The Zoonotic Potential of Campylobacteriosis and its Implications to Human Health

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INTRODUCTION

In the late 70’s, *Campylobacter* spp. had emerged as foodborne pathogens in addition to other well-known and recognized foodborne pathogens, among which is *Salmonella* spp. According to Blaser et al. (1983), *Campylobacter jejuni* causes more cases of gastroentiritis than *Salmonella* or *Shigella* species. For decades it was apparent that different species of *Campylobacter* are associated only with warm-blooded animals, but their significance as human pathogens was not established for lack of detection methods during those times. The development of selective growth media in the late 1970’s permitted laboratories to test stool specimens for *Campylobacter* (Kist 1985; Tauxe 1992). Recent advances in epidemiology and microbiology have directly resulted in association of *Campylobacter* spp. with human enteric illnesses. *Campylobacter jejuni* and *C. coli* are now recognized as major causes of diarrhea (Griffiths and Park 1990; Tauxe 1992; Taylor 1992). Most campylobacter infections appear to be sporadic rather than outbreak associated, and in majority of cases, the original source of infection cannot be determined (Cowden 1992). The development of selective media and methods to isolate the causative agents allow more laboratories to test stool specimens for *Campylobacter*. From then on, many different DNA-based subtyping schemes have been developed including pulsed-field gel electrophoresis (PFGE) and randomly amplified polymorphic DNA (RAPD) analysis (Hilton et al. 1997).

The sources of campylobacter infections are generally assumed to be foods mainly poultry products, water, unpasteurized milk, and pets (Tauxe 1992). Published information indicates that campylobacteriosis is a zoonotic disease. Pets, water, and contaminated foods are considered the main sources of sporadic infections in humans (Harris et al. 1986; Morgan et al. 1985; Svedhem and Kajiser 1981; Tauxe et al. 1988). According to Stern (1992), cross-contamination, improper handling, and cooking of foods of animal origin account for the majority of the diseases. Person-to-person transmission is uncommon (Norkrams and Svedhem 1982; Schmid et al. 1987). However, an overlap has been reported between serotypes of *C. jejuni* found in humans with those found in poultry and cattle, indicating that foods derived from these animals are significant in transmitting *C. jejuni* to humans (Nielsen et al. 1997).

Case-control studies have identified several risk factors associated with campylobacteriosis. Other significant but unrecognized sources of infection may also exist. A better understanding of the epidemiology of sporadic infection is essential for the development of intervention measures to reduce human exposure to this pathogen (Jackson et al. 1998).

This paper reviews available literature highlighting the zoonotic potential of campylobacteriosis, describing the sources of infection, as well as transmission of the causative organism from animals through the food chain and ultimately to humans.

SOURCES OF INFECTION

It is a known fact that campylobacters live as commensals in the intestinal tracts of a wide range of birds and mammals, including domestic animals most widely used for food production and as pets. So there are many
potential pathways of infections to humans. The organisms can survive in the environment for several weeks at temperatures around 4°C, and cause infections when consumed through untreated water and milk. Infection can also be acquired through direct contact with infected animals, especially among those in specialized occupations such as among veterinarians, animal husbandry personnel, butchers, meat inspectors, and animal caretakers in the farm. Pet dogs and cats are also considered sources of infections.

*Campylobacter* enteritis is essentially a foodborne disease and the principal source of infection is raw or undercooked meat (Skirrow and Blaser 1992). Any raw meat is likely to be contaminated with the organisms. Poultry is by far considered the most significant source especially broiler chickens as these are consumed in large quantities. According to Tauxe (1992), consumption of raw milk and untreated surface water is another source of infection. Based on documented evidences, a typical outbreak occurs after a school class visit to a dairy farm, when children are given raw milk to drink. This practice is hazardous and should be discouraged. The mechanisms by which raw milk becomes contaminated are likely to include fecal contamination, perhaps related to long-term biliary carriage in the bovine (Warner et al. 1986). It can also be the result of asymptomatic bovine mastitis caused by *C. jejuni*, which has been documented to be the source of human infections on two occasions (Hudson et al. 1984; Hutchison et al. 1985). *C. jejuni* is often present on retail fresh poultry and is less frequently found on fresh beef, lamb, pork, mushrooms, and raw milk (Doyle 1984; Doyle and Schoeni 1986; Stern et al. 1988). Shellfish such as clams may become contaminated by feeding in waters polluted with run-off from animal raising farms (Doyle and Jones 1992).

