CHAPTER II

REVIEW OF LITERATURES

Historical Background

In 1913 in England, the observation of spiral, curved bacteria by McFadyean and Stockman was assumed to be the first description of microaerophilic vibrios (V. fetus and now considered to be Campylobacter) in animal disease (cattle abortion). The association of similar organism with bovine abortion was also reported in 1918 (Smith 1918) and the isolated organisms were named V. fetus by Smith and Taylor in the later year (Smith and Taylor 1919).

The observation of this organism in human disease was first described by Levy in 1946. It was successful cultured from human blood (Bloodstream of 3 pregnant women who had infectious abortion) in 1947 by Vinzent et al., that its potential significance in human disease was appreciated and the first proven case was reported. Ten years later, it was recognized as a opportunistic pathogen of debilitated patients (Bokken heuser 1970, Guerrant et.al. 1978). Elizabeth King observed that V.fetus isolates could be devided into two groups on the basis of thermophilic characteristics and V. fetus that grew best at 42°C was named "related vibrios" in 1957. Furthermore she was the first to notice that the possibility of "related

vibrios" (thermophilic vibrios) were associated with diarrheal disease. Although the organism was isolated from bloodstream, the patient had had a diarrheal illness in each case as well (King 1957, King 1962).

In 1963, Sebald and Veron determined that the DNA base composition of guanine plus cytosine (G+C) of microaerophilic V. fetus group was different from other Vibrio spp.(V. fetus 29-36 mol% but Vibrio spp. 40-53 mol%), therefore a new genus, Campylobacter was proposed for microaerophilic vibrio in 1978 (Smibert 1978). Bokkenheuser concluded that this organism was probably present in feces, but could not be detected with the available laboratory technique in 1970 (Bokkenheuser 1970). The later year, the first successful effort to isolate V. fetus (C. jejuni) was made in Australia by Cooper and Slee. It was isolated from immunocompromised patient with recurrent bacteremia and diarrhea by culture onto a horse blood agar containing cephalothin discs and incubating overnight in CO_2-enriched atmosphere (Cooper and Slee 1971).

In 1972, such "related vibrios" (Thermophilic Campylobacters) were isolated in Brussel from diarrhoeic stool specimen by using the 0.65-um-membrane filter (Dekeyser et al. 1972, Butzler et al. 1973).

In 1977, the development and introduction of highly selective solid growth medium (agar medium containing

antibiotics) by Skirrow provided the break through for routine culture (Skirrow 1977).

Basis on the scheme of Veron and Chatelain (1972), and later modification by Smibert in 1978, King's "related vibrios" became C. jejuni and C. coli and the opportunistic organism became C. fetus SS. fetus, respectively (Smibert 1984, Karmali and Skirrow 1985).

Taxonomy of the Genus Campylobacter

Initially, the organism was classified into the family Vibrionaceae because of its morhology. However, there are major differences in biochemical (its inability to use sugar either oxidatively or fermentatively) growth characteristics and nucleotide base composition, a new genus Campylobacter was created. There was considerable confusion and controversy about nomenclature and classification of strains within the genus in the past. The currently accepted species classification of Campylobacter by the International Committee on Systemic Bacteriology published in the Approved List of Bacterial Names is as the followings (Skerman et al. 1980).

Family Spirillaceae

Genus I Spirillum

Genus II Campylobacter

1. Campylobacter coli

2. Campylobacter fetus

2a. C. fetus ss. fetus

2b. C. fetus ss. venerealis

3. Campylobacter jejuni

4. Campylobacter sputorum

4a. C. sputorum ss. bubulus

4b. C. sputorum ss. sputorum

and other organisms have been reported in the literature that may be Campylobacter like organisms are

a. Nalidixic acid esistant thermophil Campylobacter (NARTC)

: C. laridis

b. C. fecalis (V. fecalis)

c. Aerotolerant Campylobacter species C. cryaerophila (Campylobacter like organism.

d. Nitrogen - fixing Campylobacter like organisms.

e. "Free living" aspartate fermenting Campylobacter species

The composition of the taxonomic classification synonyms of the genus Campylobacter from the past up to now is shown in Table I.

Bacteriology of Campylobacter species

Campylobacter (derived from Greek; Campylo meaning curved and bacter meaning rod) are thin, nonsporogenic,

spirally curved, gram negative rods, 0.2 to 0.5 um wide and 0.5 to 5 um long, and can be as long as 8 um. Short, S-shaped or gull winged (two cells form short chains) and longer multispiralled, filamentous organism may also appear. Coccoid form may occur in old cultures. The organisms are rapid, darting and tumbling (corkscrew-like motion) motile with a single polar flagellum at one or both ends. They require reduced oxygen tension for growth that vary from microaerophilic to anaerobic atmosphere depending on different species. Optimum temperature for growth vary from 25°C to 43°C depending on species (Neill et al. 1979, Smibert 1984, Morris and Patton 1985).

The principal energy sources of these organisms are obtained from amino acids and tricarboxylic acid cycle intermediates not carbohydrates, therefore carbohydrate are neither fermented nor oxidized. The organisms are oxidase positive, reduce nitrate, methyl red and Voges Proskauer are negative. The guanine plus cytosine content ranges from 29 to 38 mol% (Neill et.al. 1979, Rettig 1979, Belland and Trust 1982, Smibert 1984, Morris and Patton 1985).

There are many species of genus Campylobacter as the followings :

1. C. jejuni is now as one of the most common leading causes of human gastroenteritis in many parts of the world (Brunton and Heggie 1977, DeMol and Bosmans 1978, Lauwers et.al. 1978, Linquist et.al. 1978, Blaser

et.al. 1978, Blaser et.al.1980-b, Itoh et.al. 1980. Williams and Deacon 1980, Ringertz et.al. 1980, Taglor et.al. 1980).

The organism is small tightly coiled spiral. Rapid formation of coccoid bodies occurs when exposed to air. Swarming growth occurs on moist agar plates. There are two types of colonies on primary isolation. One may be nonhemolytic, low, flat, grayish, finely granular and translucent with an irregular edge with a tendency to spread along the direction of the streak. The colony diameter can reach up to 10 mm. The other is round, raised, convex and glistening with entire edge and 1-2 mm in diameter. It has a translucent edge and a dark, dirty brownish slightly opaque center (Smibert 1965, Smibert 1984).

