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Campylobacter Enteritis in Denver

MARTIN J. BLASER, MD; L. BARTH RELLER, MD; NANCY W. LUECHTEFELD, MD, *and* WEN-LAN LOU WANG, PhD, *Denver*

To determine the relative importance of Campylobacter jejuni *as a cause of diarrheal illness in patients coming to three hospitals in Denver, we cultured stool specimens from 2,670 patients over a two-year period.* C jejuni *was identified in the feces of 124 patients (4.6 percent),* Salmonella *from 90 (3.4 percent) and* Shigella *from 77 (2.9 percent). Most* Campylobacter *isolates were obtained in the summer months and from patients 10 to 29 years old. The illness usually lasted less than two weeks; predominant symptoms were diarrhea (98 percent), abdominal pain (88 percent) and fever (82 percent); patients with severe illness frequently had objective evidence of nonspecific colitis. Occult blood and leukocytes were present in stool specimens of 71 percent and 85 percent, respectively, of the patients tested. The duration and severity of illness led to antibiotic therapy in about half of the patients; erythromycin appeared effective. This study confirms the importance of* C jejuni *as a cause of enteritis; this microorganism should be sought routinely in fecal specimens from patients with diarrhea.*

Campylobacter jejuni is being recognized with increasing frequency as an enteric pathogen of humans.[1-8] Studies on all continents and in varied climates[2-8] have shown that *C jejuni* is a ubiquitous microorganism; however, the epidemiology of *Campylobacter* enteritis and its clinical features are still being defined.

To delineate the clinical and epidemiologic features of *Campylobacter* infection, we collected data on all patients from whom *C jejuni* was isolated at three large Denver hospitals. The results of the first six months of those studies have been reported[8]; we now present data from two full years of surveillance that extend the original findings. During the two-year period of study, *C jejuni* infection was more common than either *Salmonella* or *Shigella* infection, with a distinct age and seasonal distribution.

From the Division of Infectious Diseases, Department of Medicine, University of Colorado School of Medicine, Denver (Blaser and Reller); the Microbiology Laboratory, Veterans Administration Medical Center, Denver (Luechtefeld and Wang), and the Enteric Diseases Branch, Bacterial Diseases Division, Center for Infectious Diseases, Centers for Disease Control, Atlanta (Blaser).

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Reprint requests to: Enteric Diseases Branch, Bacterial Diseases Division, Center for Infectious Diseases, Centers for Disease Control, Atlanta, GA 30333.

Materials and Methods

The study included stool specimens from all patients whose physicians requested culture for enteric pathogens at the three collaborating hospitals from March 1978 through February 1980.[8] In addition to conventional media for isolating *Salmonella* and *Shigella*,[9] a selective plate medium

(Campy-BAP) was used and incubated as described previously.[8] All fecal specimens were cultured within two hours of receipt. Colonies with typical morphology for *Campylobacter* on the Campy-BAP were examined and *C jejuni* was identified according to standard criteria.[8] Rotaviruses, *Yersinia enterocolitica* and *Clostridium difficile* were not sought. Parasitology tests, complete blood counts and blood chemistry determinations were done when requested by the primary physician.

All patients from whom fecal material was obtained were classified as to age, sex, date of submission of the specimen and pathogens found. The hospital chart of every patient with *Campylobacter* infection was reviewed and the patients or their parents were interviewed by one of us whenever possible. Complete histories were taken that emphasized the course and clinical features of the illness.

Results

Epidemiologic Findings

During the two years a total of 2,670 fecal specimens were cultured at the three hospitals; *Campylobacter* was isolated from 124 (4.6 percent), *Salmonella* from 90 (3.4 percent) and *Shigella* from 77 (2.9 percent). Four patients had mixed infections: two with *Campylobacter* and *Salmonella,* one with *Campylobacter* and *Shigella* and one with *Campylobacter, Shigella* and *Giardia lamblia.*

More *Campylobacter* isolates were found in stool specimens in the warmer months (May through August) than in the cooler months (December through March)—both in absolute numbers and as a percentage of cultures done (Figure 1). No such seasonal pattern was observed for *Salmonella* or *Shigella.* No increase was observed in the number of specimens obtained from young children during the winter months. The rates at which *Campylobacter* was isolated from male patients (5.2 percent) and female patients (4.0 percent) were not significantly different. Most *Campylobacter* isolates were obtained from older children and young adults (Table 1). *Campylobacter* was isolated from 8.4 percent of patients 10 or more years of age but from only 2.0 percent of those under 10 ($x^2=56.6$, $P<.001$). In contrast, for *Salmonella* the highest age-specific isolation rate was for patients less than a year old and for *Shigella* it was for those from ages 1 through 9. For male patients 10 through 29 years of age whose specimens were cultured in the period June through September, the isolation rate for *Campylobacter* was 21.9 percent; for female patients of that age group the comparable rate was 18.1 percent.