**Zoonotic Potential**

**Reservoirs**

Reservoirs are hosts that carry the organisms but may not show signs or symptoms of the disease. The ecology of *C. jejuni* involves wildlife reservoirs, particularly wild birds. Species reported to carry *C. jejuni* include migratory birds such as cranes, ducks, geese, and seagulls (Nielsen et al. 1997; Leutchefeld et al. 1980). Rodents had also been implicated as reservoirs of the organism. Even insects can carry them in their exoskeleton (Cabrita et al. 1992; Jacobs-Reitsma et al. 1996).

**Poultry**

The intestines of poultry are easily colonized with *C. jejuni*. Day-old chicks can be colonized with as few as 35 organisms (Kaino et al. 1988). According to the studies of Skirrow and Blaser (1992), poultry not only harbors campylobacters in the cecum but also becomes heavily contaminated during mass mechanized processing. *C. jejuni* exists within the intestinal tract of poultry, which can be considered a commensal association. Large numbers of the organism live in there (up to 10⁶ to 10⁷ CFU per g) without any apparent gross pathologic consequences for the host chicken (Stern et al. 1988). The organism resides in a comparatively rare niche within the intestinal tract where competition for space and nutrients is minimal (Beery et al. 1988). There exists to be a symbiosis between the host and parasite with few pressures to dislodge the bacterium. The organism appears to be a member of the normal flora of chickens.

In the study of Aho and Hirn (1988), findings showed very low levels of *C. jejuni* (1.7%) in the feces of broilers at 4-5 weeks of age. However, at slaughter (ca. 6-7 weeks of age), the ceca of birds yielded a higher incidence of *C. jejuni* (24%). During processing of chicken carcasses, the organisms can be spread either from the large load of bacteria within the intestinal tract or from the load of *C. jejuni* on the birds’ feathers and skin. This enormous bacterial load results in substantial contamination of processed carcasses.

Smith and Muldson (1974) presented the earliest of numerous reports on the presence of *C. jejuni* associated with chicken carcasses. In Ontario, Canada and in Ohio, USA, fresh chicken obtained at retail outlets yielded *C. jejuni* at a rate of 116 of 200 carcasses (Park et al. 1981).

In a study conducted by Notermans et al. (1981) on marketplaces in Netherlands, 16 % of the chicken yielded *C. jejuni*. In France, the isolation of rate of *Campylobacter* spp. from poultry was 44 of 45 carcasses sampled (Marinescu et al. 1987). In Poland, the organisms were found in 80 % of the chicken carcasses, 48% of duck carcasses, and 3 % of turkey carcasses examined (Kwiatek et al. 1990).

Studies conducted in the laboratory (Clark and Buesch 1986; Kazwala et al. 1990a, 1990b; Shanker et al. 1990), had indicated that birds already colonized with *C. jejuni* can rapidly spread the organisms to majority of hatchmates in less than 3 days. Fecal-oral spread is possible because chicken are coprophagic. In other studies, results showed colonization of the birds did not come from the hatchery. Carrier rats probably introduced the organisms, as rat feces frequently yield (87%) the organisms (Kazrazadeh...
and Genigeorgis 1987). Annan-Prah and Jane (1988) monitored 10 broiler flocks but did not isolate the organisms from their samples until the birds were 21 days old. They suggested that other farm animals and transmission through fomites such as the farmer’s boots could have been the sources of contamination of flocks.

**Beef and Dairy Cattle**

Cattle are considered an important source in milk-borne transmission of *C. jejuni*, but are not strongly implicated in transmission through meat products. Raw milk is presumed to be contaminated by bovine feces; however, direct contamination of milk as a consequence of mastitis also occurs (Hudson et al. 1984). *Campylobacters* are also found in red meat, and there are reports linking the role of beef cattle. In one study, *C. jejuni* was present in 5% of raw ground beef and in 40% of veal specimens (Lammerding et al. 1988). According to a Dutch report, an outbreak affected 28 military personnel living in one barrack. Steak tartare had been eaten by 93% of those affected individuals, whereas only half of the unaffected soldiers had eaten the food. Garcia et al. (1985) reported that many of the serotypes of *C. jejuni* isolated from cattle are similar to those found in human disease. The implication tells us that a proportion of human campylobacteriosis can be traced back to beef products. The organism was frequently isolated from gallbladders, large intestines, small intestines, and livers. The serogroup of the organism was similar for both humans and cattle.

