SECTION II

Excreted Bacteria

12

Campylobacter and *Campylobacter* Enteritis

THREE CHAPTERS of this book describe recently recognized causes of diarrhea that are now believed to be of major importance throughout the world. These are the rotaviruses and other viruses (chapter 11); the various pathogenic forms of *Escherichia coli* (chapter 13); and some bacteria of the genus *Campylobacter*, which are described in this chapter. Knowledge of *Campylobacter* as a cause of diarrhea in man is recent and limited. The first isolations of the organism from stools of patients with diarrhea came in 1971 in Australia (Cooper and Slee 1971) and in 1972 in Belgium (Dekeyser and others 1972). It was only during 1977 that the scale of the problem became clear in Europe; information on *Campylobacter* enteritis in the USA is even more recent. Very little is yet known about this infection in the developing countries. Several comprehensive reviews have been published since 1977 (Butzler 1978; Butzler and Skirrow 1979; Karmali and Fleming 1979; Skirrow 1977; Smibert 1978).

Description of Pathogen and Disease

The delayed recognition of the important role of *Campylobacter* as a cause of diarrhea is due to the problems of isolating these bacteria. As strict aerobes growing under low oxygen levels, they will not grow under the aerobic or anaerobic growth conditions used in most laboratories; furthermore, unless selective growth systems are used they are overgrown by other bacteria present in feces. Now that these difficulties have been overcome, it seems that campylobacters are the single most common bacterial cause of diarrhea in several countries (table 12-1). However, the mechanism by which campylobacters cause diarrhea remains obscure. Although they are commonly isolated from fecal specimens, their significance as pathogens is not always clear.

Identification

Campylobacter enteritis (also called campylobacteriosis) is an enteric infection caused by *Campylobacter fetus* subspecies *jejuni*. The consequences of the infection vary from asymptomatic excretion or mild symptoms to severe disease. In some affected patients the diarrhea is profuse and watery and is often accompanied by strong abdominal pain, headache, and fever. Dysenteric stools containing blood and mucus are fairly common, especially in children. Vomiting is uncommon. Illness usually persists for a few hours to a few days, but in some patients it may continue for weeks. Rehydration and electrolyte replacement are sometimes required. Antibiotic therapy is usually recommended in severe cases, although its efficacy is not proven. Complications include an abdominal pain of such intensity that acute peritonitis is diagnosed and surgery often undertaken. Reactive arthritis has been reported as a complication of *Campylobacter* enteritis in 2 percent (8 of 340) of cases in Finland (Kosunen and others 1980).

Occurrence

The exact distribution and importance of *Campylobacter* enteritis in various geographical regions are not yet known. It is very probable, however, that *C. fetus* ssp. *jejuni* is a major cause of diarrhea throughout the world (table 12-1).

Infectious agent

Campylobacters are microaerophilic, Gram-negative, motile, slender (0.2–0.4 micrometers in width), curved or spiral bacteria (figure 12-1). They are oxidase positive and do not attack sugars. The genus is divisible into two groups on the basis of the catalase reaction and nitrate reduction test. The organisms

Table 12-1. *Prevalence of excretion of* Campylobacter *and other enteric pathogens by individuals with and without diarrhea in twelve countries*

Country	*Age group*	*Number of persons with (+) and without (−) diarrhea*	*Prevalence of* Campylobacter *excretion (percent)*	*Prevalence of excretion of other bacterial or protozoal pathogens (percent)*	*Source*
Australia	All ages	+224	5.8 (5.4)[a]	ND[b]	Steele and McDermott (1978)
	All ages	−530	0	ND	
Bangladesh	All ages	+204	12.0	ND	Blaser and others (1980*a*)
	All ages	+97[b]	5.2	ND	
	1–4 years	+80	8.6	ND	
	1–4 years	+34[b]	5.9	ND	
	1–5 years	−141	18.0	ND	
Belgium	Children	+3200	5.8	ND	Butzler (1978)
	Children	−6500	1.7	ND	
	Adults	+600	2.3	ND	
	Adults	−700	0.7	ND	
Brazil	0–12 years	+217	6.4	ND	Ricciardi and Ferreira (1980)
England	All ages	+280	14.0 (12)	13.0	Bruce, Zochowski and Ferguson (1977)
	All ages	−156	0.6	1.9	
	All ages	+182	7.6	ND	Dale (1977)
	All ages	−60	0.2	ND	
	All ages	+860	4.2	4.4	Pearson and others (1977)
	All ages	+330	5.8	ND	Tanner and Bullin (1977)
	All ages	−120	0.8	ND	
Indonesia	0–9 years	+150	10.0	ND	Rockhill and others (1980)
	>9 years	+200	2.0	ND	
	0–9 years	+7[c]	28.0	ND	
	>9 years	+150[c]	2.0	ND	
	All ages	−ND	<1.0	ND	
Rwanda	Children	+150	11	42	De Mol and Bosmans (1978)
	Children	−58	0	31	
Scotland	All ages	+196	8.7 (7.1)	16	Tefler Brunton and Heggie (1977)
	All ages	−50	0	0	
South Africa	0–8 months	+47	32 (31)	40	Bokkenheuser and others (1979)
	0–8 months	−45	4	15	
	9–24 months	+31	39 (38)	39	
	9–24 months	−18	44	50	
Spain	All ages	+446	4.5	17	Lopez Brea, Molina and Baquero (1979)
USA	All ages	+238	4.6	ND	MMWR (1979*a*)
	All ages	+956	4.1	ND	Blaser and others (1980*c*)
	All ages	−548	0	ND	
Zaïre	Children	+70	8.6 (8.6)	ND	Butzler (1973)
	Children	−30	0	ND	

