Campylobacter jejuni Infections: Update on Presentation, Diagnosis, and Management

Olayinka Adedayo, MD
Beth D. Kirkpatrick, MD

Campylobacteriosis is a food- and water-borne zoonotic diarrheal illness caused by bacteria of the genus *Campylobacter*, with most cases caused by *C. jejuni*. *Campylobacter* species have a worldwide distribution, and campylobacteriosis is a leading cause of acute diarrhea and enterocolitis throughout the world. In the United States, approximately 1 million symptomatic *Campylobacter* infections occur each year.[1] The majority of *Campylobacter* infections are acquired via the oral route after handling raw poultry or consuming undercooked poultry.

Campylobacter species were first recognized in 1906 by John McFadyean, who described comma-shaped spiral organisms associated with abortions in cattle and sheep. Initially named *Vibrio fetus*, this pathogen was reclassified as *Campylobacter fetus* in 1973.[2,3] Human disease was first described 1959, when organisms were isolated from the blood of children with acute dysentery.[4] *Campylobacter* was first isolated from fecal specimens of patients with acute enteritis in 1972.[5] These initial cases were followed by other sporadic cases worldwide, and community outbreaks due to contaminated water, unpasteurized milk, and community meals were identified.[6–11] In 1978, a large community outbreak associated with the town water system affected 3000 people in Bennington, VT.[8]

Although campylobacteriosis is typically a self-limiting disease in otherwise healthy persons, severe gastrointestinal disease can occur in immunocompromised persons. In addition, postinfectious complications of *Campylobacter* infection, including Guillain-Barré syndrome and reactive arthritis, can occur in both immunocompromised and immunocompetent persons. This article provides an update on the presentation, diagnosis, and management of *Campylobacter* infection and its postinfectious complications.

TAKE HOME POINTS

- Infection with *Campylobacter jejuni* is a common cause of food-borne disease in the United States.
- *C. jejuni* causes self-limiting inflammatory diarrhea in healthy hosts but may be associated with severe and protracted disease in immunocompromised patients.
- Postinfectious sequelae of campylobacteriosis include reactive arthritis, irritable bowel syndrome, and the Guillain-Barré syndrome.
- Clinical judgment should be used when deciding whether to treat with antibiotics. Macrolide antibiotics (azithromycin or erythromycin) are used as first-line therapy for treatment when symptomatic infection with *C. jejuni* is deemed necessary.
- No vaccine against *Campylobacter* is available; strategies to prevent infection include avoiding the ingestion of undercooked meats and poultry and attention to hand hygiene.

EPIDEMIOLOGY

More than 16 *Campylobacter* species have been identified, but most clinically recognized infections in immunocompetent adults are due to *C. jejuni* and, less frequently, *C. coli*.[12] Campylobacters colonize the colon of farm and domestic animals, including cattle, sheep, goats, pigs, and particularly poultry, which serve as the main source of human infection.[13–15] In microbiologic surveys of raw meat products, broiler chicken appears to be a common source of contamination, with *C. jejuni* detected in 31% to 83% of samples.[15,16]

The incidence of *Campylobacter* infection varies throughout the world but appears to be declining in

Dr. Adedayo is a fellow and Dr. Kirkpatrick is an associate professor, Infectious Disease Unit, Department of Medicine, Fletcher Allen Health Care and the University of Vermont College of Medicine, Burlington, VT.