C. jejuni requires microaerophilic (5% O_2, 10%CO_2 and 85% N_2) condition, grows well at 42°C and does not grow at 25°C. The organism is oxidase and catalase positive, reduces nitrate and hydrolyzes hippurate. It is susceptible to nalidixic acid and resistant to cephalothin. Tolerance to 0.04% TTC and 1% glycine. It has DNA with G+C contents of 31 mol% (Smibert 1984, Morris and Patton 1985, Barret et al. 1988).

2. C. Coli causes disease in human similar to those caused by C. jejuni. It is very often found in healthy pigs, and intestinal tract of swine, poultry and man (Smibert 1984).

The cell is tightly coiled, 0.2-0.3 um in diameter and 1.5-5.0 um long, and fairly aerotolerant.

The colonies are generally round,raise covex,smooth, glistening and 1-2 mm in diameter with white to tan color. On moist agar, colonies are low flat, grayish color with a tendency to spread in the direction of the streak. They are nonhemolytic on blood agar (Smibert 1984).

The organism grows well at 42°C but not at 25°C under microaerophilic (5% O_2, 10% CO_2 and 85% N_2) condition. It is oxidase and catalase positive, reduce nitrate but does not hydrolyse hippurate. Sensitive to nalidixic acid and resistant to cephalothin, tolerance to 0.04% TTC, 1% glycine and 1.5% NaCl. The guanine plus cytosine ranges from 32 to 34 mol% (Smibert 1984, Morris and Patton 1985, Barrett et al 1988).

3. C. fetus ss. fetus (C. fetus ss. intestinalis) was first described as the agent of bovine abortion. The organism is also responsible for sporadic abortion in cattle. Transmission is fecal-oral rather than venereal. It rarely causes enteritis and is primatily an opportunistic pathogen capable of causing systemic illness in debilitated or immunosuppressed patients (Harvey and Greenwood 1983, Smibert 1984).

The cell is slender curved rod, 0.2-0.3 um in diameter and 1.5-5 um long. On primary isolation, the colonies are frequently low, flat, grayish to tan color and translucent with an irregular edge. They spread along the direction of the streak. However, there are several types of colonies are found on agar on primary isolation. Smooth colonies are colorless to slightly cream color, 1 mm in diameter and after incubating for 6-8 days, it become mucoid. Rough colonies are small, round finely granular, opaque and white to cream or tan color. "Cut glass" colonies are 1 mm diameter, round, raised, translucent and granular with reflecting facets and do not develop in primary cultures. Upon subculture, smooth cut glass and rough cut glass colonies will apprea (Smibert 1984). The organism grows at 25°C but usually not at 42°C. It is inhibited by cephalothin that is an antibiotic in commercially available Camplybacter isolation media. At 42°C, the temperature which enhance the growth of C. jejuni but which inhibits the growth of moist strains of C. fetus ss. fetus. This organism is differentiated from "C. hyointestinalis" by a lack of pigment, an ability of produce H_2S in TSI and good growth at 25°C. The mol% G+C of DNA ranges from 33 to 36 (Smibert 1984).

4. C. fetus ss. venerealis was first described association with disease of the fatal membrane in cattle by Smith in 1918. The organism causes abortion and infertility in cattle and is transmitted venerally. It has

not been found in human infection (Smibert 1978, Karmali and Skirrow 1985).

The organism grows at 25°C but not at 42°C and is differentiated from C. fetus ss. fetus by inability to tolerance to 1% glycine. It has DNA with G+C contents of 33-36 mol% (Smibert 1984).

5. C. laridis was first described as nalidixic acid -resistant thermophilic Campylobacter. It has been isolated from a variety of birds and animals, and occasionally been isolated from patients with diarrhea. There was the first recorded case of bacteremia due to C. laridis in immunosuppressed patient in 1984. Its role in human disease was not clearly established (Skirrow and Benjamin 1980-a, Nachamkin et al. 1984).

The colonies of the organism were 1-1.5 mm. in diameter,low convex,smooth, translucent and entire; swarming was absent on normally dried media but some strains swarmed on very moist media (Benjamin et al. 1983). C. laridis grows well at 42°C but not 25°C. The phenotypic characters of the organism are closest to those of C. coli, although some characters are shared with C. jejuni and C. fetus ss. fetus. The features that distinguishs C. laridis from other thermophilic Campylobacter, particularly C. jejuni and C. coli are resistance to a 30-ug disc of nalidixic acid, negative for hippurate hydrolysis test. The production of

H_2S in iron metabisulfite medium (FBP semisolid medium), sensitivity to 0.04% TTC, tolerance to 1.5% NaCl, may also be useful for distinguishing from C. jejuni and C. coli (Skirrow and Benjamin 1980-b, Benjamin et al. 1983, Lior 1984). Anaerobic growth in the presence of 1% trimethylamine N-oxide (TMAO) may be used as a confirmatory test for identification of C. laridis. The guanine plus cytosine content of DNA ranges from 31 to 33 mol% (Benjamin et al. 1983).

6. "C.hyointestinalis" was originally isolated from the intestine of swine with proliferative ileitis (Gebhart el al. 1983). Investigators have isolated strains with similar characteristics from pigs, cattle and hamster (Lambert et al. 1984, Gebhart et al. 1985). "C. hyointestinalis" can also be a human enteric pathogen since there are some reports of this organism was associated with human disease but its role in disease cannot be define now (Fennell et al. 1986, Edmonds et al. 1987, Minet et al. 1988).

The organism are curved gram-negative rods but appear thicker and less curved than C. jejuni. The colonies are yellow, circular, raised, smooth, slightly mucoid but nonswarming, 1.5-2.0 mm in diameter and do not have a distinctive ador (Gebhart et al. 1985). "C. hyointestinalis" requires microaerophilic atmosphere that containing hydrogen grows at 25°C and 42°C. The phenotypic characteristic of this organism are most

resemble C. fetus ss. fetus; however, these species could be distinguished by several biochemical tests (Gebhart el al. 1985). Roop et al. also found that this organism showed closer genotypic and phenotypic relationships to C. fetus ss. fetus than to any other catalase positive Campylo bacterl spp. (Roop et al. 1984). The characteristics that most consistently distinguished this organism from the others are colony morphology (pigment), ability to produce H_2S strongly in TSI agar, ability to grow anaerobically in 0.1% TMAO, resistance to nalidixic aicd, susceptibility to cephalothin, hydrogenase activity, tolerance to 3% NaCl and 0.04% TTC. The guanine plus cytosine content of DNA is 36 mol% (Gebhart et al. 1985, Edmonds et al. 1987).

7. "C. cinaedi" is the proposed name for the orgamism that was isolated from the blood and rectal swab of homosexual men with intestinal symptoms in Seattle (Totten et al. 1985). In addition, the organism has been reported to be associated with diarrhea in 1987 (Tee et al. 1987). The role of the organism in human disease is unknown now.

