Sporadic *Campylobacter* Infection in Infants

A Population-Based Surveillance Case-Control Study

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Background: *Campylobacter* is an important cause of foodborne illness in infants (younger than 1 year of age), but little is known about the sources of infection in this age group.

Methods: Eight sites in the Foodborne Diseases Active Surveillance Network (FoodNet) participated in a 24-month population-based case-control study conducted in 2002–2004. Cases were infants with laboratory-confirmed *Campylobacter* infection ascertained through active laboratory surveillance, and controls were infants in the community.

Results: We enrolled 123 cases and 928 controls. Infants 0–6 months of age with *Campylobacter* infection were less likely to be breast-fed than controls [odds ratio (OR); 0.2; 95% confidence interval (CI), 0.1–0.6]. Risk factors for infants 0–6 months of age included drinking well water (OR 4.4; CI, 1.4–14) and riding in a shopping cart next to meat or poultry (OR 4.0; CI, 1.2–13.0). Risk factors for infants 7–11 months of age included visiting or living on a farm (OR 6.2; CI, 2.2–17), having a pet with diarrhea in the home (OR 7.6; CI, 2.1–28) and eating fruits and vegetables prepared in the home (OR 2.5, CI 1.2–4.9). *Campylobacter* infection was associated with travel outside the United States at all ages (OR 19.3; CI, 4.5–82.1).

Conclusions: Several unique protective and risk factors were identified among infants, and these risk factors vary by age, suggesting that prevention measures be targeted accordingly. Breast-feeding was protective for the youngest infants and should continue to be encouraged.

Key Words: *Campylobacter*, infants, *Campylobacter* infections, campylobacteriosis, case-control studies

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Since the late 1970s, *Campylobacter* has been recognized as one of the most common causes of bacterial diarrheal illness in humans.[1] In the United States, it is estimated that ~2 million people are infected with *Campylobacter* each year, with the highest incidence in infants (children younger than 1 year of age).[2] In 2004, the incidence of laboratory-confirmed *Campylobacter* infections in the Foodborne Diseases Active Surveillance Network (FoodNet) was 12.9 per 100,000 persons for all age groups and 28.4 per 100,000 infants.

Most cases of *Campylobacter* infection occur sporadically, rather than as part of recognized outbreaks. *Campylobacter* outbreaks have been caused by ingestion of untreated water,[3–5] raw milk,[6–8] chicken[9] and cross-contaminated foods.[10,11] Sporadic *Campylobacter* infections have been associated with similar exposures[12–22] as well as contact with pets,[21,23–25] particularly those with diarrhea,[26,27] and exposure to the farm environment, primarily through farm work or animal husbandry.[27–30]

Because of their limited diets and rapidly changing developmental levels, infants represent a unique population whose sources of *Campylobacter* are likely to differ from those of older age groups. Postulated sources of *Campylobacter* infection in infants include exposure to pet chickens,[31] puppies in the house[32] and untreated drinking water.[31,33] Breast-feeding is protective against diarrhea in infants[34] and may be protective against *Campylobacter* infection.[35–37]

Because *Campylobacter* disproportionately affects infants and sources of *Campylobacter* infections in this high risk group are not well studied, we conducted a 24-month case-control study to describe associations between sporadic *Campylobacter* infections and potential exposures among infants in FoodNet sites.

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METHODS

Active Surveillance. FoodNet is a collaborative effort involving the Centers for Disease Control and Prevention (CDC), the U.S. Department of Agriculture's Food Safety and Inspection Service, the U.S. Food and Drug Administration, and 10 state health departments. FoodNet was established in 1996 as the foodborne disease component of the CDC's Emerging Infections Program. FoodNet conducts active surveillance for laboratory-confirmed pathogens commonly transmitted through food, including *Campylobacter*.[38] Surveillance personnel routinely contact >600 clinical laboratories in the FoodNet catchment area to ascertain all laboratory-confirmed *Campylobacter* cases. When this study was initiated, there were 9 FoodNet sites. We conducted this study in 8 of those 9 sites (Connecticut, Georgia, Minnesota, Oregon, Tennessee and selected counties in California, Colorado and New York), with a mean population under surveillance of 35.2 million persons, or 12.1% of the U.S. population. This study was approved by the human subjects review boards at CDC and participating sites.

