis [63]. The reported incidence of Campylobacter infection in U.S. was 20.1 cases per 100,000 in 2000 [3], and from 60 to 90 cases per 100,000 in northern Europe [33]. When taking under-reporting into consider-
ation, the true incidence rate is estimated to be 1,000–2,300 cases per 100,000 in Europe [33]. *Campylobacter* affects all age groups in developed countries, with one peak in children less than 4 years old, and in young adults from age 15 to 44 [33]. The incidence of *Campylobacter* in developed countries also showed seasonal patterns, with peaks during the warmer months of the year [33], which may be a result of increasing survival of *Campylobacter* in the environment in warm weather.

The frequency and pattern of occurrence of *Campylobacter* spp. differ between developed and developing countries, especially in the number of cases reported in adults and the presence of any seasonal patterns in occurrence. It should be noted that there is limited information on the incidence of *Campylobacter* infections from developing countries. Most developed countries in Europe and North America have surveillance programs for *Campylobacter* and other foodborne pathogens, such as FoodNet in the U.S. [3]. Establishment of similar surveillance programs would be beneficial in developing countries.

*Campylobacter* in food animals: Many different animal species maintain *Campylobacter* spp. with no clinical signs [100]. The most important species of *Campylobacter* in veterinary medicine are *C. fetus subsp. fetus* and *venerealis* [35]. Of *Campylobacter* spp. that are pathogenic in food animals, *C. fetus* can cause reproductive disorders in cattle and sheep [85], and *C. hyointestinalis* and *C. mucosalis* have been associated with enteritis in pigs and cattle [35].

There is limited information on *Campylobacter* spp. in food animals or foods of animal origin from developing countries. In Thailand, *Campylobacter* spp. was isolated from 12% of various food samples including pork, chicken and vegetables in Bangkok [87], 40% of poultry ceca in India [22], and 68–100% of poultry samples from retail markets in Taiwan [95]. The low prevalence of *Campylobacter* reported in Thailand was probably due to the fact that various types of meats and vegetables were included in the study, while the other two studies examined only poultry products. *Campylobacter* was isolated more in samples from fresh markets than in supermarkets in Taipei, Taiwan [95]. In Kenya, *Campylobacter* was found on 77% of poultry products at the market [74], while the prevalence of *Campylobacter* at the poultry farm was found to be 64–100% [58, 96]. By species, *C. jejuni* was isolated more frequently than *C. coli* in live chickens in Africa [96].

There have been many studies on *Campylobacter* spp. in food animals or foods of animal origin from developing countries. The low prevalence of *Campylobacter* reported in Thailand was probably due to the fact that various types of meats and vegetables were included in the study, while the other two studies examined only poultry products. *Campylobacter* was isolated more in samples from fresh markets than in supermarkets in Taipei, Taiwan [95]. In Kenya, *Campylobacter* was found on 77% of poultry products at the market [74], while the prevalence of *Campylobacter* at the poultry farm was found to be 64–100% [58, 96]. By species, *C. jejuni* was isolated more frequently than *C. coli* in live chickens in Africa [96].

There have been many studies on *Campylobacter* spp. in Table 1. Prevalence of antimicrobial resistance in *Campylobacter* spp. from humans