The characteristics of these species were described as the followings : growth microaerobically at 37°C but not at 25°C or 42°C, no growth aerobically or anaerobically; catalase positive; growth in 0.04% TTC, 1% glycine; nitrate is reduced; no growth in 2% NaCl, hippurate is not hydrolysed; H_2S is not produced in TSI agar; growth is

inhibited by 30 ug-disc of nalidixic acid and intermediate zone of inhibition around 30 ug-disc of cephalothin. The G+C content of DNA is 37-38 mol% (Fennelle et al. 1984), Totten et al. 1985).

8. "C. fennelliae" is the proposed name for the organism that was isolated from rectal swab of homosexual men with intestinal symptoms in Seattle. Its role in human disease is unknown (Totten et al. 1985).

The characteristics of these species are as follows: microaerophilic growth at 37°C but not at 25°C or 42°C; no growth aerobically and anaerobically; catalase positive; growth in 1% glycine, tolerance to 0.04% TTC, but no growth in 2% NaCl; hippurate is not hydrolysed; nitrate is not reduced; H_2S is not produced in TSI agar; growth is inhibited by 30 ug-disc of nalidixic acid and 30 ug-disc of cephalothin and distinctive hypochlorite odor of colonies. The G+C content of the DNA is 37-38 mol% (Totten et al. 1985).

9. C. cryaerophilia is recently designated as a new species to describe aerotolerant Campylobacter like organisms isolated from aborted-fetuses and placental tissues of pigs and cattles (Marmur and Doty 1962, Ellis et al. 1977, Ellis et al. 1978, Neill et al. 1979, Neill et al. 1980. Neill et al. 1985). The isolation of C. cryaerophilis from human was reported in 1988. It was

isolated from a single stool specimen of homosexual man who presented with intermittent diarrhea for 4 to 6 months. The clinical significance role of the organism in human disease is unknown (Tee et al. 1988)

The phenotypic characteristics of C. cryaerophila are gram negative helically curved rods which do not ferment carbohydrates, whereas catalase and oxidase are positive (Neill et al. 1985). Phimary isolation was achieved in leptospiral media in 30°C. Growth occurred at 37°C, but more readily at 30°C, under aerobic, microaerophilic and anaerobic conditions. However, there was a report of isolation of C. cryaerophila by using a conventional Campylobacter media (Modified Skirrow's medium containing trimethoprim, polymyxin B and vancomycin) which was cephalothin free(Tee et al. 1985). On the first subculture from primary plate, the organism is stickly microaerophilic manner. After a series of subculture, the organism becomes increasingly tolerant to atmospheric oxygen. The base composition of DNA (G+C) ranges from 30 to 32 mol% (Tee et al. 1985).

10. "C. upsaliensis" is the name proposed for a new group of thermophilic Campylobacter strains which differs from C. jejuni and C. coli in having a negative or weak catalase reaction. The organism was reported on the isolation from feces of diarrheal or healthy dog in 1983 (Sandstedt et al. 1983). Primary isolation of the organism

in human has been reported in the early of year 1989. The strain was isolated from stool of six children. Only three of them had signs and symptoms compatible with gastroenteritis (loose watery stool, vomiting and anorexia) at the time the positive isolates were obtained (Walmskey and Karmal 1989). Another isolation of "C. upsaliensis" is and apportunistic pathogen. The potential role of the organism as a human enteric pathogen requires further evaluation. The organism forms a genetically separated group with G+C content more than 3% higher than that of any other thermotolerant strains (Ursing et al. 1983).

The phenotypic characters are catalase negative or weak reaction, oxidase and nitrate positive, hippurate negative, negative for H_2S in TSI agar, and susceptible to cephalothin (30 ug) disc and nalidixic acid (30 ug) disc. They grow at 37°C and 42°C only. No growth occurs on Skirrowtype selective medium (blood agar plate containing vancomycin, trimethoprim, and polymyxin B or colistin) and selective media containing cephalothin (Skirrow 1977).

11. C. concisus has been isolated from the gingival crevices of humans with periodontal disease, but its pathogenicity is unknown. The mol % G+C of DNA ranges from 34 to 38 mol%. The organism requires hydrogen for growth in n atmosphere with 5% O_2, 10% CO_2 and 10-85% H_2, at 36°C, and does not produce catalase. Now growth at 25°C and 42°C. The colonies are convex, translucent, 1 mm in

diameter, with entire edge (Smibert 1984, Morris and Patton 1985).

12. C. pylori (formerly C. pyloridis) is a distinct form of spiral-shaped bacilli which were first isolated from antral biopsy specimens in 1983 (Warren and Marshall 1983). Subsequently several investigators have found an association between this organism and gastritis (The histological examination of gastric biopsy tissue has shown the C. pylori is strongly associated with active chronic gastritis, when polymorphonuclear leukocytes are present, and it is not found on normal mucosa). The organism is now identified as a potential etiologic agent in the pathogenesis of gastristis and ulcers (Marshall et al. 1985-a, Marshall et al. 1985-b, Buck et al. 1986, Goodwin et al. 1986, Blaser 1987, Rauws et al. 1988). It also has a unique ultrastructure which is different from that of all of other Campylobacter spp. and may belong to a distinct new genus (it is more closely related to Wolinella succinogenes than it is to the Campylobacter spp. (Romaniuk et al. 1987). Both urease enzyme and large amount of catalase enzyme of the organism may be important virulence factor, allowing C. pylori to occupy a protected niched in the stomach below the mucus layer but above the gastric mucosa (Goodwin et al. 1986).

C. pylori can be identified in gastric tissue specimen by culture and histologic staining technique

(modified Gram's stain : carbolfuchsin). Both of these are time consuming. Since the organism possesses a powerful urease enzyme, therefore the urease test is highly specific and leads to rapid presumptive diagnosis of C. pylori infection now (Owen et al. 1985, Westblom et al. 1988, Couldron and Kirby 1989). There have been few studies that compared recovery and growth of C. pylori on different primary media. It is found that the addition of blood to media not only enhanced the growth of C. pylori but also helped to distingnish C. pylori colonies from those of other bacteria on primary media. Although the numbers of colonies of C. pylori on different media are nearly equal, the size of the colonies differ greatly. On the basis of colony size, the addition of horse serum to fresh Skirrow medium improves the growth of C. pylori slightly and that the addition of horse serum and cholesterol improves the growth more significantly (Couldron and Kirby 1989).