ND No data.

a. Figures in parentheses refer to *Campylobacter* isolations in the absence of other known bacterial or protozoal pathogens.

b. These patients had dysentry (bloody stools).

c. These patients had suspected typhoid.

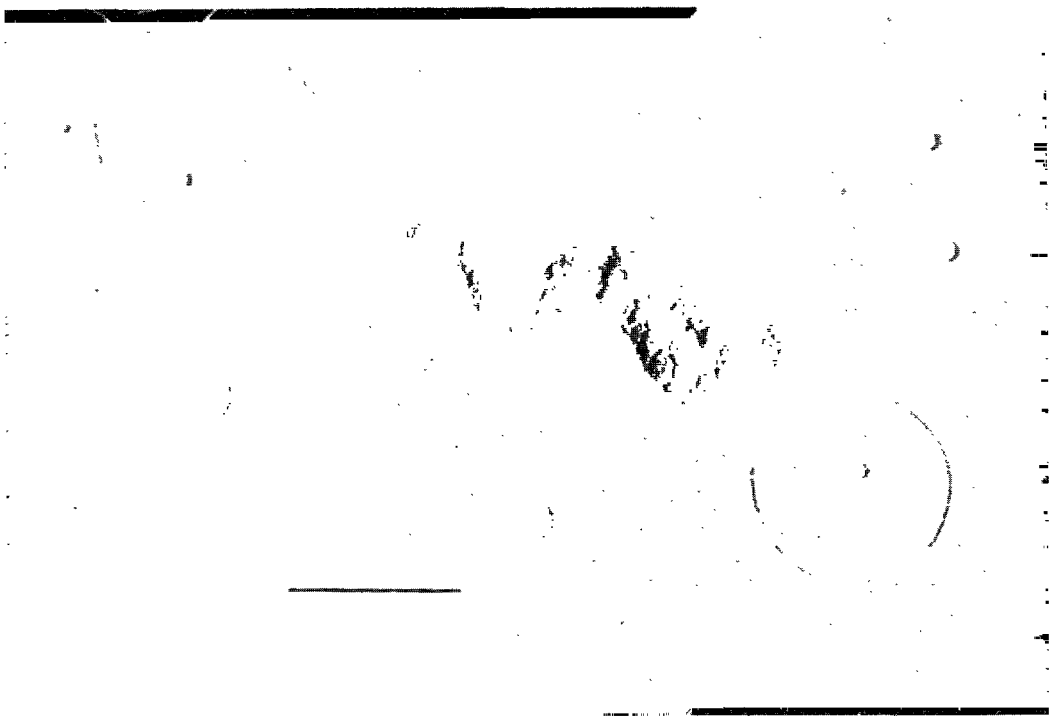

Figure 12-1. Campylobacter *under scanning electronmicroscopy.* The polar flagella are clearly seen. Scale bar = 1 micrometer. (Photo: J. P. Butzler, Hôpital Universitaire Saint Pierre, Brussels, Belgium)

considered in this chapter are catalase positive. Although campylobacters have aerobic metabolism, they are unable to grow in atmospheric oxygen. Growth occurs at oxygen concentrations of between 3 and 7 percent. Incubation on isolation media at 43°C aids the isolation of *C. fetus* ssp. *jejuni*, and incubation at 25°C favors *C. fetus* ssp. *intestinalis* and ssp. *venerealis*. *C. fetus* ssp. *jejuni* has been the most commonly described isolate associated with diarrhea, but the significance of other campylobacters has not been fully assessed. *C. fetus* ssp. *venerealis* causes enzootic sterility in cattle and is transmitted venereally. *C. fetus* ssp. *intestinalis* causes abortion in sheep and cattle, is transmitted by the fecal-oral route, and is a rare, opportunistic pathogen of man. The taxonomy of the catalase-positive campylobacters remains confused. The organism described here as *C. fetus* ssp. *jejuni* is also called *C. jejuni*, or *C. jejuni* and *C. coli*, or, in the older literature, "related vibrios."