Species of *Campylobacter* are often isolated from feces of cows. In a study conducted by Meanger and Marshall (1989), 22% of 273 rectal swabs from dairy cows yielded *Campylobacter* spp. According to studies of Svedhem and Kajiser (1981), 5% of cattle have *Campylobacter* spp. as a component of the gut flora. Contamination of milk can be of fecal origin or could occur through mastitic infection. Raw milk from cows suffering from mastitis could infect humans. Morgan et al. (1985) reported the isolation of *C. jejuni* from a naturally occurring case of mastitis in association with human illness involving the same serotype. Unpasteurized milk has been recognized as a source of diarrhea outbreaks. (Sharp et al. 1985). Regulatory authorities should require pasteurization since raw milk is a known source of human campylobacteriosis.

**Organically-raised Animals**

With increasing clamor and demand for organically raised animals, one cannot help but think about the possibility of disease transmission from these animal food sources. *C. jejuni* is a commensal organism of the intestinal tract of cattle (Fricker and Park 1989). Young animals are more often colonized than older animals. Feedlot cattle are more likely to carry campylobacters than grazing animals. In one study, colonization of dairy herds was associated with drinking unchlorinated water (Humphrey and Beckett 1987). Whereas organically-raised animals can be considered susceptible to infections as those raised under conventional farm conditions, there is a need to conduct further studies.

**Pigs**

There are varied reports implicating pigs as a major source of human campylobacteriosis. Some investigators described the presence of *Campylobacter* spp. in the gallbladders and or bile ducts of slaughtered pigs. Rosef (1981) found in Norway that 58% of the pigs sampled yielded the organisms. In Sweden, Svedhem and Kajiser (1981) reported that 95% of the pigs sampled at slaughterhouses yielded *Campylobacter* spp. On the other hand, several reports specifically considered the isolates from pigs and compared the results with the serology of *C. jejuni* isolates from humans (Banffer 1985; Munroe et al. 1983; Pokamunski et al. 1986). The reports coming from Europe and Canada concluded that isolates from pigs (mostly *C. coli*) belonged to serotypes uncommon among human isolates. These reports show that pigs do not appear to be a major source of human campylobacteriosis specifically *C. jejuni*.

**Domestic Pets**

Among domestic pets, dogs and cats have also been implicated in the transmission of *C. jejuni* to humans. In a study conducted by Deming et al. (1987), 30% of the cases they studied were accounted for by contact with cats. They observed an association of sporadic cases of campylobacter enteritis with handling kittens. Bruce et al. (1980) found that up to 45% of clinically normal cats yielded *Campylobacter* spp. Puppies may also serve as reservoirs for human infections (Blaser 1986). However, there are variable frequencies of isolation from dogs. Nair et al. (1983) recovered the organisms from 21.7% of dogs with diarrhea and 3.1% of normal healthy dogs. Other investigators have found that 49% of healthy dogs yielded *C. jejuni*.

There were also reports implicating other domestic animals and pets but, they were not considered significant sources of transmission to the general public.

**Other Sources**

*C. jejuni* is one of the bacterial etiologies of water-borne outbreaks of diarrhea (Mentzing 1981; Vogt et al. 1982; Melby et al. 1990). One explanation is that *C. jejuni* may
survive in a non-culturable form. Several waterborne epidemics have been previously described. Three well-known and well-documented epidemics occurred in Vermont, USA in 1982 (Vogt et al. 1982), in Grums, Sweden, (Mentzing 1981), and in Northern Norway in 1988 (Melby et al. 1990). C. jejuni is found at a fairly high frequency in river water and ponds, during both warm and cold seasons (Vogt et al. 1982; Bolton et al. 1987). In a study conducted by Lind et al. (1996), waterborne outbreaks that occurred in northern Norway originated from contaminated drinking water. It was concluded that the source of the organism was the polluted surface water of a small lake that is used for drinking water. They have also concluded that contamination possibly came from feces of wild birds in the surrounding area. The second outbreak was in Sweden, and the organisms originated from a small river where its water, via backflow, contaminated the drinking water system.