There are some Campylobacter spp. that generally do not cause disease in humans including C. sputorum ss. sputorum, C. sputorum ss. bubulus and C. mucosalis.

13. C. sputorum ss. sputorum is a commensal found in the human oral cavity (gingival crevice flora of man) and occasionally isolated from normal human feces (Loesche et.al 1965, Smibert 1984, Karmali and Skirrow 1985).

The organism are slender, curved rods, 0.3-0.5 um wide and 2-4 um long. They appear gull-winged and commonshaped and occasionally occur as filaments up to 8 um long. Colonies on blood agar are gray, smooth, shiny, low convex, 1-2 mm in diameter and round with thin irregular spreading edges. Some may be widely α-hemolytic. Addition of nitrate to culture media markedly enhances growth of the organism. They require microaerophilic atmosphere for growth and no growth occurs in broth or an agar under aerobic conditions. Do not produce catalase. The G+C content of DNA is 29-31 mol% (Loesche et al. 1965, Smibert 1984, Roop et al. 1985). C. sputorum ss. sputorum differs from C. sputorum ss. bubulus by ability to grow in the presence of 1% oxgall and no growth in 3.5% NaCl (Smibert 1984, Roop et al. 1985).

14. C. sputorum ss. bubulus is found in the genital tract of cattle and sheep. It is isolated from semen, preputial and vaginal mucous of normal animals and is not con-sidered to be pathogenic (Loesche et al. 1965, Smibert 1984). Most characteristics of this organism are resemble C. sputorum ss. sputorum; it can be easily differentiated by ability to grow in 3.5% NaCl and no growth in 1% oxgall (Loesche et al. 1965, Smibert 1984, Roop et al. 1985).

15. C. mucosalis (C. sputorum ss. mucosalis) is pathogenic for pigs. It was first isolated from the intestinal mucosa of pigs with porcine intestinal adenomatosis (PIA)

(Lawson and Rowland 1974). The organism has been also isolated for pigs with necrotic enteritis, regional ileitis and proliferative hemorrhagic enteropathy, as well as isolated from the porcine oral cavity (Smibert 1984).

A recently report presented DNA homology data showing that C. sputorum ss. mucosalis strains are not related to either C. sputorum ss. sputorum or C. sputorum ss. bubulus at the species level, therefore C. mucosalis is proposed for this subspecies and this name has been validly published (Roop et al. 1985).

Cells of C. mucosalis are short, irregularly curved, 0.25-0.3 um wide and 1.0-2.8 um long. Colonies are 1.5 um in diameter, circular, raised with a flat surface and have a dirty yellowish color Lawson and Rowland 1974). On moist agar, colonies tend to swarm along the line of streak (Smibert 1984). They do not grow microaerophilically in and atmosphere containing 5% O_2, 10% CO_2 and 85% N_2. They grow microaerophilic only with 3-5% O_2, 10% CO_2 and H_2 and does not grow on MacConkey agar (Lawson and Rowland 1974, Smibert 1984). C. mucosalis and C. concisus require either H_2 or formate for microaerophilic growth and either H_2 and fumarate or formate and fumarate for anaerobic growth. C.mucosalis grows at 25°C and is sensitive to cephalothin whereas C. concisus does not grow at 25°C and resistant to cephalothin (Roop et al. 1985).

The phenotypic characteristics of Campylobacter spp are shown in table 2 and table 3

Recently atypical Campylobacter strains were isolated from human with gastroenteritis in Central and South Australia (Steele et al. 1985, Tee et al. 1987). These organisms were unusual biochemical characteristics, therefore DNA. DNA hybridization dot blotting was used to differentiate these atypical Campylobacter strains (Tee et al. 1987).

Pathogenesis

Only C. jejuni has been studied in detail of this topic. Infection can be manifested in several different forms. In nature infection due to C. jejuni is most commonly gastrointestinal disease. However, extraintestinal infection including meningitis, cholecystitis, and urinary tract infection, have been reported (Darling et al. 1979, Davies and Penfold 1979, Thomas et al. 1980). At least three potentially pathogenic mechanisms have been associated withCampylobacter spp, invasiveness, toxin (cytotoxin andenterotoxin) production, and translocation.

1. Invasiveness (involves penetration and proliferation within the intestinal epithelium) is compatible with the occurence of bloody diarrhea in some infected person and often associated with endoscopic evidence of

colitis or bacteremia (Blaser et al. 1979, Lambert et al. 1979, Blaser and Reller 1981). In Campylobacter enteritis, clinical evidence exists for intestinal epithelial invasion in case with bloody diarrhea and inflammatory cells in the stool. The most commonly infection involves the terminal ileum and colon. The rectal biopsy of eight consecutive patients with C. jejuni enteritis was abnormal in the study of Price et al. (Prince et al. 1979). The lesion in the lamina propria and crypt abscess consisted of inflammatory infiltrates similar to those seen in infection with Shigella and Salmonella spp. (Blaser et al. 1980-c). Similar biopsy results have been obtained by others (Lambert et al. 1979), Duffy et al. 1980). Hemorrhagic necrosis of the ileum and jejunum was found at autopsy of a patient with Campylobacter enteritis by King (King 1962, Ward et al. 1984). However, the frequency of infection in proximal small bowel is unknown, no one has prospectively investigated small-bowel biopsies in patients with Campylobacter enteritis. Intestinal infection with C. jejuni in animal models, including young chicken, mice, hamster, rabbit, calves and gnotobiotic dogs, have been shown to produce inflammatory lesion in the bowel. (Al-Mashat and Taylor 1980, Prescott et al. 1981, Ruiz-Palacios et al. 1981, Blaser et al. 1983-b, Caldwell et al. 1983, Kazmi et al. 1984, Sanyal et al. 1984, Welkos 1984, Humphrey et al. 1985), and in some instances bacteremia was detected (Blaser et al. 1983-b, Caldwell et al. 1983, Kazmi et al. 1984, Sanyal et al. 1984).

2. Toxin production is a proposed mechanism in patient with bloody or acute watery diarrhea.

2.1 Cytotoxin : Some C. jejuni isolate produce a cytotoxic response in various tissue culture systems, including Vero, HeLa, MRC-5 and Hep-2 cell lines(Yeen et.al. 1983, Johnson and Lior 1984, Newell et al. 1985). Guerrant et al. investigated 12 clinical isolates of C. jejuni and found polymyxin B extracts from 5 strains to be toxic to HeLa cells, and 6 strains to have cytotoxic effects on CHO (Chinese hamster ovary) cells. The cytotoxic was heat labile and susceptible to trypsin, but not neutralizable with antisera prepared against Shiga-like toxin I or II, or with Clostridium difficile antitoxin or antibody to non-01 Vibrio Cholerae cytotoxin. Preliminary characterization suggests a 50-790 Kd molecule, however no significant secretion with this toxin was shown in rabbit ileal loop assays (Guerrant et al.1987).

