

AD-A271 903



1 January 1992

Reprint

An Outbreak of Bacteremic Campylobacter Jejuni Infection

Army Project Order 90PP0820

Wayne X. Shandera, M.D., Michael P. Tormey, M.P.H.
Martin J. Blaser, M.D.

Veterans Administration Medical Center
Research Service
1310 24th Avenue South
Nashville, Tennessee 37212-2637

93-26163



U.S. Army Medical Research & Development Command
Fort Detrick
Frederick, Maryland 21702-5012

Title of Project Order: Studies of the Outer Membrane Proteins of Campylobacter Jejuni for Vaccine Development

Approved for public release; distribution unlimited

Accession For	
NTIS CR&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-1	20

DTIC ELECTED
S E D
OCT 29 1993

DTIC QUALITY INSPECTED 2

Campylobacter, Vaccines, Biotechnology, ID, Diseases
RADI, Lab Animals, Volunteers

Unclassified

Unclassified

Unclassified

Unlimited

93 10 27 01 02

An Outbreak of Bacteremic *Campylobacter jejuni* Infection

WAYNE X. SHANDERA, M.D., MICHAEL P. TORMEY, M.P.H., AND MARTIN J. BLASER, M.D.

Abstract

During September 1980, an outbreak of bacteremic *Campylobacter jejuni* infection occurred in metropolitan Los Angeles. The outbreak was recognized when blood cultures obtained from 11 previously healthy persons with acute febrile illnesses (characterized in over 80% by fever, diarrhea, and headaches) were positive for *C. jejuni*. All recovered after an illness that lasted a mean of 8 days. A surveillance system failed to reveal a concomitant outbreak of gastroenteritis. Isolates had identical biochemical characteristics, susceptibility patterns to antimicrobial agents, and serotypes. Isolates from 2 patients were found to be susceptible to bactericidal activity of normal human serum. When bacteremic case-patients were matched with healthy controls, a significant association ($p < 0.05$, odds ratio 10) between illness and consumption of processed turkey was established. Although turkey was not available for culture, and processing of turkey theoretically destroys *Campylobacter*, turkey carcasses are known to be heavily contaminated with the pathogen.

CAMPYLOBACTER infections in humans typically occur with the species *jejuni*, *coli*, or *fetus*. *C. jejuni* and *coli* infections produce enteritis, *C. fetus* infections bacteremia. *C. jejuni* and *coli* infections occur in young, healthy adults, while *C. fetus* infections typically affect elderly immunocompromised adults or neonates. The modes of transmission for enteritis in adults with *C. jejuni* are established and include water and foodstuffs, especially undercooked meat products. In this re-

port, we review an outbreak of *C. jejuni* infection that manifested as bacteremia in which a larger outbreak of enteritis was not uncovered; the vehicle appeared to be processed turkey meat.

Description of the Outbreak

During September 1980, an outbreak of bacteremic *Campylobacter* infection occurred in the Los Angeles metropolitan area. The outbreak was recognized when a nurse at a health maintenance organization (HMO) alerted the county health department that within a 4-day period five persons came to a local hospital with an acute, febrile illness; although all received only nonspecific symptomatic therapy, blood cultures had been obtained and the organism *C. jejuni* was isolated from all five; when patients were notified of culture results, four of the five reported a resolution of symptoms in the absence of antimicrobial chemotherapy.

The methods of investigating this outbreak included (a) a review of the HMO laboratory records and a telephone and mail survey of 50 hospital infection-control practitioners to assess the size of the outbreak (this was all performed

Supported in part by an interagency agreement between the U.S. Army Medical Research and Development Command and the Veterans Administration.

An earlier version of this paper was given at the Epidemic Intelligence Service Conference, April, 1981, Centers for Disease Control, Atlanta, Georgia 30333.

From the Division of Field Services, Centers for Disease Control Atlanta, Georgia (WXS), Acute Communicable Disease Control, Los Angeles County Department of Health Services, Los Angeles, California (MPT), and Medical Service, Veterans Administration Medical Center, Division of Infectious Diseases, Department of Medicine, University of Colorado School of Medicine, Denver, Colorado (MJB).

