Campylobacter enteritis

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Campylobacter jejuni/coli **has recently become recognized as a common bacterial cause of diarrhea. Infection can occur at any age. The usual incubation period of campylobacter enteritis is 2 to 5 days. Fever, diarrhea and abdominal pain are the most common clinical features. The stools frequently contain mucus and, a few days after the onset of symptoms, frank blood. Significant vomiting and dehydration are uncommon. A rapid presumptive laboratory diagnosis may be made during the acute phase of the illness by direct phase-contrast microscopy of stools. Isolation of the organism from stools requires culture in a selective medium containing antibiotics and incubation under reduced oxygen tension at 42°C. The organism persists in the stools of untreated patients for up to 7 weeks following the onset of symptoms. Erythromycin may produce a rapid clinical and bacteriologic cure, and should be used to treat moderately to severely ill patients as well as patients with compromised host defences. The emergence of erythromycin-resistant strains requires close monitoring.**

The epidemiologic aspects of campylobacter enteritis will be fully understood only when methods become available for differentiating strains of *C. jejuni/coli*.

The historical background and current knowledge of campylobacter enteritis are reviewed in this paper.

On a récemment reconnu le *Campylobacter jejuni/coli* **comme une cause bactérienne fréquente de la diarrhée. Cette infection peut survenir à tout âge. La période d'incubation habituelle de l'entérite au campylobacter est de 2 à 5 jours. Les symptômes cliniques les plus fréquents comprennent la fièvre, la diarrhée et les douleurs abdominales. Les selles contiennent souvent du mucus et, quelques jours après l'apparition des symptômes, des traces manifestes de sang. Des vomissements et une déshydratation d'importance sont rares. Pendant la phase aiguë de la maladie un diagnostic de présomption rapide peut être porté en laboratoire par microscopie directe à contraste de phase des selles. L'isolation du microorganisme dans les selles exige la culture dans un milieu sélectif contenant des antibiotiques et l'incubation à 42°C sous pression d'oxygène réduite. L'organisme persiste dans les selles des patients non traités jusqu'à 7 semaines après l'apparition des symptômes. L'érythromycine peut entraîner une guérison clinique et bactériologique rapide, et elle doit être utilisée chez les patients modérément ou grièvement malades tout comme chez les patients ayant des moyens de défense diminués. L'émergence de souches résistantes à l'érythromycine exige une surveillance étroite.**

Les aspects épidémiologiques de l'entérite au campylobacter ne pourront être bien connus que lorsque des méthodes seront développées pour différencier entre les souches de *C. jejuni/coli*.

Dans cette étude on a passé en revue les données historiques au sujet de l'entérite au campylobacter; de plus, on a regardé de près nos connaissances actuelles de ce type d'entérite.

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Campylobacters are small, microaerophilic, oxidase-positive, gram-negative bacteria that are characteristically curved, S-shaped or spiral (Fig. 1). They have a single polar flagellum at one or both ends of the cell and move in a characteristic darting, corkscrew-like manner.[1]

Campylobacters were originally classified among the vibrios, the type species *Campylobacter fetus* being known as *Vibrio fetus*. The new generic term *Campylobacter* ("curved rod" in Greek) was proposed by Sebald and Véron[2] in 1963 on the grounds that the microaerophilic vibrios were different biochemically and serologically from the classical cholera and halophilic vibrios, and had a significantly different deoxyribonucleic acid base-pair ratio from both the latter.

Kreb's cycle intermediates and amino acids serve as primary energy sources for these organisms.[1] Carbohydrates are not utilized, and the subdivision of the genus *Campylobacter* on biochemical grounds is unsatisfactory. A lot of confusion has arisen over the use of different nomenclatures for the species and subspecies (Table I). The strains associated with gastroenteritis in humans correspond to the *C. jejuni* and *C. coli* (*C. jejuni/coli*) group of Véron and Chatelain,[3] the *C. fetus* ss. *jejuni* of Smibert[4] and the "related" vibrios of King.[5] All these names are used in the literature to refer to strains causing gastroenteritis in hu-

mans, and sometimes these strains are referred to simply as *Vibrio fetus*. In this paper the nomenclature of Véron and Chatelain is used unless otherwise specified.