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Method</th>
<th>CIP/FQ (%)</th>
<th>ERY/M (%)</th>
<th>CHL (%)</th>
<th>GEN (%)</th>
<th>TET (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Netherland</td>
<td>1994–1997</td>
<td>Agar diffusion</td>
<td>28.8</td>
<td>0.3</td>
<td>16.1</td>
<td></td>
<td></td>
<td>(107)</td>
</tr>
<tr>
<td>Spain</td>
<td>1995–1998</td>
<td>Disk diffusion</td>
<td>81</td>
<td>5</td>
<td>1</td>
<td>72</td>
<td></td>
<td>(84)</td>
</tr>
<tr>
<td>Spain</td>
<td>1979–1996</td>
<td>Disk diffusion</td>
<td>54</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td></td>
<td>(81)</td>
</tr>
<tr>
<td>Spain</td>
<td>1997–1998</td>
<td>Disk diffusion</td>
<td>75</td>
<td>3.2</td>
<td>0.4</td>
<td></td>
<td></td>
<td>(91)</td>
</tr>
<tr>
<td>Spain</td>
<td>1992–1993</td>
<td>Broth dilution or disk diffusion</td>
<td>30.4</td>
<td>0</td>
<td>44.3</td>
<td>(117)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>1999</td>
<td>NA</td>
<td>81–90</td>
<td>4–90</td>
<td>1–16</td>
<td>70–97</td>
<td></td>
<td>(67)</td>
</tr>
<tr>
<td>Ireland</td>
<td>1996–1998</td>
<td>Agar dilution</td>
<td>17</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>14</td>
<td>(65)</td>
</tr>
<tr>
<td>UK</td>
<td>1997</td>
<td>Agar dilution</td>
<td>11.7</td>
<td>1.7</td>
<td>5.4</td>
<td>0.1</td>
<td>29.6</td>
<td>(110)</td>
</tr>
<tr>
<td>Canada</td>
<td>1995–1997</td>
<td>Agar dilution</td>
<td>12.7–13.9</td>
<td>0</td>
<td>55.7</td>
<td></td>
<td></td>
<td>(37)</td>
</tr>
<tr>
<td>US</td>
<td>1998</td>
<td>E-test</td>
<td>10.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(97)</td>
</tr>
<tr>
<td>Kenya</td>
<td>1997–1998</td>
<td>E-test</td>
<td>24</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td></td>
<td>(94)</td>
</tr>
<tr>
<td>Nigeria</td>
<td>1998</td>
<td>Disk diffusion</td>
<td>–</td>
<td>16.7</td>
<td>33.3</td>
<td>0</td>
<td>33.3</td>
<td>(98)</td>
</tr>
<tr>
<td>India</td>
<td>1994</td>
<td>Disk diffusion</td>
<td>4.4</td>
<td>2.2</td>
<td></td>
<td>6.7</td>
<td></td>
<td>(83)</td>
</tr>
<tr>
<td>India</td>
<td>1996</td>
<td>Disk diffusion</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(18)</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1998</td>
<td>E-test</td>
<td>52–85</td>
<td>10–50</td>
<td>1–15</td>
<td>85–95</td>
<td></td>
<td>(64)</td>
</tr>
<tr>
<td>Taiwan</td>
<td>1994</td>
<td>Broth dilution</td>
<td>91</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(62)</td>
</tr>
<tr>
<td>Thailand</td>
<td>1995</td>
<td>Agar dilution</td>
<td>84</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td>(46)</td>
</tr>
<tr>
<td>Thailand</td>
<td>1994</td>
<td>Broth/agar dilution</td>
<td>69–79</td>
<td>0–31</td>
<td></td>
<td></td>
<td></td>
<td>(69)</td>
</tr>
<tr>
<td>Thailand</td>
<td>1995–1999</td>
<td>Agar dilution</td>
<td>73–77</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td>(49)</td>
</tr>
</tbody>
</table>

a) AMP-Ampicillin, CHL-Chloramphenicol, CIP/FQ-Ciprofloxacin or other fluoroquinolones, ERY/M-erythromycin or other macrolides, GEN-Gentamycin, TET - Tetracycline.
b) NA - Not available.
food animals, and foods of animal origin, in developed countries. In the past, research in cattle was limited, but has been increasing as outbreaks of human campylobacteriosis have been traced to foods of cattle origin [56]. The prevalence of Campylobacter was found to be 15% in beef calves [13], 37.7% in dairy herds [125], and 89.4% on beef cattle at slaughter [99]. The prevalence in beef cattle at slaughter peaked in the summer [99], which coincides with the seasonal peak of human Campylobacter infections [33].

Extensive research has been conducted on Campylobacter in pigs. Pigs carry higher proportions of C. coli than C. jejuni, whether they have enteritis or not [44, 101]. In the U.S., Campylobacter spp. was isolated from 76% of gilts, 100% of pregnant sows, 57.8% of newborn piglets, and 100% of weaning pigs [131]. Fifty percent of piglets were infected with the same serotype as their sows by seven days of age in the Netherlands [123]. The average number of Campylobacter colonizing the gut decreased toward the end of the rearing period [124]. A study in Belgium reported the prevalence of Campylobacter spp. on pig carcasses at slaughterhouses to be 2% [60]), and Campylobacter was found in 1.3% of samples from pork from a retail market in the U.S. [24].