Table 1. Selected Risk Factors for *Campylobacter* Infection

Study	Subjects	Risk Factor	Odds Ratio (95% CI)	PAF, % (95% CI)
Friedman et al[20]	1152 American nontravelers	Contact with farm animals (persons aged 2–11 yr)	21 (2.5–178)*	2 (0.7–2)
		Drank raw milk	4.3 (1.3–12.2)*	1.5 (0.4–3)
		Drank untreated water from lake, river, stream	3.3 (1.5–7.5)*	3 (1–4)
		Ate chicken prepared in a restaurant	2.2 (1.7–2.9)*	24 (17–30)
		Consumption of undercooked poultry	2.1 (1.2–3.4)*	3 (1–6)
		Ate meat other than poultry at a restaurant	1.7 (1.3–2.2)*	21 (13–30)
		Had contact with animal stool	1.4 (1.02–1.9)*	6 (0.9–12)
Kapperud et al[21]	212 Norwegian nontravelers	Consumption of any poultry	2.69 (1.2–5.9)†	ND
		Consumption of undercooked poultry	6 (0.6–57.7)†	ND
		Daily contact with dog	5 (1.8–14)†	ND
		Eating grilled meat at barbecue	3.94 (1.9–8.4)†	ND
		Eating homemade minced meat	6.6 (0.72–60.9)†	ND

CI = confidence interval; ND = no data; PAF = population attributable factor.

*Adjusted odds ratio, multivariate.

†Unadjusted odds ratio, univariate analysis.

industrialized countries due to improvements in poultry processing. In the United States, the Food Borne Diseases Active Surveillance Networks reported a 30% decline in incidence between 1996 and 2007.[1,17,18] In 2007, 12.79 laboratory-confirmed cases of *Campylobacter* infection occurred per 100,000 persons, second only to *Salmonella* infections (14.92 cases per 100,000 persons) as a bacterial cause of food-borne disease.[1] In the United States, the incidence of *Campylobacter* infection is highest in Alameda and San Francisco counties of California, where incidence reaches 34.4 cases per 100,000 persons and infection accounts for 52% of all infective diarrhea.[19] Sporadic cases occur in 2 peak age-groups, 0 to 4 years and 20 to 39 years, and most cases occur during the spring and summer months.[17] Factors associated with increased risk of sporadic campylobacteriosis are related to poultry consumption, eating outside of the home, international travel, and exposure to animals (**Table 1**).[20,21]

The epidemiology and clinical manifestations of disease due to *C. jejuni* differs markedly in resource-poor countries. Estimates of incidence are incomplete, but rates are thought to be dramatically higher in such countries than in industrialized nations. Infection occurs without seasonal variability in warmer climates, and *C. jejuni* is often found with other copathogens.[22] Symptomatic disease in these settings appears most often in young children, and isolation of *Campylobacter* organisms in older individuals is inconsistently associated with symptomatic disease.[22,23] *Campylobacter* species account for 8% of diarrhea of bacterial origin in Western Kenya[24] and 14% in Bangladesh.[22]

Campylobacter is also an important cause of travelers' diarrhea, second in incidence to enterotoxigenic *Escherichia coli*. In a study of 322 visitors to Jamaica who experienced diarrhea, *C. jejuni* accounted for 6% of cases.[25] *Campylobacter* accounted for 9% of bacterial causes of diarrhea in 328 expatriates to Nepal[26] and 64% in US military troops in Thailand.[27]

Person-to-person transmission of infection is rarely described in adults, but *Campylobacter* species have been reported as a cause of sexually transmitted enteric infection in homosexual men.[28] Case reports describe mother-to-infant perinatal transmission and nosocomial spread in a hospital nursery.[28–31]

PATHOGENESIS

Campylobacters cause a nonspecific acute inflammatory enteritis involving the colon and small intestine; edema of the infected area as well as an infiltrate composed of neutrophils and mononuclear cells is seen histologically.[32,33] After oral ingestion, the pathogen moves through the intestinal mucus layer via its flagellum and multiplies in the distal ileum and colon. Campylobacters cause diarrhea by damaging the gut epithelial cells either directly by invading the cells or indirectly by initiating an inflammatory response.[34] The infectious dose of *C. jejuni* varies depending on the strain but may be as low as 500 organisms in milk, as shown in a self-infection experiment.[35] In a formal challenge model involving 111 adult volunteers, the infectious dose of *C. jejuni* ranged from 800 to 2×10^9 organisms.[36] Rates of infection increased with dose, but

there was no clear relationship between dose and the development of illness, with 10% to 50% of volunteers developing fever and/or diarrhea at these doses.[36]