Historical background

Microaerophilic vibrios were first recognized in 1913 by McFadyean and Stockman,[6] who reported on the association of these organisms with abortion in sheep and cattle. This association was confirmed in 1918, when Smith[7] isolated similar organisms from aborted bovine fetuses. In 1919 Smith and Taylor[8] designated these organisms *Vibrio fetus*.

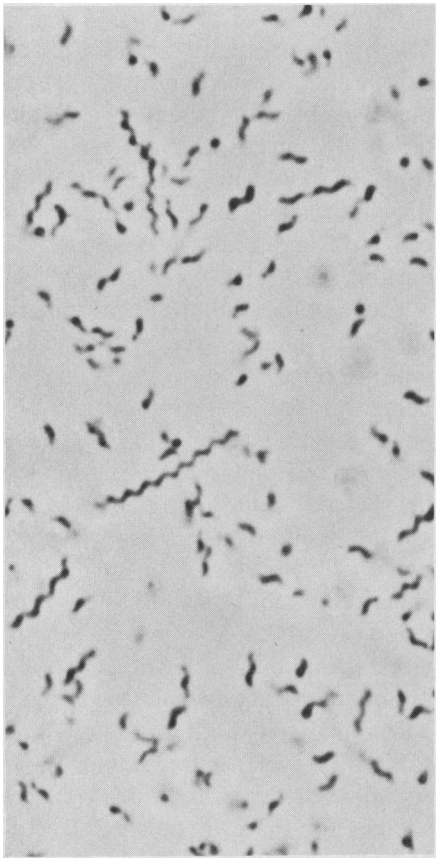

FIG. 1—*Campylobacter jejuni/coli* in 18-hour culture examined by phase-contrast microscopy (×2000).

In 1931 Jones and Little[9,10] implicated microaerophilic vibrios as the cause of a serious and occasionally fatal condition of cattle known as winter scours or winter dysentery. This disease, characterized by severe diarrhea and marked suppression of milk production, initially occurred in a few cattle and subsequently spread throughout the herd. The diarrheal stools of affected animals contained blood and mucus, and occasionally the animals exhibited signs of abdominal pain. The illness was usually self-limiting and subsided within a few days. At autopsy marked inflammatory changes were noted in the small bowel mucosa, from which microaerophilic vibrios were subsequently cultured. The disease could be reproduced in healthy animals by feeding them a pure culture of the microaerophilic vibrios designated *Vibrio jejuni* by Jones, Orcutt and Little.[11] Challenge experiments suggested an incubation period of about 3 days. Winter scours in cattle, as described by Jones and colleagues, bears marked similarities to campylobacter enteritis in humans. Curiously, winter scours remains an important problem in cattle, but its association with microaerophilic vibrios is no longer recognized. Although the precise cause of the disease remains obscure, the condition is now considered by veterinarians to be due to viral agents.[12]

In 1944 Doyle[13] suggested that the etiologic agent of swine dysentery was also a microaerophilic vibrio; Doyle termed the organism *Vibrio coli*. However, the etiologic role of *V. coli* in swine dysentery is very controversial, and the true causal agent of this condition is now thought to be a spirochete, *Treponema hyodysenteriae*.[1]

The first association of microaerophilic vibrios with diarrheal disease in humans was reported in 1946 by Levy,[14] who described a large institutional outbreak of gastroenteritis in Illinois. Vibrio-like organisms were seen microscopically in stained smears of feces from 20% of the patients but could not be cultured from the stools. However, the recovery of microaerophilic vibrios from blood cultures of 13 of 39 patients strongly implicated these organisms as the cause of the diarrhea. Epidemiologic evidence pointed to milk as the possible source of the outbreak. Levy suggested that the microaerophilic vibrios isolated in this outbreak were perhaps the same organisms that Jones and colleagues had associated with winter scours in cattle.

About 10 years later King[5] compared the characteristics of microaerophilic vibrios obtained from various sources. Among several isolates from human blood cultures she was able to distinguish two distinct groups of organisms. One group corresponded to the then existing descriptions of *V. fetus*. The second group, although closely related to *V. fetus*, differed in that they had an optimum growth temperature that was higher than normal; King therefore called this group of organisms "related" vibrios. She noted that "related" vibrios were virtually always isolated from blood cultures of patients with gastroenteritis, and she suggested that these organisms were perhaps more common as agents of gastroenteritis than was generally recognized at that time.