There is a large body of research on Campylobacter in poultry. The reported prevalence of Campylobacter in broiler flocks ranged between 35–57% in Europe [7, 77, 88, 113]. The prevalence of Campylobacter colonization was higher in organic farms (100%) when compared to extensive indoor system (49.2%) or conventional farms (36.7%) [45]. A study at Swedish slaughterhouses showed a 27% flock prevalence, which increased with bird age and flock size [9]. The prevalence of infection in chickens has been shown to increase linearly with the age of the birds [39]. At broiler farms, day-old chickens can be colonized with Campylobacter [104], with rates of 100% colonization by 3–4 weeks [54]. Up to 40% of the flocks in the U.K. were found to be colonized with Campylobacter spp. by four weeks, and up to 90% by seven weeks [30]. After transportation, counts of Campylobacter in chickens increased [105, 126], although there was no significant increase in prevalence [126]. The reported prevalence of Campylobacter spp. in retail chickens varied from 28.5–100% (Table 1). Lower levels of contamination were found in chicken pieces without skin [11, 111], but removal of skin did not change the prevalence of Campylobacter spp. found on chicken carcasses [11]. Frozen chickens had lower bacteria counts than fresh chickens [25, 102]. The highest levels of recovery usually occurred during the warmer months (Jun-Oct) [52, 103, 122, 128], and more C. jejuni (43–86%) than C. coli (11–39%) were recovered [7, 52, 95, 122]. The seasonality of Campylobacter found in poultry products at the market coincides with the peak of incidence of Campylobacter in humans, which demonstrates the importance of chicken as a source of Campylobacter infection for humans in developed countries.

There do not appear to be significantly different colonization rates of Campylobacter in food animals between developed and developing countries. However, since the housing and management of food animals differs between developing and developed countries, the rate of colonization in developing countries, which are mostly located near the equator, should be higher than those in developed countries. This speculation should be confirmed by field observation.

EXPOSURE AND TRANSMISSION OF CAMPYLOBACTER

In humans: In developed countries, Campylobacter spp. are associated with sporadic cases and outbreaks of infection. Outbreaks of Campylobacter are usually associated with raw milk [5, 56], whereas sporadic illnesses are often associated with consumption of chickens [23, 26, 57, 92, 106]. Other reported risk factors for Campylobacter spp. infection included handling of chickens or preparing chickens [47], contact with cats [23], consuming antibiotics before illness [26], eating pork [106], barbequing [57, 106], living or working on farms [106], working in slaughterhouses [15], exposure to animals with diarrhea [90], and travel abroad [92]. Traveling to developing countries was associated with Campylobacter with resistance to antimicrobial drugs [38]. Foreigners residing in countries where Campylobacter is prevalent also have high risks of infection [36]. In addition to traditional outbreak investigational techniques, various molecular identification techniques are now available for epidemiological typing of Campylobacter spp. [121]. These techniques have been used to trace outbreaks back to broiler or dairy farm and food handlers [56, 73, 76]. A recent molecular study also suggested a link between the Campylobacter spp. found in farm environments and those causing diseases in local communities [31].

In developing countries, chicken products were found to be an important source of Campylobacter in humans in both Asia [87] and Africa [96], and chickens were also found to be a potential source of Campylobacter in farm workers [96]. Although higher prevalences of Campylobacter on poultry products were reported in developing countries, the local customs of eating well-cooked meat and poultry may reduce the risk of infection, when compared to developed countries, where the consumption of undercooked meat is more common.