Less is known about the specific bacterial virulence properties of campylobacters compared with other enteric gram-negative pathogens, such as salmonellae. Completion of the *Campylobacter* genome has shown extensive interstrain variability in several virulence genes, particularly in the organism's capsule, lipooligosaccharides, and flagellum.[37] Specific virulence factors of *Campylobacter* include its motility via a polar flagella, which is important in host colonization and cell invasion; the lipooligosaccharide, which facilitates immune avoidance and is associated with autoimmune disorders (*see* Guillain-Barré syndrome in Postinfectious Complications); and the capsule, which contributes to serum resistance and facilitates invasion of epithelial cells and colonization. The multifactorial process of host cell invasion also requires the proteins of a flagellar export apparatus system similar to those of type III protein secretion systems as well as a cytolethal distending toxin. Interestingly, host adaption also appears to play a role in pathogenesis, and chromosomal rearrangements and genetic material exchange occur in vivo.[33,37]

Table 2. Clinical Presentation of Campylobacteriosis in Immunocompetent Individuals

	Blaser et al[40]	Pitkanen et al[41]	Ponka et al[42]
Location	Denver, CO	Finland	Finland
Subjects	124 patients	188 inpatients	524 outpatients
Features, %			
Diarrhea	98	99	98
Blood in stool	52	27	–
Mucus in stool	35	21	–
Malaise	95	92	70
Abdominal pain	88	90	87
Abdominal tenderness	–	53	–
Fever	82	88	78
Nausea	55	65	–
Vomiting	35	51	–
Headache	< 30	55	51
Myalgia	< 30	35	–
Arthralgia	< 30	28	19

CLINICAL PRESENTATION

Many individuals with *Campylobacter* infection are thought to be asymptomatic. Rates of asymptomatic infection vary widely by age and region. In a study conducted at 2 large academic hospitals in Baltimore, MD, and New Haven, CT, *Campylobacter* was isolated from 0.9% of healthy individuals of all ages without symptoms of diarrhea but was not found in any healthy adult control subjects in a separate trial conducted in Sweden.[38,39] In symptomatic individuals, onset of clinical disease occurs 1 to 7 days after ingestion of the bacteria. Acute diarrhea is the most common presenting feature, occurring in 98% to 99% of symptomatic patients.[40–42] Classic dysentery may occur with small-volume mucoid stool containing occult or gross blood. However, large-volume fluid losses without dysentery may also occur. In immunocompetent patients, other prominent symptoms include abdominal cramps, nausea, vomiting, fever, headache, and myalgias. Fever and gastrointestinal symptoms, including abdominal cramping and nausea, but without diarrhea, have also been reported (**Table 2**). Illness in otherwise healthy adults is usually self-limiting and lasts less than 2 weeks. Illness with severe diarrhea, abdominal pain, or high fever are considerations for hospital admission and fluid replacement.[41] Carriage of *Campylobacter* organisms following infection is usually less than 3 weeks even in untreated patients.[14]

Severe gastrointestinal disease, including chronic diarrhea, bacteremia with or without extraintestinal dissemination, and postinfectious syndromes are infrequently seen in healthy patients. Prolonged and severe disease more frequently occurs in individuals with immunodeficiency syndromes, including HIV/AIDS.[43] In a series of 38 patients with HIV and *Campylobacter* infection, most patients presented with acute diarrhea, fever, and abdominal pain; however, 4 (11%) had bacteremia, and 8 (21%) experienced chronic diarrhea.[43] Infrequently, acute extraintestinal complications, prolonged disease, bacteremia, and disseminated disease occur in the elderly and in patients with underlying diseases, including malnutrition, diabetes, malignancy, and alcoholism.[44,45] Rare systemic and extraintestinal complications include meningitis, acute septic arthritis, septic abortion, severe gastrointestinal hemorrhage, cholecystitis, urinary tract infection, abscesses, gram-negative sepsis, toxic megacolon, and endocarditis.[45–48] Extraintestinal manifestations are more common in non-*jejuni Campylobacter* species.[44,48]

POSTINFECTIOUS COMPLICATIONS

Postinfectious complications associated with *Campylobacter* infections include Guillain-Barré syndrome, reactive arthritis, postinfectious irritable bowel syndrome,