2.2 Enterotoxin : The recent demonstration of enterotoxin production by C. jejuni has supported this mechanism in the pathogenesis of the organism. One third of C. jejuni isolates in South India, and 75% of strains isolated in Mexico from young children with secretory-type diarrhea produce an enterotoxin that is heat-labile stimulates cyclic AMP, and is structurally and immunologically related to both cholera toxin and E. coli heat-labile toxin (LT) (Ruiz-Palacio) et al. 1983, Klipstein

and Engert 1984-a, Klipstein and Engert 1984-b, Mathan et.al. 1984, Mc Cardell et.al. 1984, Klipstein and Engert 1985). However, Mathan et.al. compared toxin production in isolates from children with acute diarrhea and asymptomatic children in South India, they found no difference in the prevalence of enterotoxigenic strains between the two groups (Mathan et al. 1984). Recently Klipstein et al., using fresh C. jejuni isolates, to show differences in toxin production among strains isolated from patients with asymptomatic illness, watery diarrhea or dysentery. None of the C. jejuni strains from asymptomatic patients had any demonstrable virulence attributes, six isolates from the bloody-diarrhea patients produced cytotoxin as measured in Vero and HeLa cell assays, but broth infiltrates from these organisms did not cause fluid accumulation in ligated rat ileal loops (no enterotoxin) and also exhibited invasive properties. Sixstrains isolated from secretory-type diarrhea patients elaborated enterotoxin and cause fluid secretion in ligated rat ileal loops, but only one of these isolates produced a cytotoxin (Klipstein et al. 1985).

In later study of Klipstein et al. in 1986, enterotoxin production and or invasiveness were exhibited by 75% of C. jejuni faccal isolates. Relationship between pathogenic propOerties of the infecting strain and clinical manifestations was observed again (Klipstein et al. 1986). However, this distinction is not supported by majority of the data from the others and is therefore questionable.

3. Translocation : In translocation, the organisms penetrate the intestinal mucosa, resulting in minimal damage and proliferative in the lamina propria and mesenteric lymph nodes. The involvement of C. jejuni with the mesenteric lymph node is well described clinically (Skirrow 1977, Butzler and Skirrow 1979). Youssef et al. recently showed that C. jejuni translocates to the mesenteric lymph node in gno- tobiotic mice (Youssef et al. 1985).

It remains to be determined whether the variability in the disease presentation is due to inherent differences among strain of C. jejuni or to host responses.

Chemotaxis and adhesins have also been suggested as possible factors for colonization by Campylobacter spp. Hugdahl and Doyle found that positive chemotactic responses were direct toward L-fucose, which is a constituent found in both bile and mucin, and suggested that this may be an important factor causing the colonization of the organism in the intestine and gall bladder (Hugdahl and Doyle 1985). Although C. jejuni lacks fimbriae, it may possess other adhesins. The flagellum may contain adhesins for epithelial cells, an aflagellated variant of C. jejuni was reported to adhere poorly to INT 407 cells, which suggests that the presence of adhesins on flagellum. However, in suspension, aflagellated organisms attach better than the parenteral flagellated type to target cells, suggesting the possibility of multiple adhesins (McBride and Newell 1983).

Other surface structures of C. jejuni that could be important is adhesion to the epithelium are outer membrane proteins (OMPs), lipopolysaccharide (LPS) and glycocalyx material. McSweegan and Walker were able to show that tritiated OMPs and LPS extracted from C.jejuni adhere to INT 407 cells (McSweegan and Walker 1985).

For the other Campylobacter spp, the role of pathogenic potential for human diseases cannot define now. Further studies emphasizing Microbiology, Seroepidemiology and clinical patterns are required to determine firmly establish the etiological role of these organisms in human diseases.

Epidemiology

Since infection due to C. coli is closely related to C. jejuni, and appears to share many clinical and epidemiologic characteristics, therefore C.jejuni and C.coli will be considered together in this topic.

A. Clinical features

Symptomatic infection due to Campylobacter spp. is marked by a gastrointestinal illness (Kaplan 1980), but the manifestations of this infection cannot be readily distinguished from illness due to other enteric pathogens. Manifestation of Campylobacter infection may vary from asymptomatic or either invasive-type bloody or secretory type watery diarrhea to fulminant illness. Mild infection may produce symptoms lasting for 1 day resembling those seen in a viral gastroenteritis. Fulminant illness mimics acute relapse of ulcerative colitis leading to death (Lambert el al. 1979, Blaser et al. 1980-c). The illness often begins with 1 or 2 days of prodomal symptoms including fever, headache, myalgias, arthralgias, and back pain. The predominant symptoms of infected person are diarrhea, abdominal pain, malaise, fever, nausea, vomitting and history of bloody diarrhea (Blaser et al.1979, Blaser et al. 1983-a). However, C. jejuni had rarely been reported to be associated with extraintestinal infection symptoms including bacteremia (Kaplan 1980), meningitis (Thomas et al. 1980), cholecystilis (Darling et al. 1979, Mertents and DeSmet 1979), urinary tract infection (Davies and Penfold 1979), appendicitis (Rettig 1979) etc. The incubation period of diarrhea is variable (1-7 days), usually self-limited, lasting 2-7 days, but persistent and relapsing symptoms are as well reported (Blaser et al. 1983-c).

The clinical features of C. jejuni-C.coli infections in developed and developing countries are substantially different. In developed countries, Campylobacter spp. is recognized as one of the most frequent bacterial causes of diarrheal disease (Blaser et al. 1983-c). Campylobacter enteritis can be a severe illness characterized by fever, bloody diarrhea and fecal leukocytes (Blaser et al. 1979, Blaser et al. 1983-c). Asymptomatic infections and infection with multiple enteric pathogens are apparently rare (Blaser and Reller 1981), and the mean duration of convalescent phase Campylobacter excretion after an acute infection is 2 to 3 weeks (Karmali and Flaming 1979, Svedhem and Kaijser 1979).

In developing countries, Campylobacter infection may lead to mild illness or be asymptomatic. This made it more difficult to determine its actual importance as pathogen. The infection is less often associated with bloody diarrhea than are infections in person in developed countries. Among Bangladeshi children, the duration of convalescent phase excretion was short. Because Campylobacter spp. can be isolated from well children and with other pathogens from children with diarrheal disease, the association between Campylobacter spp. and illness is less clear-cut in the developing world than in the developed world (Glass et al. 1983).