ANTIMICROBIAL RESISTANCE

Because of indiscriminate use of antibiotics, there is an increasing rate of human infections caused by antimicrobial resistant strains of C. jejuni. This continuing practice makes clinical management of campylobacteriosis cases more difficult (Piddock 1995; Murphy et al. 1996). Antimicrobial resistance can prolong illness and compromise treatment of patients with bacteremia. The rate of antimicrobial-resistant enteric infections is highest in developing countries, where the use of antimicrobial drugs in humans and animals is relatively unrestricted. A 1994 study found that most clinical isolates of C. jejuni from U.S. troops in Thailand were resistant to ciprofloxacin (Murphy et al. 1996). Experimental evidence demonstrates that fluoroquinolone-susceptible C. jejuni become drug-resistant in chickens when these drugs are administered (Jacobs-Reitsma et al. 1996). In a 1997 study conducted in Minnesota, USA, 12 of 60 (20%) C. jejuni isolates from chicken purchased in grocery stores were ciprofloxacin-resistant (Smith et al. 1998).

HEALTH IMPLICATIONS

The above-mentioned documented evidences show the zoonotic potential of campylobacteriosis and the possible sources of infections to humans. The usual manifestations of Campylobacter spp. infection is a form of enteritis that is a very unpleasant attack of acute diarrhea lasting about 5 days (Skirrow and Blaser 1992). There is also an acute inflammatory entero-colitis and examination of the stools that shows the presence of cellular exudates. Frank blood is visible in the stools of about one-quarter of the patients affected. Fever and other signs of acute infections are common in the early stages of the disease. In one study, approximately half of the patients with laboratory confirmed campylobacteriosis reported a history of bloody diarrhea (Blaser et al. 1983).

In a study of Sorvillo et al. (1991), the incidence of campylobacteriosis in Human Immunodeficiency Virus (HIV)-infected patients is higher than in the general population. Common complications of campylobacteriosis in HIV-infected patients are recurrent infection and infection with antimicrobial strains (Perlman et al. 1988). A number of reported cases of C. jejuni bacteremia have occurred in immuno compromised patients, such as with hypogammaglobulinemia, acquired immune deficiency syndrome (AIDS), malignant neoplasms, recipients of corticosteroid therapy and persons at the extreme age (Peterson et al. 1993; Peterson 1994)

In recent decades, serologic and cultural studies have suggested that C. jejuni is one of the most significant triggers of Gullain-Barré syndrome (GBS) (Enders et al. 1994; Nakanishi et al. 1985; Allos and Blaser 1995; Nachamkin et al. 1998). Up to 40% of patients with the syndrome have evidence of recent campylobacter infection (Allos 1997). GBS is a neurologic disease characterized by ascending paralysis that can lead to respiratory muscle compromise and death (Hughes and Rees 1997; Allos et al. 1998). Case-control studies have shown that GBS is frequently preceded by acute infectious illness. Culture confirmation of preceding C. jejuni infection in 8-50% of GBS patients has been achieved (Allos and Blaser 1995). Among the serotypes isolated from stools of GBS patients, O19 strains account for 83% and 29% of GBS-associated C. jejuni isolates in Japan (Fujimoto et al. 1992; Kuroki et al. 1993) and in the US, respectively (Allos et al. 1998). The complete genomic sequence of C. jejuni was published in Nature at the beginning of 2000. There were hypervariable sequences, however, many of them involved in genes for surface structures, possibly related to C. jejuni’s survival strategy, or to the development of the neuromuscular disorder GBS for which C. jejuni is a frequent antecedent (Parkhill et al. 2000).

Campylobacteriosis has also been associated with Reiter’s syndrome, a reactive arthropathy. Multiple joints can be affected, particularly the knee joint. Pain and incapacitation can last for months or becomes chronic. This was found in approximately 1% of patients with campylobacteriosis, the sterile post-infection process occurring 7-10 days after the onset of diarrhea (Allos 1997).
The pathogenesis of *C. jejuni* involves both host, and pathogen-specific factors. The health and age of the host, and *C. jejuni*-specific humoral immunity from previous exposure influence clinical outcome after infection (Tauxe, 1992; Blaser et al. 1987). Rates of infection increased with the ingested dose, and rates of illness appeared to increase when inocula were ingested in a suspension buffered to reduce the acidity of the stomach (Black et al. 1988).