Clinical Features of Campylobacter Infection

Symptoms. A prodrome of one or more days of malaise, myalgia, headache and fever was noted by 18 percent (22/124) of patients. For 62 percent of the patients the onset of illness was sudden, with abdominal cramps and diarrhea often severe enough to wake them from sleep. The symptoms noted when the patients were seen initially at the hospital are shown in Table 2. Studying the group of patients who had stool specimens taken for culture biases the results toward persons with diarrhea; nonetheless *Campylobacter* was identified from three patients who had no diarrhea. Two of them had specimens taken for culture because of sudden abdominal pain and fever, and one infant had a culture done after she passed a grossly bloody stool. Two thirds of the patients had eight or more bowel movements on the worst day of the

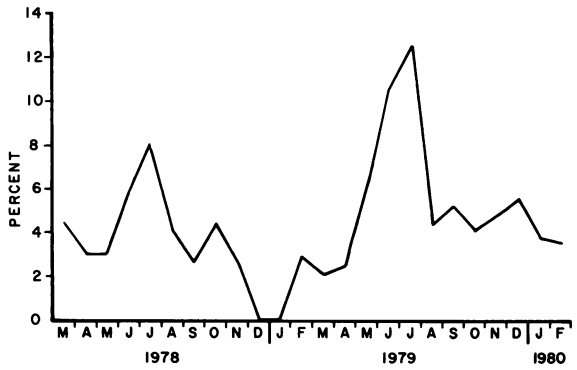

Figure 1.—Rate of isolation of *Campylobacter* from fecal specimens at three Denver hospitals by month, March 1978 through February 1980.

TABLE 1.—*Rate of Isolation of Three Enteric Pathogens From Fecal Specimens Submitted to Three Denver Hospitals by Age of Patient, March 1978 Through February 1980*

Age (yr)	Number of Fecal Specimens	Positive Fecal Specimens (%)		
		Campylobacter	*Salmonella*	*Shigella*
<1	875	12(1.4)	35(4.0)	2(0.2)
1-9	656	20(3.0)	19(2.9)	45(6.9)
10-29	554	68(12.3)	20(3.6)	17(3.1)
30-49	252	17(6.7)	5(2.0)	8(3.2)
50-69	204	6(2.9)	4(2.0)	0(0.0)
>70	73	1(1.4)	3(4.1)	3(4.1)
Unknown	56	0(0.0)	4(7.1)	2(3.6)
TOTALS	2,670	124(4.6)	90(3.4)	77(2.9)

TABLE 2.—*Symptoms of 124 Patients With* Campylobacter *enteritis Seen at Three Denver Hospitals*

Symptom	Percentage With Symptom: All Patients	Children (<10 yr) (n=31)	Older Children and Adults (n=93)
Diarrhea	98		
Defecation ≥8 on worst day	65	45†	71†
Gross blood present	52	48	53
Bile-stained stools	36		
Mucus in stools	35		
Malaise*	95		
Abdominal pain*	88		
Fever	82	57†	91†
Nausea*	55		
Vomiting	35	33	35

*Could not be evaluated for very young children. For these symptoms, n=110 patients.
†$P < .01$.

illness and about half noted gross blood in their stool.

Cramping abdominal pain, either periumbilical or involving the lower quadrants, frequently was noted. Nausea and vomiting rarely were the principal features of the illness but generally accompanied the most severe stages of cramping and diarrhea. Abdominal distention and tenesmus were rare complaints. Most patients had anorexia; however, almost all those who were ill for less than a week lost less than 2.3 kg (5 lbs).

Those who reported having fever said it was present either before the onset of the gastrointestinal symptoms or coincident with the first two days of diarrhea. Of patients under age 1, 36 percent had a history of fever, as did 68 percent of those 1 to 9 years old and 91 percent of those over 10 years old. Persistent fever was unusual but was reported by those patients with the most severe enteric symptoms. Rigors, noted by 10 percent of patients, occasionally heralded the onset of illness. Headache, backache, myalgia and arthralgia were each reported by less than 30 percent of patients; frank arthritis was not noted.

Signs and laboratory findings. The initial physical examination of the patients and the related laboratory findings usually were normal or nondiagnostic. Eight patients had postural changes in their blood pressure and pulse, but no other signs of dehydration were seen. Fever (temperature of greater than 37.5°C [99.5°F] and as high as 39.7°C [103.5°F]) was recorded for 40 percent of patients. Abdominal tenderness was noted for about half of the patients but was always generalized; no point or rebound tenderness, abdominal distention or organomegaly was observed.