Address reprint requests to Wayne X. Shandera, M.D., Department of Internal Medicine, Baylor College of Medicine, Ben Taub Hospital, 2-001, Texas Medical Center, Houston, TX 77030.

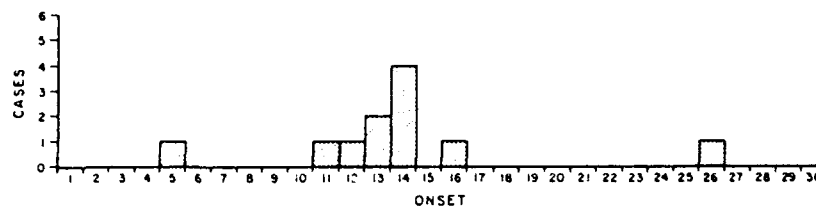


Fig. 1. Dates of isolation of bacteremic *C. jejuni* infections, Los Angeles County, September 1980.

within a month of the outbreak); (b) personal interviews with each of the identified cases and their family members, regarding exposures; (c) Kirby-Bauer (1) antibiotic susceptibility testing; (d) serotyping of 2 available isolates by the Penner system using somatic heat-stable antigens (2, 3); (e) susceptibility testing of the 2 isolates to the bactericidal activity of human serum (4, 5); and (f) a case-control study examining four possible common exposures using a matched-pair analysis with two controls matched per case for age, sex, and neighborhood of residence.

The review of laboratory records and the survey of infection control practitioners demonstrated that during the month of September a total of 11 persons in the Los Angeles metropolitan area sustained an acute febrile illness associated with *C. jejuni* bacteremia. The dates of isolation clustered around September 14 (Fig. 1). Furthermore, the isolation rate of *C. jejuni* from blood cultures at the HMO laboratory increased from a background rate of 0.5 per month (95% confidence intervals, 0.16 to 1.17) during the preceding 32 months to 10 during the month of September, 1980. The number of positive stool cultures during September elicited from the survey was 33, contrasting with 17 during August; additional data on stool samples was not available.

The 11 case-patients who had *C. jejuni* infection during September lived in a range of locales throughout the Los Angeles metropolitan area and included eight males and three females; their mean age was 16 years (range 2 to 32 years) and the mean duration of their symptoms was 8 days. Only two of the cases knew one another (the case on the 26th was a son of a woman who became ill on the 14th, and hence a secondary case) and there were no apparent common exposures.

All 11 had fever (mean maximal temperature was 102.6°F) and 82% developed diarrhea, typically after the onset of fever. Headaches were also reported by 82% and abdominal pain by 73%; abdominal pain, chills, and bloody stools were all reported by more than half (Table 1). Mean pulse rate on examination was 102/min. Data is not available on stool examination (guaiac, white blood cell stain). Laboratory studies included a mean hematocrit of 38.9% (range, 28 to 48.4) and a mean white blood cell count of 7900 (range,

4500 to 16,300). Renal function was unimpaired. One patient was hospitalized for suspect appendicitis. None received antimicrobial therapy.

Isolates were identified at the HMO laboratory using a Bactec system. All isolates had identical sensitivity patterns to antimicrobial agents, including sensitivity to ampicillin, colistin, chloramphenicol, kanamycin, gentamicin, and carbenicillin. Two isolates that were tested according to the Penner system were of the same serotype (one). Both isolates were susceptible to the bactericidal activity of normal human serum (\log_{10} killing 1.37 ± 0.28), similar to the susceptibility of fecal isolates (\log_{10} killing 1.51 ± 0.42) and unlike that of blood stream isolates from previously healthy hosts (\log_{10} killing 0.64 ± 0.32).

Although only 6 of the 11 patients recalled having eaten processed turkey, the case-control study showed that case-patients had eaten turkey more often during the 2 weeks before illness than controls, with an odds ratio of 10.0 ($p < 0.05$) (Table 2). No controls had been ill. No single brand of processed turkey was implicated.