Case-Control Study. During a 24-month period from 2002 to 2004, all infants with a laboratory-confirmed *Campylobacter* infection residing in the catchment area of participating FoodNet sites were eligible for the study. FoodNet personnel made at least 15 attempts to interview the parents/guardians of all eligible cases by telephone within 45 days of specimen collection. Eligible cases were excluded from the study if they were asymptomatic at the time of specimen collection or if they were part of an outbreak that was investigated by the health department in which a vehicle of transmission was identified.

Infants in the communities from which the cases occurred served as controls. This study was conducted concurrently with a case-control study of infant *Salmonella* infections; the same set of controls was used for each study. Controls were frequency matched to cases by 1-month age categories based on the historical incidence of *Salmonella* and *Campylobacter* infections in the participating sites from 1998 to 2000. The mean annual number of cases for each site was calculated for each age group by month of occurrence. Controls for each age group were then randomly selected from birth registries in each state. For the last 3 months of the study, New York used newspaper-published birth announcements to select controls.

A standard questionnaire was administered by telephone to parents/guardians of cases and controls. Interviews were conducted in English or Spanish and, in California, in Cantonese or Mandarin. Information was collected on both the infant (age, sex and medical history, including prior antimicrobial use) and the interviewee (education level and income). Questions included environmental exposures (household exposures, child care settings, animals, petting zoos and farms and international travel) and food exposures (breast-feeding, formula, water and solid food). We asked about exposures in the 5 days before illness onset for cases and 5 days before interview for controls. Because of the time lag in the availability of birth registries, information for controls with a target age of 0–2 months was gathered for a prespecified 5-day period in the first 12 weeks of life. Verbal informed consent was obtained from parents and guardians before beginning the interview. Some sites offered $10 gift certificates or checks to cases and controls upon completion of the questionnaire.

Statistical Analysis. Multivariable unconditional logistic regression models were applied with factors selected based on a priori knowledge regarding their association with *Campylobacter* infection and results from bivariate analyses. All models were adjusted for age. We also conducted age-specific analyses for 2 age groups, younger than 6 months of age and 6 months of age or older; we split at 6 months because infants begin to eat solid food and begin to move independently around this age. There were not enough cases to further split the youngest group of infants and conduct meaningful analyses.

Population attributable fractions, the estimates of the fraction of the total disease in the population that would not have occurred if the effect associated with the risk factor of interest were absent, were calculated for the factors associated with disease in the multivariable models.[39] All statistical analyses were conducted using the statistical package SAS version 9.1 (SAS Institute, Cary, NC).

RESULTS

Study Population. During the 24-month study period, 8492 cases of laboratory-confirmed *Campylobacter* infection were ascertained in participating FoodNet sites; 191 (2%) were in infants. Of these, 123 (64%) were enrolled in the study. Among the 68 cases not enrolled, the most common reasons for not enrolling were inability to reach the parents/guardians (49%), refusal (25%) and not speaking one of the study languages (10%). Other reasons for nonenrollment were inability to provide an onset date for illness onset (4%) and inability to answer questions (3%). Enrolled and nonenrolled cases did not differ significantly by gender, age, type of specimen from which *Campylobacter* was isolated, month of year in which their specimen was collected or outcome. All cases ascertained represented sporadic infections; that is, none of the ascertained cases was determined to be outbreak associated.

Nine hundred twenty-eight infants from the community were enrolled as controls. Controls were similar to enrolled cases with respect to gender (51% female among cases and controls) and age (mean age: 7 months among cases; 6 months among controls). Parents/guardians of cases had less formal education (39% had more than a high school education versus 75% of control parents/guardians, $P < 0.001$), were more likely to report a lower household income (53% reported an income of $30,000 or more versus 76% of control parents/guardians, $P < 0.001$) and were more likely to be insured through Medicaid (40% versus 24% of control parents/guardians, $P < 0.001$).