In food animals: There have been several studies on the epidemiology of Campylobacter in poultry in developed countries. Sources of infection were more likely to be horizontal contamination from the environment [51, 112] or water system [58, 75], rather than from direct flock-to-flock transmission [77]. Although prevalence of Campylobacter spp. is high (67%) in breeder flocks, serotyping of the organism did not support the hypothesis of vertical transmission [19, 50, 78]. Additional risk factors for Campylobacter colonization include housing with no air circulation, more than two workers working in the same poultry house, more than three poultry houses, acidified drinking water, the presence of insects or litter in worker changing rooms [88], batch depletion of the flock (not all in/all out) [41], and the
presence of other animals (pig, cattle, sheep) on the farm [113]. Wild birds have been found with *Campylobacter* spp., with prevalences up to 50% in birds near chicken houses [21] and 40% in dead wild birds found in broiler houses [55], and has been found in wild birds not associated with poultry facilities [17].

A longitudinal study that followed the same flock of chickens from farm to processing plant and market found the highest prevalence of *Campylobacter* at the processing plant (32.5%), especially on carcasses after chilling (52%), suggesting that contamination of carcasses most likely occurred at the processing plant [55]. Counts of *Campylobacter* were highest in caeca and colon of birds at slaughter [10], and the number of *Campylobacter* declined after scalding, but increased during picking and evisceration [10, 127], which suggested that the caecum and colon are the most probable sources of contamination in the slaughterhouses, which has been confirmed by molecular typing [71]. After processing contaminated flocks, *Campylobacter* spp. can be found on all slaughter equipment [8, 71], making cross-contamination between different flocks at slaughter possible [9, 127]. Other risk factors for the isolation of *Campylobacter* at slaughterhouses include short empty period between flocks, the lack of strict barriers such as changing boots between houses, wet litter or bedding, the presence of other poultry on the farm, staff handling other poultry on the farm, dividing the flock before slaughter, slaughterhouse staff loading birds from several different farms, and the presence of mice [9].

In developed countries, the permanent colonization of *Campylobacter* spp. in pigs is probably related to constant exposure to other colonized pigs, since experiments have shown that pigs reared off-sow had less prevalence of *Campylobacter* spp. [43].

Very little research has been done on the epidemiology of *Campylobacter* in food animals in developing countries. In one study, *Campylobacter* were isolated frequently from surface water and foot baths, which may be a potential source of *Campylobacter* on the farm [58]. Because of the differences in the rearing systems and the slaughtering processes, risk factors for *Campylobacter* contamination in food animals in developing countries may be significantly different from those in developed countries. Some factors on the farm, such as biosecurity measures and the presence of wild birds, may be similar between developed and developing countries. In many developing countries, the majority of the slaughterhouses that process meat for local consumption commonly have lower standards of hygiene, which may also result in higher prevalence of *Campylobacter* on their products. However, meat in local markets in developing countries usually does not remain in the market more than one day after slaughter, so bacteria do not have the opportunities to multiply as much as in developed countries, especially for slow-growing organism like *Campylobacter*. Epidemiological studies of *Campylobacter* in food animals under different rearing systems in developing countries should be conducted to clarify the risk factors associated with the presence of *Campylobacter* in food animal and food animal products.

**CLINICAL EXPRESSION OF CAMPYLOBACTER INFECTION IN HUMANS AND ANIMALS**

*In humans:* *Campylobacter jejuni* and *Campylobacter coli* have been recognized as important etiologic agents of gastrointestinal infection since the 1970s [70]. In developed countries, typical clinical feature of *Campylobacter* spp. infection include acute, self-limiting gastroenteritis, characterized by diarrhea, fever and abdominal cramps, with a 24 to 72 hr incubation period [4]. Diarrhea is initially watery, which may last more than two weeks in travellers’s diarrhea [34], or may become bloody as a result of diffuse inflammatory colitis and enteritis [12]. An important post-infection sequel of *Campylobacter jejuni* infection is Guillain-Barre syndrome (GBS), an acute demyelinating disease of the peripheral nervous system that results in a flaccid paralysis [3, 5].

In developing countries, the clinical picture of *Campylobacter* infection is characterized by a milder form of gastroenteritis [72], and symptomatic infection is uncommon in adults [12]. Severe diarrhea requiring hospitalization is usually the result of co-infection with other virulent bacteria or viruses [115]. The severity of clinical symptoms and fecal excretion in children was inversely related to age [109]. Although the severity of *Campylobacter* infection in adults was different between developed and developing countries, the clinical symptoms of infection in adults resulting from infection in developing countries was similar to those in developed countries [72].