Discussion

This outbreak is distinctive in two respects. First, it represents an outbreak of *C. jejuni* infection in which the primary manifestation of disease was bacteremia. Second, it provides additional epidemiologic support for the role of poultry products in the transmission of *C. jejuni*.

***C. jejuni* Bacteremia.** *C. jejuni* bacteremia is well recognized among immunocompromised patients and among the very young and very old (5-9). However, among previously healthy persons, bacteremia is an infrequent manifestation of *Campylobacter* infections, particularly when contrasted with the large number of fecal isolates that are reported (7). It has been postulated that bacteremia may infrequently follow *C. jejuni* gastroenteritis, since most *C. jejuni* organisms are susceptible to the bactericidal activity of normal human serum (8). However, bacteremia may have been recognized in this outbreak because blood cultures were obtained (transient bacteremia may occur more often than is recognized, since blood cultures are usually not obtained from patients with acute gastroenteritis (9) and because

C. jejuni is not always easy to isolate using blood cultures [10]).

No previous outbreaks of extraintestinal infection among immunocompetent hosts have been described, although an outbreak of *C. jejuni* meningitis has been reported among neonates (11). Since the presentations were primarily a systemic illness and the gastrointestinal symptoms developed secondarily, this outbreak may have been limited to bacteremia. It is possible that the cases of bacteremia represented most readily recognizable infections among an outbreak of predominantly nonbacteremic gastrointestinal illnesses, since stool culture isolations of *C. jejuni* identified through the surveillance system increased during September, and the serum sensitivity of 2 isolates tested were akin to that of typical gastrointestinal isolates; however, no major outbreak of gastrointestinal illnesses was identified at the time of the outbreak though passive or active (telephone calls of emergency rooms) surveillance, and the only data available suggests that the outbreak was one limited to bacteremic infection.

C. jejuni is known to cause frank colitis (10, 12–14) and mucosal invasion (15, 16), although bloodstream infections are uncommon (5) with *C. jejuni*, unlike *C. fetus*, an organism well-known to cause extraintestinal disease (16–18). The reason extraintestinal infections are limited to certain strains is not well understood (4). Both strain characteristics and host factors are responsible for producing *C. jejuni* bacteremia: such infections are more common among strains that are carbohydrate-rich and presumably contain long-chain lipopolysaccharide molecules (8) that confer serum resistance. Such strains are more likely to occur among the immunocompromised, the young, and the elderly (6, 7). Neither strain characteristic or host factors can explain the occurrence of this outbreak. By analogy, *Salmonella* infections often produce bacteremia in previously healthy hosts, and the strain serotype is a major determinant of the propensity toward extra-intestinal spread (19).

Processed Turkey as Source. The case-control study implicated consumption of processed turkey as the common source of the outbreak. Turkey is a highly plausible vehicle for *Campylobacter* transmissions; at slaughterhouses 100% of turkey carcasses are contaminated with *C. jejuni* (20); even after chilling in solution with high chlorine levels, over 80% of turkey carcasses remain culture-positive (21). When turkey wings reach the consumer, more than 50% remain contaminated with *C. jejuni* (22). Similarly, most chicken meat is contaminated, both at the slaugh-

TABLE 1
Symptoms associated with *C. jejuni* infection,
Los Angeles County, 1980

Symptom	Cases	%
Fever	11	100
Diarrhea	9	82
Headache	9	82
Abdominal pain	8	73
Chills	8	73
Bloody stools	6	55
Vomiting	4	36
Arthralgias	4	36
Cough	3	27
Rash	2	18

All controls were asymptomatic.

terhouse and when it reaches consumers (21, 23). Handling or consumption of undercooked chicken has been shown to be responsible for epidemic *Campylobacter* infections prior (24) and subsequent (25–27) to the current one, as well as sporadic infections (27–29). In England, an outbreak of enteritis due to *C. jejuni* and *Salmonella hadar* was associated with consumption of a boned, stuffed, and rolled turkey (30).