Clinical Illness. Of the 123 enrolled cases, 122 (99%) reported diarrhea, 82 (67%) had fever and 54 (44%) reported vomiting. Eighty-nine (72%) cases were treated with an antibiotic for their illness. Of 60 (67%) who could recall the name of the antibiotic, 54 (90%) had taken a macrolide.

Nineteen (15%) cases were treated with intravenous fluids for their illness, and 14 (11%) were admitted overnight to the hospital for a mean length of stay of 3 nights. There were no deaths among cases enrolled in the study.

A member of the family missed work (median, 3 days) as a result of the infant's illness in 58 (47%) of the cases. Twenty-three (19%) cases and 211 (23%) controls attended day care in the 5 days before their illness onset.

Risk Factor Analysis. In multivariable regression analysis, *Campylobacter* infection was associated with drinking well water, eating fruits and vegetables prepared in the home, having a pet in the home with diarrhea, visiting or living on a farm, riding in a shopping cart next to meat or poultry and traveling outside the United States. Infants with *Campylobacter* infection were significantly less likely to be breast-fed or to be in a household where hamburger was prepared than control infants (Table 1).

In age-specific analyses using 2 age groups (younger than 6 months and 6 months of age or older), travel outside the United States remained a significant risk factor for both age groups. In infants younger than 6 months of age, breast-feeding remained protective. Factors associated with infection in infants younger than 6 months of age were drinking well water and riding in a shopping cart next to meat or poultry. Factors associated with infection in infants 6 months of age or older were eating fruits and vegetables prepared in the home, having a pet in the home with diarrhea and visiting or living on a farm (Table 2).

DISCUSSION

We believe that this is the largest case-control study conducted to investigate potential sources of laboratory-confirmed *Campylobacter* infection in infants. Potential sources of *Campylobacter* infection identified in this study include drinking well water, eating fruits or vegetables prepared in the home, having a pet in the home with diarrhea and visiting or living on a farm. Breast-feeding was protective. A novel finding was that infants with *Campylobacter* infection were more likely than well infants to have ridden in a shopping cart next to meat or poultry. *Campylobacter* infection was also associated with international travel, a finding seen in studies of *Campylobacter* in the general population,[19] but in our population international travel accounts for a small fraction (6%) of cases, suggesting that most infections in infants in the United States are acquired domestically.

While riding in a shopping cart next to meat or poultry, infants can come into direct contact with *Campylobacter* by touching the contaminated packaged meat or poultry and then putting their hand or contaminated toys into their mouth. Infants could also become infected through indirect exposure to *Campylobacter*, for example by touching the contaminated shopping cart or via the contaminated hands of caretakers who have handled the packaged meats. There is microbiologic evidence for the external contamination of retail meat packages; in the United Kingdom, the exterior of 3% of tested, unopened chicken packages yielded *Campylobacter*.[40] Although control families might report less shopping cart exposure for reasons unrelated to *Campylobacter*, the association is strong and persisted in multivariable analysis. A similar finding was observed in the concurrent *Salmonella* case-control study.[41] Additional studies would be helpful to confirm transmission of *Campylobacter* in this situation, to better understand parental behaviors around infants and shopping carts and to suggest specific measures for prevention.

Consistent with previous studies, our results show that breast-feeding is protective against *Campylobacter* infection. This protection is seen for all age groups of infants, although it is most pronounced in the youngest infants. Breast-feeding in accordance with published guidelines should be encouraged. The American Academy of Pediatrics recommends breast-feeding for at least the first 12 months of life.[42]

Drinking well water was a risk factor for *Campylobacter* infection in infants younger than 6 months of age; these infants primarily have a liquid diet, usually including breast milk, formula, juice or water. Previous studies have identified untreated surface water as a source for sporadic and

TABLE 1. Multivariable Analysis of Exposures, Adjusted for Age, in the 5 Days Before Illness Onset Caused by *Campylobacter* Infection: FoodNet Sites, 2002–2004