Table 3. Frequency of Joint Involvement in Postinfectious Reactive Arthritis

Involved Joint	Frequency, % (n = 45)
Knees	36
Proximal interphalangeal, hand	36
Metacarpophalangeal	33
Ankles	29
Shoulder	27
Metatarsophalangeal	24
Distal interphalangeal	24
Wrist	22

Data from Hannu T et al.[58]

and potentially immunoproliferative small intestinal disease (IPSID). Guillain-Barré syndrome is a rapidly progressive acute flaccid paralysis that results from inflammatory demyelination of peripheral nerves and is the most severe and life-threatening postinfectious sequelae of campylobacteriosis. It is reported in 1 per 1000 to 3000 *Campylobacter* infections.[49] The association of Guillain-Barré syndrome with *Campylobacter* was first reported in a 45-year-old man who presented with bloody stool and developed progressive flaccid paralysis.[50] Approximately 36% to 38% of Guillain-Barré syndrome cases are preceded by symptomatic or asymptomatic *Campylobacter* infection, and cases of Guillain-Barré syndrome associated with this infection appear to be more clinically severe.[51–53]

The development of Guillain-Barré syndrome following *C. jejuni* infection is linked to autoimmune molecular mimicry between terminal sugar molecules shared by human peripheral nerves and *C. jejuni* antigens. As discussed earlier, *C. jejuni* organisms express lipooligosaccharides, and the outer core of lipooligosaccharides of strains associated with Guillain-Barré syndrome contain the same terminal sugars (NeuNAC) found in gangliosides of peripheral nerves. "Molecular mimicry" occurs as antibodies to *C. jejuni* lipooligosaccharides cross-react with the sugars in peripheral nerve gangliosides, resulting in immune reaction against myelin or axons of peripheral nerves and causing demyelination.[54] Investigators have isolated *C. jejuni* strains associated with "classic" Guillain-Barré syndrome (acute inflammatory demyelinating polyradiculoneuropathy and, particularly in patients with *Campylobacter*-associated disease, acute axonal degeneration) and found that these serotypes most frequently develop antibodies to GM1 or GD1a gangliosides. In contrast, *Campylobacter* strains that induce antibodies to GQ1b, GT1a, or GD3 gangliosides are associated with the Miller-Fisher variant of Guillain-Barré syndrome, which is associated with ataxia, ophthalmoplegia, and nonreactive pupils.[55,56]

Reactive arthritis is a seronegative spondylarthropathy that occurs after approximately 2% to 7% of *Campylobacter* infections.[57,58] Unlike Guillain-Barré syndrome, reactive arthritis appears to be associated with host genetic factors, not the bacterial strain. *Campylobacter* as well as *Salmonella, Shigella, Yersinia,* and *Chlamydia* are similarly associated with postinfectious reactive arthritis; disease manifestations do not differ based on the associated pathogen.[59] The mechanisms by which these species induce reactive arthritis is poorly understood, but they are thought to result from an autoimmune phenomenon caused by cross-reaction between bacteria antigens and an autologous joint peptide found predominately in genetically predisposed human leukocyte antigen (HLA)-B27–positive patients.[59] Between 65% and 95% of white patients and between 30% and 50% of African American patients with reactive arthritis carry the HLA-B27 allele.[60] Antibiotic treatment of campylobacteriosis does not prevent reactive arthritis; however, patients who subsequently develop reactive arthritis have a longer duration of diarrhea are more likely to have required antibiotic therapy.[61] Both large and small joints can be involved in postinfectious reactive arthritis, as demonstrated in large population studies (**Table 3**).[58] Twenty-two percent of affected individuals recover within 1 month, but 55% remain symptomatic at 6 months. Occasionally, patients develop full Reiter syndrome, including uveitis.[62]