B. Prevalence and Incidence

1. Geographic distribution

C. jejuni appears to be an important cause of diarrheal illness on all continents, it has been isolated from patients and travellers returning from tropical temperature, and arctic climates. In developed countries, cases of Campylobacter infection usually occur sporadically (Blaser and Reller 1981, Blaser et al. 1983-a). C. jejuni is an important cause of acute diarrheal illness. It has been isolated from the stool 3 to 14% of patients with diarrhea who seek medical attention(Blaser and Reller 1981). Asmptomatic infections are uncommon. Several surveys of healthy persons have shown the isolation rate from fecal specimens to be less than 1%. Infections with multiple enteric pathogens are apparently rare. (Brunton and Heggie 1977, Skirrow 1977, Blaser et al. 1979, Ringertz et al.1980, Pai et al. 1979, Blaser and Reller 1981). Studies conducted in several different localities in the United States and Canada show that Campylobacter infection are at least as common as Salmonella or Shigella infections or more so among patients with diarrheal diseases. The incidence of Campylobacter infections whether symptomatic or not is about 1-2% per year (Butzler et al. 1973, Bruce et al.1977,Brunton and Heggie 1977, Blaser et al. 1979, Skirrow 1979, Blaser et al. 1983-c).

In developing countries, Campylobacter infection is hyperendemic, and epidemics have rarely been reported (Blaser et al. 1980-b, Glass et al. 1983). The vast majority of infection occur in the first five years of life. Isolation rates are highest during the first two years of life and then rapidly declined. The prevalence of C. jejuni infection in some developing countries may be much grater than in the industrialized countries. Higher rates of isolation from both ill and well children in developing countries suggest that Campylobacter exposure is considerably more frequent than in developed countries (Glass et al. 1983, Tayler et al. 1988)

2. Age and Sex

Information on age-specific and sex-specific rates of infection is based largely on culture surveys of patients with diarrhea. The isolation rates peak in infants (less than 5 years old) and again in young adult(20-29 years old) (Finch and Riley 1984). In several surveys based on Clinical Microbiology laboratory isolations from symptomatic individuals, the highest rate of positivity were from specimens submitted from persons 10-29 years of age (Blaser et al. 1983-c). In a population-based study in England showed that the highest age specific isolation rates were in children under five (Butzler and Skirrow 1979).

In poor - hygienic areas of developing world, the prevalence of infection appears to be highest in young children during the first 2 years of life and then rapidly decline (Blaser et al. 1980-b, Rajan and Mathan 1982). Studies of healthy persons in South India demonstrated that infection is prevalence in all age groups. In Bangladesh, the prevalence of infection is inversely related to age (Glass et al. 1983). In improved-hygienic condition areas, such as Indonesia, isolation of C. jejuni from healthy persons was uncommon and rates resembled those seen in the developed countries (Ringertz et al. 1980).

The earlier literature implied that the male sex was a risk factor for Campylobacter (V. fetus) infection (Bokkenheuser 1970). Data from an eight-hospital cooperative study in the United States showed that culture from males were performed more frequently, but the isolation rates were approximately the same for males and females (Blaser et al. 1983-c)

3. Season

In studies of the temporal distribution of Campylobacter infection in England, Belgium, the United States, and South Africa, the peak rate of isolation was in the summer. Both the absolute number of isolates and the isolation rate from the submitted stools increased in the warm months (Butzler and Skirrow 1979, Blaser et al.

1983-c). From the Communicable Disease Surveillance Center (CDSC) data, a second smaller peak in isolation during the winter months has been reported (Blaser et al. 1983-a). In Zaire, where mean temperatures are constant throughout the year, isolation of Campylobacter spp. from patients with diarrhea was much more frequent in the wet season than in the dry season (Bokkenheuser 1970, Blaser et al. 1983-a). In developing countries, there is no seasonal peak. In Thailand, Campylobacter was found throughout the year with the highest incidence in February and May and the lowest incidence in July (Supavej et al. 1987).

C. Reservoirs

1. Animal reservoirs

C. jejuni or C. coli organisms exist as commensals in the intestinal tracts of a wide variety of wild and demestic animals. The organisms from animals cause disease in humans is now known from data obtained in a few outbreaks in which an animal or animal product was ultimately identified as a source. Furthermore, some of the same serotypes of Campylobacter that cause disease in humans have been isolated from animals (Luechtefeld et al. 1981, Luechtefeld and Wang 1982, Hudson and Roberts 1982).

1.1 Poultry : Avian species are reservoirs for Campylobacter spp. C.jejuni has been isolated from the feces

of 30-100% of chickens, turkeys, water fowl, and other wild birds. Feces from these animals also may contaminate the surface of eggs. Thus, attempts to eradicate the organism from commercial operations may fail (Bruce et al. 1977, Grant et al. 1980, Luechtefeld et al., Svedhem and Kaijser 1981).

1.2 Cattle : C.jejuni is a commensal of cattle. Stool positivity rates peak in the summer months and decline in the winter. Individual cows excrete the same serotype for at least several months (Robinson 1982). Transmission to calves occurs but has not been shown among adult cows. Several different serotypes may be present in a herd at a given time. Unpasteurized milk has been implicated as a vehicle in numerous outbreaks of Campylobacter enteritis. Either contamination with fecal contents or mastitis is the likely condition leading to introduction of C. jejuni into milk. The presence of C. jejuni in the herd does not necessarily lead to contamination of milk (Lander and Gill 1980, Robinson and Jones 1981, Potter et al. 1983).

1.3 Swine : Swine commonly carries C. coli and occasionally C. jejuni as intestinal commensal (Svedhem and Kaijser 1981, Luechtefeld and Wang 1982).

1.4 Sheep : C. jejuni is an important cause of epizootic infectious abortion in sheep. Surveys of the intestinal contents of sheep have shown that isolation of C. jejuni is common, but contamination of carcasses

occurs less often (Luechtefeld and Wang 1982, Hudson and Roberts 1982).

1.5 Dogs and Cats : C. jejuni and Campylobacter spp. are often present in the stools of both healthy dogs and those with diarrhea. It is now clear that C. jejuni may be isolated from both healthy and diarrheal dogs, isolation rates are higher in puppies than in mature dogs. (Blaser et al. 1980-d).