Exposure	Cases Exposed (n = 123)	Controls Exposed (n = 928)	Odds Ratio	Population-Attributable Fraction (%)
Breast-feeding	26/123 (21)*	408/926 (44)*	0.3 (0.2–0.6)†	—
Drinking concentrated formula	24/122 (20)	110/921 (12)	1.8 (0.9–3.3)	8.7
Drinking well water‡	26/117 (22)	73/900 (8)	2.6 (1.3–5.3)	13.7
Started on solid foods	93/123 (76)	611/925 (66)	1.0 (0.4–2.2)	0
Eating fruits and vegetables prepared at home‡	50/89 (56)	240/559 (43)	2.0 (1.1–3.6)	28.1
Consuming unpasteurized dairy products	5/93 (5)	13/611 (2)	1.5 (0.3–5.8)	1.8
Attending child care	23/122 (19)	211/926 (23)	0.7 (0.4–1.2)	—
Independently walking	13/123 (11)	51/918 (6)	0.8 (0.4–1.9)	—
Having a pet with diarrhea in the home‡	9/123 (7)	17/928 (2)	5.3 (1.8–15.5)	5.9
Visiting or living on a farm‡	25/122 (20)	41/923 (4)	4.1 (1.9–8.9)	15.5
Preparing hamburger in the home	57/113 (50)	502/907 (55)	0.6 (0.3–0.9)	—
Preparing chicken in the home	83/115 (72)	629/910 (69)	1.2 (0.7–2.0)	12
Riding in a shopping cart next to meat or poultry‡	15/116 (13)	54/905 (6)	2.2 (1.1–4.6)	7.1
Traveling outside the United States‡	7/123 (6)	4/925 (0.4)	19.3 (4.5–82.1)	5.4

*Numbers in parentheses, percent.
†Numbers in parentheses, 95% confidence interval.
‡Risk factors significantly associated with disease.

TABLE 2. Age-Stratified (Younger Than 6 Months and 6 Months of Age or Older) Multivariable Analysis of Exposures, Adjusted for Age, in the 5 Days Before Illness Onset Caused by *Campylobacter* Infection: FoodNet sites, 2002–2004

Exposure	Younger Than 6 mo				6 mo of Age or Older			
	Cases Exposed (n = 52)	Controls Exposed (n = 514)	Odds Ratio	Population-Attributable Fraction	Cases Exposed (n = 71)	Controls Exposed (n = 414)	Odds Ratio	Population Attributable Fraction
Breast-feeding	12/52 (23)*	284/513 (55)*	0.2 (0.1–0.6)†	—	14/71 (20)*	124/413 (30)*	0.5 (0.3–1.1)†	—
Drinking concentrated formula	15/51 (29)	63/508 (12)	1.9 (0.8–4.9)	13.9	9/71 (13)	47/413 (11)	1.5 (0.6–3.6)	4.2
Drinking well water‡	9/49 (18)	29/499 (6)	4.4 (1.4–14.2)	14.2	17/68 (25)	44/401 (11)	1.6 (0.6–4.2)	9.4
Started on solid foods	26/52 (50)	207/512 (40)	1.2 (0.4–3.4)	8.3	67/71 (94)	404/413 (98)	0.4 (0.1–2.2)	—
Eating fruits and vegetables prepared at home‡	4/23 (17)	27/161 (17)	1.6 (0.4–6.1)	6.5	46/66 (70)	213/398 (54)	2.5 (1.2–4.9)	41.8
Consuming unpasteurized dairy products	1/26 (4)	3/207 (1)	4.9 (0.4–59.9)	3.1	4/71 (6)	10/414 (2)	1.3 (0.3–6.3)	1.3
Attending child care	9/52 (17)	101/512 (20)	0.8 (0.3–2.1)	—	14/70 (20)	110/414 (27)	0.6 (0.3–1.3)	—
Independently walking	—	—	—	—	13/71 (18)	49/410 (12)	0.9 (0.3–2.1)	—
Having a pet in the home with diarrhea‡	2/52 (4)	10/514 (2)	3.4 (0.4–31.2)	2.7	7/71 (10)	7/414 (2)	7.6 (2.1–27.8)	8.6
Visiting or living on a farm‡	8/21 (38)	22/511 (4)	1.9 (0.5–7.8)	18.0	17/71 (24)	19/412 (5)	6.2 (2.2–17.3)	20.1
Preparing hamburger in the home	26/47 (55)	292/496 (59)	0.7 (0.3–1.5)	—	31/66 (47)	210/411 (51)	0.5 (0.3–1.0)	—
Preparing chicken in the home	34/50 (68)	344/497 (69)	0.9 (0.4–2.0)	—	49/65 (75)	285/413 (69)	1.5 (0.8–3.1)	25.1
Riding in a shopping cart next to meat or poultry‡	7/45 (16)	19/497 (4)	4.0 (1.2–13.0)	11.7	8/71 (11)	35/408 (9)	1.7 (0.6–4.5)	4.6
Traveling outside the United States‡	4/52 (8)	3/512 (0.6)	22.6 (3.5–144.5)	7.4	3/71 (4)	1/413 (0.2)	18.2 (1.2–284.2)	4.0