Our understanding of the role of *C. jejuni* in causing human infection has increased over the past two decades. We now know that *C. jejuni* causes more cases of bacterial gastroenteritis as reported by several studies conducted in the developed world even surpassing *Salmonella* or *Shigella* species in most studies (Blaser et al. 1983). In 1996, 46% of laboratory-confirmed cases of bacterial gastroenteritis reported in the Center for Disease Control and Prevention/U.S. Department of Agriculture/Food and Drug Administration Collaborating Sites Foodborne Disease Active Surveillance Network were caused by Campylobacter species. Campylobacteriosis was followed in prevalence by salmonellosis (28%), shigellosis (17%), and *Escherichia coli* O157 infection (3%) (Altekruse et al. 1999). Although *C. jejuni* is a common gastrointestinal tract pathogen, bacteremia caused by the organism is rare comprising only 0.4% of all campylobacter species infections (Riley et al. 1985). Bacteremia typically occurs in conjunction with gastroenteritis and affects persons at the extremes of age and those with underlying medical conditions such as cirrhosis, diabetes, renal failure, cancer, and HIV diseases (Peterson 1994). Although serious complications are rare, this emerging foodborne disease should not be overlooked. In cases of bacteremia caused by this pathogen, early institution of antimicrobial therapy, especially to those patients who have risk factors associated with high morbidity and mortality (Wang et al. 1998).

**CONCLUSION**

The fact that campylobacters live as commensals in the intestinal tracts of a wide range of animals, including domestic animals used for food production and pets, we must be on the lookout for this potential pathogen. There are many routes of infection as discussed in this paper and the fact that *C. jejuni* is found in many foods of animal origin establishes campylobacteriosis as a foodborne zoonosis. An overlap is reported between serotypes of *C. jejuni* found in humans, poultry, and cattle, indicating that foods of animal origin may play a major role in transmitting *C. jejuni* to humans (Nielsen et al. 1997). Mishandling of raw poultry and consumption of undercooked poultry are the major risk factors for human campylobacteriosis (Altekruse et al. 1999).

Control of *Campylobacter* contamination on the farm may reduce contamination of animal carcasses and poultry. Epidemiologic studies indicate that strict hygiene reduces intestinal carriage in food-producing animals (Humphrey et al. 1993; Kapperud et al. 1993; Kazwala et al. 1990). Slaughter and processing provide opportunities for reducing *C. jejuni* on food animal carcasses. The use of chlorinated water and maintenance of clean working surfaces resulted in a 10- to 100-fold decrease in carcass contamination (Patterson 1995). Reinforcing strict hygienic practices at each link in the food chain, for example, from farm gate to plate is critical in preventing the disease. The emergence of fluoroquinolone-resistant infections in Europe and in the US, temporally associated with the approval of fluoroquinolone use in veterinary medicine, can be considered a public health concern (Altekruse et al. 1999). Since studies have shown that the rate of antimicrobial-resistant enteric infections has been found to be highest in the developing world including the Philippines, it is high time to put a stop and restrict the use of antimicrobials particularly in animal feeds. Strict adherence to and implementation of Good Agricultural Practices (GAP) and disease prevention programs, including regulation and control in the use of antimicrobials would ensure that potential pathogens are kept under control as much as possible.

In a developing country such as the Philippines, asymptomatic and possibly multiple infections may occur, so much so that there is a need to conduct surveillance studies for the presence of this pathogen. There is probably a lack of awareness regarding the significance of this pathogen because there are few studies conducted so far. The focus of most studies in the country is still on more common diarrheagenic organisms such as *Escherichia coli, Vibrio cholerae*, and *Salmonella*. Since the organism is a microaerophilic thermophile, there is difficulty in isolation and identification of the organism. There was one study conducted in 2000 at the University of the Philippines National Institutes of Health (UP-NIH) on the prevalence of *Campylobacter* spp. from Philippine foods, which utilized conventional methods of isolation and identification (Bungay et al. unpublished). There is still a need to establish cost-effective laboratory methods with the present set-up. In outbreaks caused by enteropathogenic organisms, there is an urgent need for a rapid, reliable, and simple typing procedure in order to detect and eliminate the source of infection. Considering the zoonotic potential of this organism, there is a need for more accurate assessment in terms of incidence and prevalence. Government, research and academic institutions involved in food and food animals should actively participate in surveillance and monitoring of this pathogen.
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