Table I — Nomenclature and characteristics of campylobacters

Nomenclature			Characteristics				
				Growth at			
Véron and Chatelain[3]	Smibert[4]	King[5]	Catalase	25°C	37°C	42°C	Growth in 1% glycine
C. fetus ss. *fetus*	*C. fetus* ss. *intestinalis*		+	+	+	−	+
C. fetus ss. *venerealis*	*C. fetus* ss. *fetus*	*Vibrio fetus*	+	+	+	−	−
C. jejuni/coli	*C. fetus* ss. *jejuni*	"Related" vibrios	+	−	+	++	
C. sputorum	*C. sputorum*		−				

Over the ensuing 15 years there appeared in the literature a number of sporadic case reports[15-21] describing patients with enteric symptoms from whom "related" vibrios were isolated from blood cultures. Blood and mucus were frequently noted in the stools.[22]

The first successful attempt to isolate campylobacters from the stools was made in 1971 by Cooper and Slee[23,24] in Australia. These workers noted that a campylobacter isolated from the blood culture of a patient with diarrhea was resistant to cephalothin. Cephalothin discs were therefore applied to the surface of a blood agar plate inoculated with the patient's feces. Following incubation of the culture under microaerophilic conditions, campylobacter colonies were noted within the zone of the cephalothin disc.

In 1972 Dekeyser and colleagues[25] described a method for isolating campylobacters from the stools that consisted of selectively filtering stool suspensions through a 0.65-μm membrane filter (Millipore®). Whereas most fecal organisms were too large to pass through the filter, campylobacters could be filtered and subsequently cultured in solid media. With this method Dekeyser and colleagues were able to isolate "related" vibrios (*C. jejuni/coli*) from the stools of two adults with diarrhea.

The following year Butzler and associates[26] used the selective filtration technique to examine the stools of a large number of patients with diarrhea. They were able to isolate *C. jejuni/coli* from 5.2% of 800 children and 4.0% of 100 adults with diarrhea. This contrasted with an isolation rate for this organism of 1.3% in 1000 children without diarrhea. These findings were clearly significant but appeared to go unnoticed for another 4 years.

In 1977 Skirrow[27] described a method for recovering campylobacters from the stools that eliminated the need to use the somewhat cumbersome filtration technique. His method consisted of inoculating stools directly onto a selective culture medium containing antibiotics. Skirrow examined the stools in about 800 sporadic cases of diarrhea and found that *C. jejuni/coli* was the most common enteric bacterial pathogen cultured. In contrast, the organism could not be isolated from the stools of approximately 200 patients without diarrhea.

The high frequency of campylobacter enteritis in Skirrow's series of patients has been confirmed in several countries.

Incidence and geographic distribution

Campylobacter enteritis has been reported from Belgium,[26,28] the United Kingdom,[27,29-34] Canada,[35-40] Holland,[41,42] the United States,[5,14-18,43-48] Sweden,[49] Rwanda,[50] Zaire,[51] Australia[23,24,52,53] and South Africa,[54-56] which indicates that this disease is widely distributed in tropical as well as temperate areas of the world.

C. jejuni/coli has been cultured from between 5% and 6% of patients with diarrhea in Belgium.[26,28] Skirrow,[27] in the United Kingdom, examined stools from about 800 patients with diarrhea, and isolated *C. jejuni/coli* from 7.1% and other enteric bacterial pathogens from 6.2% of these cases; thus, *C. jejuni/coli* appeared to be more common than all other enteric bacterial pathogens together. Similar findings have been reported from other laboratories in the United Kingdom.[30-34] Severin,[41] in Holland, examined the stools of 584 patients with diarrhea, and isolated *C. jejuni/coli* from 11% and *Salmonella* sp. from 10%. Steele and McDermott,[52] in Australia, isolated *C. jejuni/coli* from 5.8% of patients with suspected infectious diarrhea. In a recent South African study[56] *C. jejuni/coli* was cultured from about 30% of black infants with diarrhea, but the frequency of this organism in the stools of asymptomatic children was also high.