The median leukocyte count was 9,400 per μl and a count over 10,000 was recorded in 34 percent. Occult blood was found in the stools of 42 (71 percent) of 59 patients tested, including 17 patients who did not have grossly bloody stools. All eight children tested had occult blood in their stools, but only 30 of 51 adults tested had this finding ($P=.02$, Fisher's exact test). Of 71 patients whose stools were examined 60 (85 percent) had polymorphonuclear leukocytes present. Of 14 patients with fever who had blood cultures, *C jejuni* was found in one culture.

There were 18 patients (13 male, 5 female) among the most seriously ill who had sigmoidoscopies, usually because of grossly bloody stools or prolonged diarrhea. The rectal mucosa appeared abnormal in 17 of the 18 patients; the findings ranged from erythema and edema to those indistinguishable from acute ulcerative colitis. Rectal biopsy specimens obtained from eight patients all showed inflammation of the lamina propria, with increased numbers of polymorphonuclear leukocytes and mononuclear cells. Abnormalities of the mucous glands were seen in all biopsy specimens, ranging from flattening of the epithelium and depletion of mucous cells to destruction of glands with formation of crypt abscesses. One specimen showed mucosal ulceration.

Course of the illness. One patient was in the hospital for treatment of a malignancy when he had diarrhea; all the others became ill at home. The median hospital stay for the 20 patients who were admitted to hospital was five days (range 3 to 37 days).

Of the 70 patients for whom the duration of illness was assessed, 37 were not treated with antimicrobial agents because their symptoms were diminishing or absent when *Campylobacter* infection was diagnosed; 68 percent had illness lasting a week or less. The 37 untreated patients were ill from 1 to 20 days (median 5 days) and 11 percent had relapses; 33 treated patients were ill from 3 to 31 days (median 8 days) and 30 percent had relapses before treatment. Of the 33 treated patients, 29 received erythromycin. No relapses occurred after treatment with erythromycin, but stools were not recultured.

Discussion

In a laboratory-based investigation such as ours, the population studied is biased toward those considered by a physician to be ill enough to

have specimens taken for culture. This form of selection favors recognizing the more severe and chronic manifestations of infection. Despite this phenomenon, or perhaps as a result of it, during the two years of our study *Campylobacter* was more frequently isolated than *Salmonella* or *Shigella* from the stools of patients with diarrhea. The seasonality of *Campylobacter* infection in Denver resembled that seen in England and Belgium.[1] The slightly higher rate at which *Campylobacter* was identified in male patients perhaps reflects their more frequent exposure to infection. Although the initial studies of *Campylobacter* infection were done in children's hospitals,[1,4,10] our study shows it clearly affects adults also. The high rate of isolation of *Campylobacter* from young men during the summer months further emphasizes its importance in adults.

The symptoms of *Campylobacter* infection could not be differentiated easily from those of infection due to other bacterial or viral causes of acute gastroenteritis,[11] and the severity of illness varied greatly. The frequent findings of fever, blood in stools and fecal leukocytes were helpful because enterotoxigenic *Escherichia coli* and rotaviruses, which commonly cause diarrhea, are not associated with such findings, even in laboratory-based surveys.[11] Thus the presence of blood and neutrophils in the feces of a febrile patient strongly suggests an inflammatory bacterial process[11-14] such as that caused by *Campylobacter, Salmonella, Shigella, Yersinia* or *Clostridium difficile.*

Occasionally abdominal pain may be the primary symptom of *Campylobacter* as well as *Yersinia* and *Shigella* infections[11,13]; patients having laparotomy or appendectomy because of severe pain have been reported.[15] We observed no extra-intestinal complications of *Campylobacter* infection, though such complications as convulsions, meningitis and arthritis have been reported.[16-18] The finding that a subset of patients with severe illness had pathologic changes in the colon should be interpreted with caution. Changes seen in several other patients[19-21] suggest that the small intestine may be the primary target organ. Therefore, colonic involvement in more severe *Campylobacter* infections may represent a so-called spill-over phenomenon, sequential sites of attack or may relate to the vulnerable site for infection in that patient.[22,23]

In this review the patients who were ill longer and had suffered relapses were more likely to be treated with erythromycin. Only a prospective controlled clinical trial will determine the proper role of erythromycin or other agents in the treatment of *Campylobacter* enteritis. Until such data are available it seems prudent to give erythromycin to patients with persistent or severe enteritis due to *C jejuni.*

The 124 patients discussed in this report indicate the wide spectrum of gastrointestinal illness caused by *C jejuni. Campylobacter* infection may cause an illness that ranges from mild diarrhea to severe enteritis, or inflammation that mimics ulcerative colitis.[22,23] Because it is such a common enteric pathogen, *C jejuni* should be sought routinely in fecal specimens from patients with diarrhea.

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