*Numbers in parentheses, percent.
†Numbers in parentheses, 95% confidence interval.
‡Risk factor significantly associated with disease in either or both age groups.

outbreak *Campylobacter* cases.[18,23,28] A recent study in Sweden also identified the presence of a well in the home and drinking untreated water as risk factors for *Campylobacter* infection in children younger than 24 months of age.[43] Although the United States Environmental Protection Agency does not regulate private, individual wells, it does recommend yearly testing of wells for total coliform bacteria counts. Additionally testing of wells after events such as floods or heavy rainfall is prudent. Treating well water by boiling, filtration or chlorination before giving it to infants might lower the risk.

Having pets with diarrhea in the home was identified as a risk factor for *Campylobacter* infection for infants 6 months of age or older; this is consistent with the findings of previous studies.[23,26,27,43,44] Infants older than 6 months of age are more mobile than younger infants and have the potential to be physically closer to household pets and their environments, which offers more opportunity for transmission. Washing hands with soap and running water after contact is an effective way to prevent the transmission of bacteria from animals to humans; it is important to emphasize this simple step to parents of young children with pets. Separation of infants from pets with diarrhea might also mitigate the risk of infection.

Our finding that visiting or living on a farm is a risk factor for *Campylobacter* infection is consistent with other studies.[30] The farm environment is likely to include more opportunities for exposure to *Campylobacter* than other environments. Although we did not specifically inquire as to the presence of animals on the farms, there are other exposures, such as well water or unpasteurized milk in the farm environment that might offer the potential for transmission of *Campylobacter*. Additionally, among children living in rural areas, those who reside on farms are more likely to have higher antibody titers to *Campylobacter*.[45]

Among infants eating solid foods, eating fruits or vegetables prepared in the home was associated with illness. It is likely that this finding is a measure of cross-contamination in the household kitchen. The question specifically asked about fruits and vegetables that had been physically handled during preparation (ie, pureed or chopped), as there are opportunities for cross-contamination to occur during this manipulation. Although capturing the effects of cross-contamination is difficult in epidemiologic studies, there have been attempts to measure cross-contamination in the domestic setting.[46–50] Cross-contamination may be an important route of infection in infants.

Parents and guardians of enrolled children were requested to provide detailed histories of their infants' exposures during a specific time period. Although the possibility exists that parents and guardians of cases were more likely to remember their infants' exposures more accurately, the potential for recall bias was taken into account in the design of the questionnaire. Detailed explanations and prompts for the questions were included to ensure that respondents were clear on what was being asked and the period for which it was being asked, thus reducing the potential for recall bias.

Cases and controls differed significantly with respect to the interviewee's income and education levels. We were unable to adjust for this factor in our multivariable modeling because of large amounts of differentially missing data.

When restricting to the subset of data with complete income and education data, however, the results of the multivariable model did not differ from those presented here.

This large, population-based case-control study identified several potential sources for sporadic *Campylobacter* infection in infants. Risk factors for *Campylobacter* infection among infants vary by age, and prevention measures should be targeted accordingly.

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