1.6 Other animals : Healthy rodents frequently excrete Campylobacters. Laboratory-raised hamsters, mice and rats, and wild rodents may excrete in their feces. C. jejuni has not been isolated from reptiles and other poikilotherms because C.jejuni will not multiply below 30°C. Campylobacter was found in 18% of healthy monkeys and 60% of monkeys with diarrhea (Fernie and Park 1977, Tribe et al. 1979).

2. Human reservoirs

In the developed countries, since asymptomatic excretion of Campylobacter is so uncommon (Blaser and Reller 1981). In developing countries, human carriage could play a larger role in the transmission of infection (Blaser et al. 1983-a).

3. Inanimate reservoirs

Campylobacter organisms found in water may be due to fecal contamination by wild or domestic animals. C. jejuni did not multiply when kept at several different

temperatures in stream water. C. jejuni survived for up to 4 weeks when kept at 4°C. However, survival at higher temperatures was reduced (Blaser et al. 1980-a). C. jejuni has been isolated from stream and river waters (Knill et al. 1982),from sea water (Knill et al. 1978). In England, river waters from a single site were sampled over the course of a year, isolations peaked during June and July (Khan 1982). In another study, Campylobacters were isolated from 50.4% of 540 riverine water samples, but only when Escherichia coli also was present. After heavy rains isolation rates diminished. Isolation rates were lower from brackish water than from fresh water, and in estuarial waters, isolation rates were also higher at low tide (Knill et.al. 1982). In seeding experiments, Campylobacters were found to survive in soil for at least 10 days and for 20 days when the ambient temperature decreased to 6°C (Lindenstruth and Ward 1948).

D. Transmission to Humans

Campylobacter spp. may be transmitted from its animal and inanimate reservoirs to humans by direct contact with contaminated animals or animal carcasses or indirectly through the ingestion of contaminated food or water; person-to-person transmission also can occur.

1. Direct animal contact :

Campylobacter enteritis has been reported in children and young adults who before their illnesses had close contact with infected puppies (Skirrow 1977, Blaser et al. 1978). Identical Campylobacter sero-or biotypes have been isolated from both animals and humans (Blaser et al. 1982-b). Puppies with diarrhea appear to be more important than adult dogs in transmitting C. jejuni to humans (Blaser et al. 1980-d, Svedhem and Kaijser 1981). Transmission of Campylobacter from cats appears to be common than from dogs (Gruffydd-Jones et al. 1980, Skirrow et al. 1980). Direct contact with domestic farm animals and their feces may also be important in transmitting infection (Blaser et al. 1980-c). In sheep and cattle C. jejuni may cause septic abortion (Smibert 1978).

2. Milkborne transmission

The first documented milkborne outbreak associated with a Campylobacter like organism occurred in 1938. In England and Wales, unpasteurized milk was identified as the vehicle of transmission of C. jejuni infection in 13 outbreaks involving an estimated 4500 persons in the period 1978-1980 (Robinson and Jones 1981). To demonstrate the disease potential of C. jejuni in milk, two volunteers drank milk experimentally contaminated with either 10^6 (Steele and McDermott 1978), or 500 (Robinson 1981) colony-forming units of C. jejuni; both developed typical illness. Milk experimentally inoculated with

Campylobacter and kept at 4°C yield viable organisms for up to 3 weeks (Blaser et al. 1980-a).

3. Foodborne transmission

Raw or undercooked poultry has been frequently suggested as a vehicle for foodborne Campylobacter enteritis (Svedhem and Kaijser 1981, Skirrow et al. 1981). Studies of traveller's diarrhea have shown that contaminated food and water are the most likely vehicles for Campylobacter infection (Merson et al. 1986, Tjoa et al. 1977).

4. Waterborne transmission

Potable water has been directly implicated in several large outbreaks of Campylobacter enteritis (Mentzing 1981, Vogt et al. 1982). In rural areas where surface water is used for drinking, communities and individuals may be at increased waterborne Campylobacter enteritis. In England and Iceland, C. jejuni has been isolated from both salt and fresh water sources by filtration and enrichment techniques. Fecal coliforms have always been isolated from specimens containing Campylobacter (Knill et al. 1978, Bolton et al. 1982, Steingrimson and Alfreosson 1982). Estuary water contained up to 230 colony forming units of C. jejuni per 100 ml, while in river water, counts were up to 36 colony forming units of C. jejuni per 100 ml (Bolton et al. 1982). Campylobacter enteritis can be acquired from drinking

contaminated water from mountain streams (Taylor et al. 1983).

5. Person-to-person transmission

In a Canadian study, an illness compatible with Campylobacter infection was documented in 18 of 72 houschold contacts of infected children in six of 24 families. The dates of onset suggest that both common-source exposure and person-to-person transmission had occured (Pai et al. 1979). In an outbreak at a nursery in Japan, where 35 children one to five years old became ill over a seven day period, only one episode of diarrheal illness, in a child's father, was thought to represent secondary spread (Itoh et al. 1980). Campylobacter proctitis has been reported in homosexual men who had passive anal intercourse and ora-lanal contact (Carey and Wright 1979, Quinn et al.1980).

6. Perianal transmission

Although most C.jejuni infections are associated with enteritis, bacteremia in pregnant women, as in pregnant sheep, may be associated with a severe systemic infection in the fetus. A woman who was 18 weeks pregnant had a three-week febrile illness without diarrhea or vaginal discharge which resulted in fetal death. C. jejuni was subsequently isolated from multiple maternal blood cultures, placenta, and fetal spleen (Gribble et al. 1981). A newborn child

delivered by caesarean section developed diarrhea on the third day of life. C. jejuni was isolated from the feces of mother and baby. A blood culture taken from the baby shortly after delivery yielded C. jejuni, suggesting that infection may have been acquired in utero (Blaser et al. 1983-a). In most cases, the neonate appears to acquire the infection during or shortly after delivery because of fecal contamination of the birth canal (Anders et al. 1981, Vesikari et al. 1981).

Epidemiology of the other Campylobacter spp. are unknown now. Further studies emphasizing the Microbiology, reservoirs or sources of infection, pathogenesis, clinical patterns, transmission and seroepidemiology of these organisms are need for more work to understand their epidemiology.

Diagnosis of Campylobacter infection

Rapid diagnosis of Campylobacter enteritis may be determined by dark field or phase contrast microscopy of freshly fecal specimens, searching for characteristic darting motility of the organism, which is recognizable by the trained microscopist (Paisley et al. 1982). Confirmation of the diagnosis is achieved by isolating organism from stool, or occasionally from blood. Chevrier et al. (1988) reported the application of molecular biology, DNA hybridization utilizing 2-acetyl aminofluorene,

were sucessful to identify clinically significant strains of Campylobacter isolated from human feces after a short primary culture (Chevrier et al. 1988). Serological testing may also be useful, and Black et al. (1988) showed a rise in IgA and IgM peak levels in volunteers at 11 days, although they did not find any significant elevation in IgG (Black et al. 1988).