C. jejuni/coli is a very common bacterial cause of diarrhea in Canada.[36,40] The relative frequency of different enteric bacterial pathogens cultured from children attending the Hospital for Sick Children, Toronto, over a 1-year period (Nov. 1, 1977 to Oct. 31, 1978) is shown in Table II. Clearly *C. jejuni/coli* is a common and a cosmopolitan enteric pathogen.

Age and sex distribution

Campylobacter enteritis affects all age groups.[26,27,29,30] Although it is difficult to estimate the true age incidence, it has been suggested that the incidence is highest in young children.[26,27] The male:female ratio of the 100 children with this disease seen at our hospital over the 1-year period was 3:2.

Clinical features

Skirrow[27] has estimated from circumstantial evidence that the incubation period of this disease ranges from 2 to 11 days. Evidence from other reports suggests that the typical incubation period is about 2 to 5 days.[34,47,52,57,58]

The most common clinical features of campylobacter enteritis[27,36] are fever, bloody diarrhea and abdominal pain. Vomiting and dehydration are not prominent.[26,27,36] Fever may be accompanied by marked malaise, headache, musculoskeletal pain and, sometimes, rigors and delirium.[27,36,47] Some patients, particularly infants, may remain afebrile.[26,36] Diarrhea usually occurs at the onset of illness but may be preceded by a variable period of abdominal pain.[36] Typically the diarrhea is mild to moderate, but it may be profuse, watery and frequent. A recent prospective clinical study of Canadian children[36] showed that about 90% of patients had blood in

Table II—Relative frequency of campylobacter enteritis at the Hospital for Sick Children, Toronto, between Nov. 1, 1977 and Oct. 31, 1978

Pathogen	No. of children
C. jejuni/coli	100
Salmonella typhimurium	64
S. typhi	6
Other *Salmonella* sp.	70
Enteropathogenic *Escherichia coli* serotypes	61
Shigella sp.	29
Yersinia enterocolitica	12

the stools and that the blood appeared characteristically a few days after the onset of symptoms.

Abdominal pain is an early symptom, which may precede the diarrhea by as much as 2 weeks.[36] Some patients have abdominal pain as the only major symptom and may be admitted to a surgical ward because of suspected appendicitis.[31] The pain is typically periumbilical or epigastric, intermittent and colicky, and may radiate to the right iliac fossa or the lower abdomen. It is most prominent just prior to defecation and is relieved by the passage of stool or flatus.[27,36]

Although significant dehydration and vomiting are not usually prominent in this condition, they may be severe and contribute to a fatal outcome.[21,59]

In most cases campylobacter enteritis is a mild to moderate self-limiting illness that subsides within a week. In some cases mild abdominal pain may persist for up to 6 weeks after the onset of symptoms,[36] and occasionally the illness is persistent or relapsing.[15,16,27,60] Skirrow[27] found that a premature return to the ingestion of solid food was associated with recurrence of symptoms. In the recent Canadian study[36] relapse in some hospitalized patients was associated with a nosocomially acquired rotavirus infection. Severe illness may occur in patients whose immune mechanisms are compromised, and death has occurred in patients with cirrhosis,[17,19] malnutrition[33,55] and lymphoma.[23] Recently campylobacter enteritis was associated with arthritis in a patient in whom tissue typing showed an HLA-B27 pattern.[61]

A study of campylobacter enteritis in children attending our hospital showed that biochemical abnormalities were not a feature and that leukocytosis was present in less than half the patients.[36]

Laboratory diagnosis

A rapid presumptive diagnosis of campylobacter enteritis can be made during the acute phase of the illness by direct phase-contrast microscopy of stools.[36] The diagnosis can be confirmed by isolation of *C. jejuni/coli* directly from stools cultured onto a selective medium containing antibiotics. Skirrow's medium consists of a special nutrient agar base (Oxoid blood agar base no. 2), with 7% lysed horse blood, containing vancomycin (10 μg/ml), trimethoprim (5 μg/ml) and polymyxin B sulfate (2.5 IU/ml).[27] We have found that by increasing the concentration of polymyxin B sulfate to 50 IU/ml in a modified Skirrow's medium (containing Columbia agar base, Grand Island [New York] Biological Company) better suppression of resistant fecal flora can be achieved.[36] The selective medium used by Butzler[28] contains bacitracin (25 IU/ml), novobiocin (5 μg/ml), actidione (50 μg/ml), colistin (10 IU/ml) and cephalothin (15 μg/ml). Wang, Blaser and Cravens[62] have found it helpful to add amphotericin B (2.0 μg/ml) to Skirrow's selective medium to suppress yeasts.