Persistent gastrointestinal symptoms may occur in some patients after the resolution of acute campylobacteriosis. Postinfectious irritable bowel syndrome occurs following bacterial diarrhea caused by *Campylobacter, Shigella,* and *Salmonella.*[63,64] Approximately 9% of patients with campylobacteriosis may develop postinfectious irritable bowel syndrome, particularly after protracted illness, and postinfectious irritable bowel syndrome should also be considered a cause of persistent diarrhea in travelers.[64,65] Although incompletely understood, the mechanisms may involve the inability to downregulate inflammatory markers after persistent inflammation[65] as well as serotonin-mediated effects from enterochromaffin cell hyperplasia.[64]

Finally, a recent report has associated *C. jejuni* infection with a rare form of mucosa-associated lymphoid tissue lymphoma, IPSID/α chain disease.[66] Patients with early IPSID had previously been known to be antibiotic (tetracycline) responsive.[67] *Campylobacter* DNA was subsequently found in biopsy specimens of an antibiotic-responsive index patient and in 4 of 6 archived specimens from other IPSID cases.[66] The proposed

mechanism of IPSID pathogenesis is via an autoreactive B cell clone that secretes α chains, possibly stimulated by *C. jejuni*–specific T lymphocytes. Causality has not yet been shown, and since *C. jejuni* is not known to chronically colonize humans, *C. jejuni* may be part of a multifactorial process of IPSID development.[67]

DIAGNOSIS

Campylobacter infection should be suspected in patients with fever and acute diarrhea, particularly those with visible blood and mucus in the stool, including international travelers. Because the clinical presentation is similar to that seen with other common enteric bacterial pathogens such as *Salmonella, Shigella, Yersinia, Clostridium difficile,* and *E. coli* O157:H7, a presumptive diagnosis based on clinical presentation cannot be made. Diagnosis is made by isolating campylobacters from stool samples.

Specimens for culture should have minimal exposure to oxygen and be processed within 24 hours. Campylobacters are gram-negative spiral or S-shaped rods that are nonspore-forming and are highly motile. Gram's staining of diarrheal stool demonstrates curved or spiral-shaped gram-negative rods, and darting motility in darkfield or phase contrast microscopy is seen.[68,69] Definitive diagnosis is based on stool culture in a microaerophilic condition (5%–10% oxygen, 1%–10% carbon dioxide, 85% nitrogen) using selective, blood-based, antibiotic-enriched media, such as Blaser or Skirrow's media. All *Campylobacter* species are oxidase- and catalase-positive and grow at 37°C. *C. jejuni* and *C. coli,* however, grow optimally at 42°C, and this differential growth is used in the clinical microbiology laboratory. *C. jejuni* alone can be distinguished by its ability to hydrolyze hippurate. Campylobacters are slow growing, and incubation of stool cultures is performed for a minimum of 48 hours. These organisms are also generally fragile and can be destroyed by heat, desiccation, acidity, and disinfectants.

TREATMENT

Most cases of campylobacteriosis are self-limiting in immunocompetent patients without systemic signs of infection, requiring only supportive treatment with adequate hydration. A recent meta-analysis demonstrated that antibiotic treatment was beneficial when begun early, decreasing diarrhea duration by a mean of 1.32 days as well as shortening the microbiologic carriage duration.[70] However, no randomized clinical trial has supported the use of antibiotics, as noted in current guidelines for the management of infectious diarrhea.[71] Two randomized controlled trials have demonstrated the benefit of antibiotics in the eradication of fecal carriage but did not show a change in the course or duration of illness.[72,73] Since there is no clear standard of care for treatment of immunocompetent individuals, clinical judgment should be used when deciding whether to treat with antibiotics. Prudent use of antibiotics will favor patients with visible blood in the stool, fever, a large number of stools, and/or worsening of symptoms, as with other inflammatory diarrheas.[18,71] Pregnant women and individuals with immunosuppressive medical conditions, including HIV/AIDS, should also receive antibiotics.[12,74] Reasons to withhold antibiotics include the self-limited nature of infection in healthy populations and the rising problem of antibiotic resistance among *Campylobacter* species due to veterinary use.[18]