Reservoirs

Although it is known that a wide variety of animals and birds may excrete *C. fetus* ssp. *jejuni*, the reservoirs that are functionally important for human infection have not been determined. Studies in developed countries have implicated domestic animals (especially puppies), caged birds, poultry (alive or undercooked), pigs, sheep, and cows as possible sources of human infections (Blaser and others 1980*c*; Bruce, Zochowski and Ferguson 1977; Butzler and Skirrow 1979; MMWR 1978*b*, 1979*a*, 1979*b*; Pearson and others 1977). The degree to which man is an important reservoir for human infection is not clear. Most studies listed in table 12-1 found a very low prevalence (0–1.7 percent) of *Campylobacter* excretion among healthy individuals. By complete contrast, the data from Bangladesh and South Africa (table 12-1) showed that *Campylobacter* are excreted by a substantial proportion of healthy children. The important reservoirs of *Campylobacter* in poor communities in developing countries remain to be elucidated.

Transmission

Transmission is presumed to be fecal-oral, from the feces of infected people, animals, or birds. Infected persons with diarrhea excrete 10^6–10^9 *C. fetus* ssp. *jejuni* per gram of feces. In affluent communities there is little evidence of direct person-to-person spread, except among young children in nurseries. In poor communities and developing countries it is very probable

that person-to-person spread is of considerable importance, although studies are required to confirm this. Several reports in developed countries indicate transmission via undercooked poultry (Butzler and Skirrow 1979; MMWR 1979*a*) and unpasteurized milk (Blaser and others 1979; MMWR 1978*b*; Robinson and others 1979; Taylor, Weinstein and Bryner 1979), and human infection from contact with infected pet animals and birds is also suspected (Blaser and others 1978, 1980*c*; Butzler and Skirrow 1979; MMWR 1979*b*). The organism can persist in chicken and turkey carcasses during preparation and refrigeration for commercial marketing (Simmons and Gibbs 1979). Waterborne transmission was suspected in one major outbreak in the USA (MMWR 1978*a*).

Data on infective dose are not yet available, but a medical laboratory technician in Australia successfully infected himself by ingesting 10^6 *C. fetus* ssp. *jejuni* in milk (Steele and McDermott 1978).

Incubation period

Incubation periods for *Campylobacter* enteritis are somewhat longer than is common for other bacterial enteric infections. Recorded or estimated incubation periods are from 1.5 to 11 days, but usually are between 3 and 5 days.

Period of communicability

One study in the USA (Blaser and others 1980*c*) found that fecal carriage of *C. fetus* ssp. *jejuni* was for a median period of 15 days from the onset of illness. Most patients were not excreting the organism after 21 days, and the maximum period of excretion recorded was 7 weeks. Jones (1979) reported excretion of the pathogen for 18–39 days by 12 adult patients employed at a food factory in England.

Resistance

The disease has been described in both children and adults. Circulating antibody can be detected, and it may well be that some immunity is conferred by infection.

Epidemiology

The epidemiology of *Campylobacter* enteritis is poorly understood in the developed countries and totally obscure in the developing countries. It seems clear that it is a zoonosis, and it may be that the nearest known parallel is with the epidemiology of the zoonotic salmonelloses (chapter 15). It is possible that the dominant route of transmission, in developed countries, is from infected animals to man, either as a result of handling pets or farm animals or as a result of ingesting poorly cooked meat (especially poultry) or unpasteurized milk. If this is the case, then its epidemiology in developed countries should indeed be very similar to the salmonelloses. This interpretation would also explain why *C. fetus* ssp. *jejuni* is such a prominent cause of bacterial diarrhea, even in affluent communities with high standards of environmental sanitation (table 12-1). Reportings of *Campylobacter* enteritis tend to peak during the warm summer months in England and Wales, Belgium, and the USA (Butzler and Skirrow 1979).