C. jejuni/coli is a strict microaerophile and grows best in an atmosphere in which the oxygen tension has been reduced to between 5% and 10%.[63] Such an atmosphere can be achieved by evacuating two thirds of the air from an anaerobic jar (without catalyst) and replacing the evacuated air with a mixture of carbon dioxide and nitrogen or carbon dioxide alone. It is best to incubate the jars at 42°C, the optimal growth temperature of *C. jejuni/coli*. Cultures are usually positive after 48 hours of incubation and often after 24 hours.

Transport of clinical specimens to the laboratory does not appear to require special precautions. Hartigan and colleagues[38] were able to culture *C. jejuni/coli* from stools transported in buffered glycerol saline that had been been in transit for 1 to 8 days.

A number of serologic tests have been used to demonstrate significant antibody responses to *C. jejuni/coli* in patients with campylobacter enteritis. These include the agglutination test,[27] the complement fixation test,[51] a serum bactericidal assay[36] and an indirect immunofluorescence test.[47]

Significant serologic responses have been demonstrated in patients with positive stool cultures.[27,36,47,51] A serologic diagnosis in patients with negative cultures can be made only during an outbreak of diarrhea in which an isolate of *C. jejuni/coli* is available from at least one of the affected patients.[34] Such a diagnosis cannot be made in sporadic cases of diarrhea, nor can seroepidemiologic surveys be carried out, because there is considerable serologic heterogeneity among *C. jejuni/coli* isolates (our unpublished observations). Detection of antibodies to a common *C. jejuni/coli* antigen or a pool of different serotypes is not yet practical.

Excretion of the organism in stools of convalescing and asymptomatic persons

Untreated children continue to excrete *C. jejuni/coli* in their stools for a few weeks following the onset of symptoms.[36,40] The incidence of asymptomatic excretion of *C. jejuni/coli* has been estimated at 1.3% in Belgian children[26] and 13% in black South African children.[56] The extent to which convalescing and asymptomatic excretors of *C. jejuni/coli* constitute a public health hazard is not known.

Treatment

Most patients with campylobacter enteritis have a mild to moderate illness that resolves spontaneously in a few days. A short course of intravenous fluid replacement may be required in the more severely ill patients, but most are able to take fluids orally.[36] A premature return to the ingestion of solid foods may result in the recurrence of symptoms.[27] Antidiarrhea agents such as diphenoxylate hydrochloride (Lomotil®) and kaolin–pectin compounds should be avoided. These agents may adversely affect patients with other infectious diarrheas,[64] and anecdotal evidence from the literature[16,47] and from our experience suggests that they may also adversely affect patients with campylobacter enteritis.

Antibiotic susceptibility data[36,65,66] indicate that *C. jejuni/coli* is usually highly sensitive to erythromycin, furazolidone, gentamicin and tetracycline, sensitive to chloramphenicol, variably sensitive to ampicillin and resistant to a number of cephalosporins.

Erythromycin has been recommended as the preferred antibiotic for the treatment of campylobacter enteritis.[27,65] It has been clinically successful in the treatment of this condition and has been shown to rapidly eradicate *C. jejuni/coli* from the stools.[36,44] However, a controlled clinical trial has not been carried out. Concern has recently been expressed about erythromycin resistance of *C. jejuni/coli*.[67] Moderate resistance (minimum inhibitory concentration [MIC] of erythromycin 3.12 μg/ml) was noted in about 5% of strains tested by Butzler, Dekeyser and Lafontaine,[65] and recently Vanhoof and colleagues[66] have described a few strains for which the MIC was greater than 50 μg/ml. Walder and Forsgren[67] have found 10% of their strains to be highly resistant to erythromycin. However, a frequency of erythromycin resistance of less than 1% has been reported from the United Kingdom,[68] and in a recent Canadian survey[36] no erythromycin-resistant strains of *C. jejuni/coli* were found. Thus, while it is clear that erythromycin appears to be a highly effective agent in the treatment of campylobacter enteritis, a substantial increase in the frequency of resistant strains will reduce its reliability as the drug to be used before the results of susceptibility tests are available.