Why the outbreak resolved in the absence of specific preventive therapy is not known. The actual source of this outbreak could not be traced, but it was postulated that a breakdown in processing occurred. (Processing involves mixing boneless, skinless turkey meat with an emulsion of carcass skins, wing meat, and wing skin; stuffing the mixture into fibrous casings pneumatically and cooking at 180°F for 2–3 hours [31], which should destroy *C. jejuni* present). A breakdown in heating process could have permitted transmission. Consumers typically do not cook this food after purchase, and refrigeration should be associated with a low rate of *C. jejuni* isolation. However, FDA studies demonstrate persistence of *C. jejuni* in processed meat held at 4°C up to 21 days. Viability in several milieus, including poultry, has been shown to be greater when organisms are maintained at 4°C than at 25°C (32, 33).

TABLE 2
Case-Control Study, Bacteremic *C. jejuni* Outbreak, Los Angeles County, September 1980, Consumption of Processed Turkey

Cases	Controls			Total
	Both ate	1 ate 1 did not	Neither ate	
Ate	0	2	4	6
Did not eat	0	1	4	5
Total	0	3	8	11

$$\chi^2 = 5.79 (34)$$

$$p < 0.05$$

$$\text{odds ratio} = 10.0$$

In summary, this article reports an outbreak of bacteremic *C. jejuni* infection in immunocompetent hosts. A larger outbreak of gastroenteritis, if present, was not readily evident. The serum susceptibility pattern of 2 isolates from the outbreak provided no evidence that unusual virulence was responsible for the bacteremia and infection. Although the actual mechanism of contamination of the food was not determined, a widely distributed product, processed turkey meat, was suggested as the source of the outbreak. The improved control and prevention of *C. jejuni* infections will require the continued investigation into its epidemiology and pathogenesis.

Acknowledgments

The authors thank Phyllis Fliegel, R.N., and William Weinstein, M.D., for collection of data; John Penner, Ph.D., for serotyping the strains; and Frank Sorvillo, M.P.H., Paul Blake, M.D., M.P.H., and Robert Gunn, M.D., M.P.H.