The data in table 12-1 show that *C. fetus* ssp. *jejuni* has been associated with 4–14 percent of diarrhea cases in developed countries. In these same countries, the prevalence of *Campylobacter* excretion by healthy persons is low (0–1.7 percent). The picture in developing countries is unclear. In some (for instance, Indonesia, Rwanda, and Zaïre) the prevalences of *Campylobacter* infection among those with and without diarrhea are similar to the prevalences reported from developed countries. In Bangladesh and South Africa, however, a very different picture has emerged. In Bangladesh, 18 percent of 141 village children (1–5 years old) were excreting *Campylobacter* during the dry season, whereas only 2 percent were excreting *Shigella*, and none were excreting *Salmonella* (Blaser and others 1980*a*). Fifty-two percent (13 of 25) of these *Campylobacter*-positive children had had no history of diarrhea in the 30 days prior to specimen collection. The prevalence of *Campylobacter* excretion in the 12–23 months age group was 39 percent. Similarly, in Soweto (South Africa), Bokkenheuser and others (1979) reported a 44 percent prevalence of *Campylobacter* excretion among healthy, black children age 9 to 24 months (see also Koornhof and others 1979). While it seems certain that *C. fetus* ssp. *jejuni* is a cause of some diarrhea in developing countries, the relative importance of this etiologic agent in comparison with other known major agents (especially enterotoxigenic *E. coli* and rotavirus) remains undetermined.

Data from England (Butzler and Skirrow 1979; Dale 1977) suggest that the highest incidence of disease occurs among people 5 to 34 years old, whereas some reports from developing countries suggest that infants and young children are the most affected (Blaser and others 1980*a*; DeMol and Bosmans 1978; Ricciardi and Ferreira 1980). This, in turn, suggests the possible importance of person-to-person transmission in

developing countries. However, Blaser and others (1980*a*) found that *Campylobacter* infection among children in a rural area of Bangladesh was not clustered by household and considered that there might be "relatively little person-to-person transmission."

An outbreak of *Campylobacter* enteritis affected 2,000 out of the 10,000 inhabitants of Bennington (Vermont, USA) during a 2-week period in May–June 1978 (MMWR 1978*a*). All parts of the town were involved, and there was no evidence of secondary person-to-person spread. The town water supply was partially chlorinated, but not otherwise treated, and several areas of the town were receiving water with no residual chlorine over the period of the outbreak. No *Campylobacter* was isolated from the water, but the water supply was strongly implicated as the common source of the outbreak.

Control Measures

Very little can be said with certainty about the control of *Campylobacter* enteritis until its epidemiology is further understood. Hygienic excreta disposal, good personal and domestic cleanliness, adequate cooking of poultry and care in handling pets and farm animals are all presumed to be important protective measures.

Occurrence and Survival in the Environment

Although it is known that *C. fetus* ssp. *jejuni* is excreted by a wide variety of animals and birds, almost no data exist on the presence of these organisms in the environment. Knill, Suckling and Pearson (1978) isolated *C. fetus* ssp. *jejuni* from 21 percent (7 of 34) of seawater samples, and from 74 percent (37 of 50) of river and pond samples, in the Southampton area (UK). All positive water samples also contained *E. coli.*

Very little is yet known about the survival of *C. fetus* ssp. *jejuni* in various environmental habitats. In one study, *C. fetus* ssp. *jejuni* was enumerated in stored feces, urine, water, and milk (Blaser and others 1980*b*). In naturally infected feces, a 7 to 9 log reduction occurred in 9 to 22 days at 4°C and in 3 to 8 days at 25°C. In urine, high initial concentrations became undetectable in less than 2 days at 37°C, but organisms were viable for up to 35 days at 4°C. In autoclaved stream water, a 7 log reduction took 5 to 33 days at 4°C and 2 to 4 days at 25°C. In pasteurized milk, maximum survival times were 22 days at 4°C and less than 3 days at 25°C. Comparative studies in acid and water showed that survival was significantly curtailed at pH values of less than 3. A 7 log reduction occurred in 20 minutes at pH 2.4

Of peripheral interest are the experiments of Lindenstruth and Ward (1948) with *Vibrio fetus*, which might now be classified as *Campylobacter fetus* ssp. *intestinalis*. They showed that, at 20°C and 37°C, inoculations of 1.5×10^9 organisms survived for 10 days but not for 20 days in hay, soil, and sheep manure. At 6°C, the same inoculation in the same environments survived for 20 days but not for 30 days.

Inactivation by Sewage Treatment Processes

No information is available on the destruction of *C. fetus* ssp. *jejuni* by sewage treatment processes or on the occurrence of this organism in sewage.

Inactivation by Night Soil and Sludge Treatment Processes

No information is available on the destruction of *C. fetus* ssp. *jejuni* by night soil and sludge treatment processes or on the occurrence of this organism in night soil and sludge.

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