Furazolidone also appears to be useful for the treatment of campylobacter enteritis[65,66] but is not marketed in many countries.

Gentamicin administered parenterally has been successful in the treatment of *C. jejuni/coli* septicemia.[66] The value of oral therapy with nonabsorbable antibiotics such as gentamicin in campylobacter enteritis is not known. Butzler and associates[65] have treated some cases successfully with neomycin administered orally.

C. jejuni/coli is usually sensitive to therapeutically achievable blood concentrations of chloramphenicol, and this agent could be used in selected cases in which the organism is resistant to other suitable antibiotics. However, the potentially serious adverse side effects of chloramphenicol are likely to limit its use. In one patient treated with chloramphenicol therapeutic failure was associated with an eightfold increase in the resistance of the campylobacter to chloramphenicol.[23]

Most strains of *C. jejuni/coli* are sensitive to tetracycline, and this antibiotic has been used successfully in the treatment of campylobacter enteritis.[65,66] Vanhoof and colleagues[66] found 5% of strains to be resistant to tetracycline, while we found 10% of strains to be resistant to this drug.[36] While tetracycline is contraindicated in children, it should be of value in adults infected with sensitive strains.

There is a high frequency of resistance of *C. jejuni/coli* to ampicillin and penicillin G,[36,41,66] and the use of these antibiotics clinically has been associated with therapeutic failure.[66] Severin[41] showed that ampicillin resistance of *C. jejuni/coli* was associated with the production of β-lactamase. The mechanism of resistance of *C. jejuni/coli* to various cephalosporins is unknown.

In summary, erythromycin is the preferred drug for the treatment of campylobacter enteritis. While it can produce a rapid clinical and bacteriologic cure, the illness is usually mild and most patients recover without antibiotic therapy. Erythromycin therapy should not be withheld from patients with moderate to severe illness. The value of antibiotics in the treatment of patients with mild symptoms as well as convalescent or asymptomatic excretors of *C. jejuni/coli* is likely to be related to the extent to which such patients constitute a public health hazard.

Periodic surveys of antibiotic susceptibility patterns need to be conducted to determine the frequency and changes in patterns of resistance of *C. jejuni/coli* to various antibiotics. Attempts should also be made to standardize methods of antibiotic susceptibility testing so that results can be compared between laboratories and between countries.

Epidemiologic aspects

Organisms indistinguishable, by presently available criteria, from strains of *C. jejuni/coli* that affect humans have been isolated from many mammalian and avian species.[1] Chickens were first suspected of being sources of campylobacter enteritis in humans by King,[5,17] who found that isolates of microaerophilic vibrios from cases of avian infectious hepatitis were indistinguishable from human strains of *C. jejuni/coli*. She also reported a fatal case of campylobacter enteritis in a chicken farmer, and suggested that the infection in this man may have resulted from occupational exposure to the organism.[5,17]

More recently Bruce, Zochowski and Ferguson[33] isolated *C. jejuni/coli* from 62% of 63 chicken carcasses from a common source. They also isolated *C. jejuni/coli* from 114 (68%) of 167 cecal samples from apparently previously healthy poultry. Smith and Muldoon[69] isolated this organism from commercially processed poultry. Severin[41] has cultured *C. jejuni/coli* from chicken feces and from crates used to transport slaughtered chickens. Butzler and associates[70] have demonstrated experimental infection of the bowel wall in chicks fed *C. jejuni/coli* isolates from humans. Hayek and Cruickshank[34] described an outbreak of campylobacter enteritis possibly related to ingestion of contaminated chicken.