Isolation of Campylobacter

The first isolation of Campylobacter(related vibrio) from fecal specimens was successful and reported in 1972 by Dekeyser et al. The fecal specimen was filtered through a 0.65 um-Millipore filter, which was plated on a blood thioglycollate agar medium(containing 25 I.U. of polymyxin B sulfate, 0.005 mg of novobiocin and 0.05 mg of actidione per ml) to isolate Campylobacter (Dekeyser etal. 1972). The method has not been generally used by diagnostic laboratories because it involved centrifugation steps and special apparatus which had to be sterilized. In this instance, Skirrow used selective technique for culturing Campylobacter in 1977. The isolation method was performed by using selective medium containing polymyxin B, vancomycin and trimethoprim, then antibiotic selective media were used preferably for culturing these bacteria directly from specimens (Skirrow 1977). Several selective media have been developed for Campylobacter isolation. The most commonly used selective media are Skirrow's, Butzler's

and Blaser's (Skirrow 1979, Butzler and Skirrow 1979, Blaser et al. 1979).

1. Skirrow's selective media consisted of Oxoid blood agar base No. 2, 7% of lysed horse blood, vancomycin (10 mg/ml), polymyxin B (2.5 IU/ml) and trimethoprim (5 mg/ml) (Skirrow 1977).

2. Butzler's selective media consisted of thioglycollate agar, 15% of defibrinated sheep blood, bacitracin (25 U/ml), colistin (10 U/ml), novomycin (5 ug/ml), actidione (50 ug/ml) and cefazolin (15 ug/ml) (Dekeyser et al. 1972, Butzler and Skirrow 1979).

3. Blaser's selective media were named Campy-BAP. It consisted of Brucella agar, 10% of defibrinated sheep blood, cephalothin (15 ug/ml), amphotericin B (2 ug/ml) and also the antibiotics using in Butzler's medium (Blaser et al. 1979).

Enrichment with 5% blood improved the recovery of the organisms, but more than 5% was not necessary (Blaser 1984). Blood-free containing antibiotics such as blood-free charcoal-based selective media have also been used successfully. The several supplements including charcoal, hematin, iron salts, sodium pyruvate, sodium metabisulfite etc., can effectively replace in media for growing Campylobacter. These supplements acted as quinching agents of photochemically generated toxin oxygen derivatives rather than as enrichment factors (Bolton et al. 1984, Karmali

et al. 1986, Goosens et al. 1986). Several enrichment media have been found to increase the number of Campylobacter isolates recovered (Rubin and Woodard 1983, Shimada and Tsuji 1986).

Some Campylobacters were inhibited by cephalothin or colistin that were contained in the selective media, or by incubation at 42°C (Fennelle et al. 1984, Steele et al. 1985, Tee et al. 1987). To correct this disadvantage, filtration technique was used again, Campylobacters would pass through a 0.45 um cellulose triacetate filter placed on the surface of antibiotic free blood agar plate and plate was incubated at 37°C (Steele et al. 1985). Taylor et al. (1987) found that there was nearly a twofold increase in the Campylobacter isolation rate when the 0.45 um-membrane filter was used and compared with standard plating on selective media (Table 4).

Biotyping

A biotyping scheme for Campylobacter has been proposed and developed. Skirrow and Benjamin proposed a simple biotyping scheme based on hippurate hydrolysis, hydrogen sulfide production in iron-contaning medium, and sensitivity to nalidixic acid (Skirrow and Beniamin 1980-b). Hebert et al., proposed a scheme based on hippurate hydrolysis, DNA hydrolysis and growth on charcoal yeast extract agar (Hebert et al. 1982). Weaver et al., proposed

a scheme based on hippurate hydrolysis, DNase activity and alkaline phosphatase activity (Weaver et al. 1982). Lior proposed a biotyping scheme for C. jejuni, C. coli, and C. laridis strains and the method is based on hippurate hydrolysis, rapid H_2S production, and DNA hydrolysis (Table 3, Lior 1984).

Serotyping

Serotyping of the organism was used for epidemic evaluation. The two most widely used serotyping scheme for C. jejuni and C. coli were the Lior system and the Penner system. The Lior system was developed based on slide agglutination of heat-labile (flagella, H) antigen with antisera. It has been further extended to 62 serotypes, and the technique has been greatly simplified for screening purposes by the initial use of four polyvalent pools which contain antisera to the 25 most common serotypes representing 90% of the typable isolates from many areas of the world. Confirmation of the serotype was need by using the monospecific absorbed antisera (Lior 1984). The Penner system identified soluble, heat-stable (somatic, O) antigens by passive hemagglutination. This system using unabsorbed antisera. (Penner and Hennessy 1980). The Lior method was simpler to perform and gave more rapid results than did the Penner method. Campylobacter isolates frequently reacted in multiple antisera with the Penner method, whereas multiple reaction were rare with the Lior

method. Thus the results were easier to interprete with the Lior system (Patton et al. 1985).

Treatment

Campylobacter enteritis is usually self-limited and short duration, fluid replacement without antibiotics is the most important and sufficient therapy. The antibiotic treatment is indicated when the patients are febrile, bloody prolonged diarrhea or severe Campylobacter enteritis. Erythromycin is the recommended therapy because most Campylobacter strains are susceptible to it. The role of antibiotics is controversial. In a number of clinical trials performed in adults and children, erythromycin has not been shown to significantly alteration the clinical course of Campylobacter infection (Karmali et al. 1979, Anders et al. 1982, Taylor et al. 1987, Black et al. 1988). However, results of one study found that when Peruvian children with bloody diarrhea due to Campylobacter isolates were treated early in the course of illness with erythromycin, they improved earlier than children given placebo (Salazar-Lindo et al. 1986). Patients with bacteremia or septic complications have been treated successfully with an aminoglycoside or chloramphenicol. C. jejuni is usually sensitive in vitro to erythromycin, tetracycline, aminoglycosides and chloramphenicol, but is often resistant to penicillin, ampicillin, and trimethoprim/sulfamethoxazole (DuPont et al. 1987).

In Thailand, erythromycin resistance is common among Campylobacter strains in Bangkok, especially in an institutional setting, which may account for the lack of efficacy of erythromycin for treatment (Taylor et al. 1987).