*In food animals:* In cattle, *C. fetus subsp. venerealis* is the most frequently encountered *Campylobacter* in bovine abortion or infertility, while *C. fetus subsp. fetus* causes sporadic abortion in cattle and enzootic abortion in sheep [35]. Bovine venereal campylobacteriosis is a chronic infection of the female genital tract, characterized by mild endometritis and transient infertility [35]. Infection in bulls is accompanied by neither histological changes nor modifications in the characteristic of semen [35]. *C. fetus subsp. fetus* infection in ewes resulting in abortion commonly in the last six week of gestation [35].

The role of *C. jejuni* as a primary pathogen in farm animals is uncertain. *C. jejuni* can be found in feces of diarrheic and healthy calves [86] and piglets [101], but both *C. jejuni* and *C. coli* can cause a mild self-limiting enteritis and bacteremia when inoculated orally to newborn calves [86]. In cows, there has been a single report of mastitis caused by *C. jejuni* [68].

**ANTIMICROBIAL RESISTANCE IN CAMPYLOBACTER**

Antimicrobial resistance has become a major public health concern in both developed and developing countries in recent years [49, 129]. Resistance to antimicrobial agents
Mechanism of resistance to antimicrobial agents in *Campylobacter* spp: Resistance to aminoglycosides is normally mediated by enzymes that modify the drugs [1]. Mechanism of resistance to chloramphenicol depends on the ability to produce enzymes that block binding of the drug to the ribosome, which is the target site of action [1]. In *C. jejuni* and *C. coli*, resistance to tetracycline was found to be located on a transmissible plasmid encoding ribosomal protection gene [1]. Macrolide resistance in *C. jejuni* is chromosomally mediated through mutation of the 23S RNA gene [29]. Mechanism of fluoroquinolone resistance in *C. jejuni* was also found to be chromosomally mediated through mutation of the gyrA gene [119] and parC gene [40]. Resistance to azithromycin was found to be correlated with resistance to quinolones [49]. Resistance to more than one group of antimicrobial agents in *C. jejuni* may be the result of efflux mechanism [16].

Antimicrobial susceptibility testing: There are several methods currently being used for antimicrobial susceptibility testing of *Campylobacter*. Agar dilution, commonly used in Europe, gives qualitative results but requires a high level of standardization for comparison [14]. Broth dilution provides quantitative data and is highly reproducible, but is more expensive than agar dilution [14]. The E-test (AB Biodisk, Culver city, CA) was found to give results comparable to the agar dilution test [48], but is also expensive. Various genetic methods for assessing antimicrobial resistance are also available [20]. Comparisons of the results of antimicrobial susceptibility testing should be made with care, since different methods from the same laboratory or similar methods in different laboratories may yield different results [14]. For surveillance, quantitative data may be more desirable, since it can detect trends that indicate reduced susceptibility, and interventions can be implemented before high levels of resistance have developed [118].

Antimicrobial resistance in human isolates. Increasing prevalence of quinolone-resistant *Campylobacter* spp. has been observed in the Netherlands since the early 1990’s [27, 107], where resistance to fluoroquinolones increased from 11% in 1994 to 29% in 1997 [107]. Quinolone-resistant *Campylobacter* have recently been reported in many other countries, including Canada [37] and Spain [84]. In the U.S., *Campylobacter* with resistance to nalidixic acid increased from 1.3% in 1992 to 10.2% in 1998 [97].

Resistance to erythromycin appeared in the Netherlands in the 1990s [107]. Resistance to macrolides has been reported to be as high as 90% in Spain [67], but trends over time for erythromycin resistance show stable and low rates in Japan, Canada and Finland [29]. Resistance to macrolides was found to be more prevalent in *C. coli* than *C. jejuni* [67, 91].