References

- Bauer AW, Kirby WM, Sherris JC, Tenckhoff M. Antibiotic susceptibility testing by a standardized single disk method. *Am J Clin Pathol* 1966; 45:493-496.
- Penner JL, Hennessy JN. Passive hemagglutination technique for serotyping *Campylobacter fetus* subspecies *jejuni* on the basis of soluble heat-stable antigens. *J Clin Microbiol* 1980; 12:732-737.
- Lastovica AJ, Penner JL. Serotypes of *Campylobacter jejuni* and *Campylobacter coli* in bacteremic, hospitalized children. *J Infect Dis* 1983; 147:592.
- Blaser MJ. Extraintestinal *Campylobacter* infections. *West J Med* 1986; 144:353-354.
- Blaser MJ, Perez GP, Smith PF, Patton C, Tenover FC, Lastovica AJ, Wang WL. Extraintestinal *Campylobacter jejuni* and *Campylobacter coli* infections: host factors and strain characteristics. *J Infect Dis* 1986; 153:552-559.
- Dhawan VK, Ulmer DD, Nachum R, Rao B, See RC. *Campylobacter jejuni* septicemia—epidemiology, clinical features and outcome. *West J Med* 1986; 144:324-328.
- Riley LW, Finch MJ. Results of the first year of national surveillance of *Campylobacter* infections in the United States. *J Infect Dis* 1985; 151:956-959.
- Blaser MJ, Smith PF, Kohler PF. Susceptibility of *Campylobacter* isolates to the bactericidal activity in normal serum. *J Infect Dis* 1985; 151:227-235.
- Blaser MJ, Reller LB, Luechtefeld NW, Wang WL. *Campylobacter* enteritis in Denver. *West J Med* 1982; 136:287-290.
- Wang WL, Blaser MJ. Detection of pathogenic *Campylobacter* species in blood culture systems. *J Clin Microbiol* 1986; 23:709-714.
- Goossens H, Henocque G, Kremp L, Rocque J, Boury R, Alanio G, Vlaes L, Hemelhof W, van den Borre C, Macart M, Henocque G, Butzler JP. Nosocomial outbreak of *Campylobacter jejuni* meningitis in newborn infants. *Lancet* 1986; 2:146-149.
- Drake AA, Gilchrist MJ, Washington JA, Huizenga KA, van Scoy RE. Diarrhea due to *Campylobacter fetus* subspecies *jejuni*: A clinical review of 63 cases. *Mayo Clin Proc* 1981; 56:414-423.
- Skirrow MB. *Campylobacter* enteritis: A "new" disease. *Br Med J (Clin Res)* 1977; 2:9-11.
- Lambert ME, Schofield PF, Ironside AG, Mandal BK. *Campylobacter colitis*. *Br Med J (Clin Res)* 1979; 1:857-859.
- Duffy MC, Benson JB, Rubin SJ. Mucosal invasion in *Campylobacter* enteritis. *Am J Clin Pathol* 1980; 73:706-708.
- Butzler JP, Skirrow MB. *Campylobacter* enteritis. *Clin Gastroenterol* 1979; 8:737-765.
- Blaser MJ, Reller LB. *Campylobacter* enteritis. *N Engl J Med* 1981; 305:1444-1452.
- Guerrant RL, Lahit RC, Winn WC, Roberts RB. *Campylobacteriosis* in man: pathogenic mechanisms and review of 91 bloodstream infections. *Am J Med* 1978; 65:584-592.
- Blaser MJ, Feldman RA. *Salmonella* bacteremia: reports to the Centers for Disease Control, 1968-1979. *J Infect Dis* 1981; 143:743-746.
- Luechtefeld NW, Wang WL. *Campylobacter fetus* subsp. *jejuni* in a turkey processing plant. *J Clin Microbiol* 1981; 13:266-268.
- Simmons NA, Gibbs FJ. *Campylobacter* subspp. in oven-ready poultry. *J Infect* 1979; 1:159-162.
- Rayes HM, Genigeorgis CA, Farver TB. Prevalence of *Campylobacter jejuni* on turkey wings at supermarket level. *J Food Protect* 1983; 46:292-294.
- Blaser MJ, Taylor DN, Feldman RA. Epidemiology of *Campylobacter jejuni* infections. *Epidemiol Rev* 1983; 5:157-176.
- Brouwer R, Mertens MJA, Siem TH, Katchaki J. An explosive outbreak of *Campylobacter* enteritis in soldiers. *Antonie Van Leeuwenhoek* 1979; 45:517-519.
- Istre GR, Blaser MJ, Shillam P, Hopkins RS. *Campylobacter* enteritis associated with undercooked barbecue chicken. *Am J Public Health* 1984; 74:1265-1267.
- Rosenfeld JA, Arnold GJ, Davey GR, Archer RS, Woods WH. Serotyping of *Campylobacter jejuni* from an outbreak of enteritis implicating chicken. *J Infect* 1985; 11:159-165.
- Tauxe RV, Pegues DA, Hargrett-Bean N. *Campylobacter* infections: the emerging national pattern. *Am J Public Health* 1987; 77:1219-1221.
- Hopkins RS, Scott AS. Handling raw chicken as a source of sporadic *Campylobacter jejuni* infections. *J Infect Dis* 1983; 148:770.
- Oosterom J, den Uyl C, Banffer JR, Huisman J. Epidemiological investigations on *Campylobacter jejuni* in households with a primary infection. *J Hyg (Lond)* 1984; 93:325-332.
- Communicable Disease Surveillance Center. Surveillance of food poisoning and salmonellosis. *Communicable Disease Report* 1981; 26:5.
- Kramlich WE, Pearson AM, Tauber FW. Meat cookery and cooked meat products. In: Kramlich WE, Pearson AM, eds. *Processed meats*. Westport CT: Avi Publishing Company, 1984:96-107.
- Blaser MJ, Hardesty HL, Powers B, Wang WL. Survival of *Campylobacter fetus* subspecies *jejuni* in biological milieus. *J Clin Microbiol* 1980; 11:309-313.
- Blankenship LC, Craven SE. *Campylobacter jejuni* survival in chicken meat as a function of temperature. *Appl Environ Microbiol* 1982; 44:88-92.
- Mantel N, Haenzel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst* 1959; 22:719-748.

Submitted for publication February 1990.

Final revision received July 1991.