C. jejuni/coli has also been isolated from other birds, such as pigeons, blackbirds, starlings and sparrows.[1] In one case of campylobacter enteritis in a human the patient gave a history of contact with canaries, and *C. jejuni/coli* was subsequently isolated from the canary cage, although no illness was noted in the birds.[31]

The first case of campylobacter enteritis associated with contact with a sick dog was described by Wheeler

and Borchers[16] in 1961. They reported a case of bloody diarrhea in a 9-week-old boy who had a positive blood culture for *C. jejuni/coli*. The infant had had close contact with the family puppy, which also had bloody diarrhea. Vibrio-like organisms were seen in a stained smear of feces from the puppy, but the organisms could not be isolated in culture. The association of human illness with dog contact was also reported by Skirrow[27] and by Lindquist, Kjellander and Kosunen,[49] who isolated *C. jejuni/coli* from symptomatic pet dogs of patients with campylobacter enteritis. Blaser and colleagues[47] recently provided strong epidemiologic evidence linking *C. jejuni/coli* infection in humans to contact with dogs with campylobacter enteritis. Peel and McIntosh[71] described campylobacter enteritis occurring in both a nurse and her dog after they had eaten the same luncheon meat. The dog died following severe disseminated *C. jejuni/coli* infection. Experience from one veterinary clinic[72] suggested a high incidence of campylobacter-associated diarrhea in dogs. There is, thus, increasing epidemiologic evidence that campylobacter enteritis also affects dogs, but the extent to which this contributes to infection in humans is not known. Although natural infection is known to occur in dogs, successful experimental infection of these animals has not so far been reported.[58]

Winter scours in cattle was at one time thought to be due to campylobacters,[9-11] but this association is no longer recognized.[12] *C. jejuni/coli* can, however, be isolated from the feces of cattle.[1] Unpasteurized milk was first incriminated as a source of campylobacter infection in humans by Levy[14] in 1946. More recently raw milk was considered to be the vehicle of infection in a small outbreak of diarrhea in Colorado.[46] Recent reports from the United Kingdom[73-77] have implicated unpasteurized milk in several large outbreaks of campylobacter enteritis, one of which[76] affected more than 2000 persons. It is clear from these reports that unpasteurized milk must now be considered an important source of infection with *C. jejuni/coli* in humans.

C. jejuni/coli occurs as a commensal in the intestinal tract of sheep, and occasionally may be responsible for abortion in pregnant ewes.[1] Duffell and Skirrow[57] recently described campylobacter enteritis in a shepherd who 2 days previously had been lambing pregnant ewes. The lambs were either moribund or dead at birth, and *C. jejuni/coli* was cultured from the lambs as well as from the shepherd. This case provides a good epidemiologic link between abortion in ewes and "shepherd's scours". Smibert[1] has reported the isolation of *C. jejuni/coli* from birds such as pigeons, starlings, sparrows and blackbirds that are usually found around sheep pens and barns. He suggested that droppings from such birds might play an important role in the epidemiology of abortion in sheep.

C. jejuni/coli has also been isolated from rodents,[78] monkeys,[70] pigs[1] and cats.[47,73] Pearson and Knill and their associates[31,79] isolated *C. jejuni/coli* from samples of sea water and fresh water. A waterborne source of infection was thought to be responsible for a recent outbreak of diarrhea in Vermont.[45]

Clearly *C. jejuni/coli* is widely distributed in the animal kingdom and may also be present in environmental sources of water. It will not be possible to understand fully the epidemiologic aspects of *C. jejuni/coli* infection until suitable methods become available for differentiating strains. Campylobacters are rather inert biochemically; hence, biotyping is unlikely to help in differentiating strains. The presence of considerable serologic heterogeneity among *C. jejuni/coli* isolates suggests that the most practical strain differential system will result from the development of effective serotyping methods. Bryner and colleagues[80] have isolated bacteriophages from campylobacters and suggested that phage-typing may become a useful adjunct to serotyping. But despite the lack of a typing system, circumstantial evidence is strengthening the concept that the strains causing infection in humans may be the same as those found in domestic and farm animals, poultry and wild birds. The complex chains of transmission that result in the infection of extremely diverse species within the animal kingdom may be difficult to unravel. However, the varied distribution of *C. jejuni/coli* could be explained if we assume that wild birds and poultry are the primary reservoirs of this organism. The thermotolerance of *C. jejuni/coli* is compatible with adaptation to a habitat in avian species. Smibert[1] has isolated *C. jejuni/coli* from wild birds and has emphasized the possible epidemiologic link of abortion in sheep to the contact of these animals with the droppings of wild birds. It is possible that a similar epidemiologic link contributes to infection in other animals, such as cattle, dogs and cats. Pearson and associates[31] suggested that wild birds could also easily contaminate water supplies with their droppings, but that such contamination could also result from sewage pollution.