There are several risk factors associated with the isolation of antimicrobial-resistant *Campylobacter*. Isolation of *Campylobacter* with resistance to quinolones was found to be associated with foreign travel and use of quinolone prior to isolation [97]. Exposure to fluoroquinolones in both humans and animals was found to induce resistance in *Campylobacter* [66, 93, 130]. The frequency of isolation also showed seasonal patterns with lower levels of resistant isolates in the summer months, when the overall incidence of *Campylobacter* isolation was higher [107]. Consumption of contaminated foods is also a source of resistant bacteria: it has been estimated that, in the worse case scenario where prevalence of resistance *Campylobacter* is as high as 84%, 3–4 people per year in US will die as a result of infection with fluoroquinolone resistant *Campylobacter* spp. from beef consumption [6].

Antimicrobial resistance in human *Campylobacter* isolates has been found in developing countries. In Kenya, 51% of diarrhea patient had isolates of bacteria that were not susceptible to antimicrobial treatment, and 24% of *Campylobacter* was resistance to nalidixic acid [94]. In Thailand, resistance to azithromycin remained low (6%) [49] and therefore may be used empirically to treat gastroenteritis [61]. Similar to developed countries, resistance to macrolides was found to be more prevalent in *C. coli* than *C. jejuni* in Taiwan [64], with resistance to erythromycin in 50% of *C. coli* isolated from human patients [64]. In Thailand where fluoroquinolones are widely used in broiler farms to control respiratory disease, the prevalence of quinolone resistance *Campylobacter* spp. was found to increase from 0% in 1987 to 84% in 1995 [46].

Antimicrobial resistance in isolates from food animals: The resistance to fluoroquinolones in food animal was observed in the Netherlands since early 1990’s [27]. Since then, there have been several reports of antimicrobial resistance in *Campylobacter* spp. isolated from food animals in both developed and developing countries (Table 2). High level of resistance to fluoroquinolones and tetracycline were reported in the Netherlands [53], Spain [91], Ireland [65] and Taiwan [64]. Resistance to tetracycline was much higher in Taiwan compared to other countries in Europe (Table 2). Resistance to gentamycin was relatively low in Spain [91], Ireland [65] and Taiwan [64]. Only resistance to chloramphenicol was found in *Campylobacter* spp. isolated from chickens in Switzerland [32].

Link between resistance in food animal isolates to resistance in human isolates: There has been speculation that the use of antimicrobial agents, such as quinolones, in food animals resulted in increasing the prevalence of quinolone resistance in *Campylobacter* spp. from humans [28, 38, 80] followed the approval of fluoroquinolone use in food ani-
mals. There seems to be a temporal relationship between the use of fluoroquinolones in animals and the finding of resistant *Campylobacter* in humans [29]. In Spain, the proportion of human isolates of *Campylobacter* resistant to quinolones was found to be 72%, while 99% of *Campylobacter* isolated from broilers and pigs were resistant to quinolones [91]. In Taiwan, 52% of *C. jejuni* isolated from human patients were resistant to ciprofloxacin, while 92% of isolates from chickens were resistant to the same agent [64]. Since *C. coli* was the most common species of *Campylobacter* isolated from pigs [101], resistance to macrolides in human isolates may reflect the use of macrolides in pork production in Taiwan. In Denmark, it was shown that the proportion of *Enterococcus* with resistance to avoparcin, tylosin, erythromycin, Virginiamycin, and avilamycin reduced after those agents were banned from the market [2]. This observation indicated a significant association between antimicrobial use as growth promoters in food animals and the prevalence of resistant bacteria. Similar phenomena may be observed in *Campylobacter* spp., which should be confirmed.

In summary, resistance was observed at high levels in food animals in both developed and developing countries. Studies suggested an association between antimicrobial use in food animals and the development of resistance in human isolates in developed countries. Traveling to developing countries has also been related to the isolation of resistant *Campylobacter*. However, there have been few reports of risk factors for the development of antimicrobial resistance in developing countries. In most developing countries, while antimicrobial use is usually less regulated than developed countries, economic necessity may limit the use of newer, more expensive antimicrobial agents. An epidemiological study of risk factors associated with the development of antimicrobial resistance in developing countries will be valuable, in order to prolong the usefulness of the available antimicrobial agents for treatment of important human pathogens.

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CAMPYLOBACTER SPP. REVIEW