Ingestion of infected or contaminated foodstuffs, such as poultry and milk, probably accounts for most cases of infection in humans; a smaller proportion are probably due to close contact with domestic animals.

The extent to which infection in humans may be acquired by direct person-to-person contact is not known. Butzler and colleagues,[28,60,66] observing outbreaks of campylobacter enteritis in five day-care nurseries in the Brussels region, considered that infection was spread by person-to-person contact. If future studies show that this is indeed an important mode of transmission, particularly in certain high-risk settings, such as day-care nurseries, then the indications for antibiotic therapy will need to be extended to include selected asymptomatic and convalescent excretors of *C. jejuni/coli*.

There are insufficient data at present to draw conclusions about the seasonal incidence of campylobacter enteritis, although it is suggested that the incidence is highest in the summer.[28]

Pathological and pathogenetic aspects

The pathological manifestations of *C. jejuni/coli* infection in humans suggest that the disease should more correctly be referred to as an enterocolitis. Hemorrhagic lesions in the jejunum and ileum have been noted at autopsy,[17,21] and inflammation of the ileum has been observed during laparotomy.[27] Small bowel disease is also reflected in the frequent occurrence of colicky central or upper abdominal pain.[27,36] The organism has been recovered from aspirates taken from different levels of the small bowel.[60] *C. jejuni/coli* infection has also been associated with mesenteric lymphadenitis and acute appendicitis.[31] The frequency of blood, pus and mucus in the stools[26,27,36] suggests that the large bowel is also commonly involved. Sigmoidoscopic and radiologic investigations of the large bowel in adults with campylobacter enteritis have revealed inflammatory changes in the colonic mucosa that are often indistinguishable from changes due to other causes of inflammatory bowel disease.[41,81]

The pathogenesis of this disease requires further investigation. Evidence for the pathogenicity of *C. jejuni/coli* can be summarized as follows:

- Studies of symptomatic and asymptomatic patients have shown that the presence of *C. jejuni/coli* in the stools is clearly associated with disease.[26,27]
- The organism disappears from the stools during convalescence.[36]
- *C. jejuni/coli* has been isolated from blood cultures of patients with diarrhea.[5,14-21,25]
- Significant antibody titres develop in patients with campylobacter enteritis.[27,36]
- Clustering of symptomatic cases occurs.[14,34,60,66,73-75]
- Diarrhea and abdominal pain resulted in a human volunteer who ingested a pure culture of *C. jejuni/coli*,[52] and also in a laboratory worker who accidentally infected himself with the organism.[58]
- Treatment with an antibiotic to which the organism is sensitive in vitro leads to the rapid disappearance of *C. jejuni/coli* from stools and the clinical resolution of symptoms.[36]
- There is evidence to suggest that in dogs infected with *C. jejuni/coli* a diarrheal illness develops that is similar to the illness in humans.[16,27,47,49]
- Stools from patients with campylobacter enteritis have been examined for other bacterial pathogens, viruses and parasites. No other known pathogens have been detected in most patients with campylobacter enteritis.[36]

Conclusion

C. jejuni/coli is now firmly established as an important cause of diarrhea; the incidence of campylobacter enteritis is comparable to that of *Salmonella* enteritis. The illness can often be recognized clinically. Unusual and postinfection manifestations may yet become apparent as the full clinical spectrum begins to unfold. The laboratory diagnosis of campylobacter enteritis has become relatively straightforward. Patients can be successfully treated with antibiotics if necessary. The sources and modes of transmission of *C. jejuni/coli* will only become clear when an effective method becomes available for typing isolates of this organism. The pathogenesis of this infection as well as the nature and duration of the host's immune response require further study.

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