C. jejuni have been historically sensitive to macrolides, tetracyclines, fluoroquinolones, aminoglycosides, imipenem, and chloramphenicol but resistant to trimethoprim.[74] Erythromycin has been the cornerstone of therapy, demonstrating consistent bacteriologic cure of sensitive strains when compared with placebo but with an inconsistent benefit for clinical cure, as discussed above.[72,75] With the introduction of the fluoroquinolones, ciprofloxacin became the mainstay of empiric treatment for acute community-acquired bacterial diarrhea and for travelers' diarrhea.[76,77] However, rapid emergence of fluoroquinolone-resistant *Campylobacter* strains was noted in Europe in the 1980s (0% in 1982 and 11% in 1989), which coincided with the introduction of quinolone use in poultry.[78] In the United States, ciprofloxacin resistance rose from 0% in 1989 to 19% in 2001 and has reached 90% in Thailand.[79–81] Currently, macrolide antibiotics are the preferred treatment for outpatients with *Campylobacter* infection acquired in the United States who require therapy: erythromycin (500 mg twice daily for 5 days) or azithromycin (500 mg orally daily for 3 days).[71,82] Azithromycin should be used for travelers' diarrhea due to *Campylobacter* infection and empirically where quinolone resistance is anticipated.[71] In US military personnel in Thailand, azithromycin was shown to be as effective as ciprofloxacin in shortening symptomatic illness and in microbiologic cure rates.[82] More severe, systemic disease can be treated with a variety of intravenous antibiotics, including cefotaxime, imipenem, ampicillin, and parenteral aminoglycosides, but antimicrobial sensitivities should always be checked.

PREVENTION

There is no licensed vaccine against *Campylobacter* species that most frequently cause clinical disease (ie,

C. jejuni and *C. coli).* Prevention of infection with *Campylobacter* involves attention to handling raw poultry and ingestion of undercooked poultry as well as contaminated water and food. Between 50% and 70% of sporadic infections are attributable to poultry; thorough cleaning of cutting boards, proper cooking (to 170°F–180°F) and hand washing after handling chicken should be encouraged in the home.[36,83,84] International travelers, immunocompromised individuals, and pregnant women should follow general precautions to protect against diarrhea, including the ingestion of clean drinking water, avoidance of unpasteurized milk and undercooked meats, and strict attention to hand hygiene.

CONCLUSION

Campylobacteriosis is a common cause of diarrhea and enterocolitis worldwide. Although commonly self-limiting, infection can be associated with severe complications, including reactive arthritis and Guillain-Barré syndrome in previously healthy hosts as well as systemic and recurrent disease in immunocompromised patients. The rapid emergence of quinolone resistance has limited antibiotic options for treating symptomatic disease. **HP**

Test your knowledge and comprehension of this article with the *Clinical Review* Quiz on page 42.

Corresponding author: Beth D. Kirkpatrick, MD, University of Vermont College of Medicine, 110 Stafford Hall, 95 Carrigan Drive, Burlington, VT 05405; beth.kirkpatrick@uvm.edu.

REFERENCES

1. Centers for Disease Control and Preventions (CDC). Preliminary FoodNet Data on the incidence of infection with pathogens transmitted commonly through food—10 States, United States, 2007. MMWR Morb Mortal Wkly Rep 2008:57–70.
2. Skirrow MB. John McFadyean and the centenary of the first isolation of *Campylobacter* species. Clin Infect Dis 2006;43:1213–7.
3. Smith T. Some morphological and biological characters of the spirilla [*Vibrio fetus*] associated with disease of the fetal membranes in cattle. Int J Syst Bacterriol 1919;23:122–34.
4. King EO. Human infections with *Vibrio fetus* and a closely related vibrio. J Infect Dis 1957;101:119–28.
5. Dekeyser P, Gossuin-Detrain M, Butzler JP, Sternon J. Acute enteritis due to related vibrio: first positive stool cultures. J Infect Dis 1972;125:390–2.
6. Lindquist B, Kjellander J, Kosunen T. *Campylobacter* enteritis in Sweden [letter]. Br Med J 1978;1:303.
7. Pearson AD, Suckling WG, Ricciardi ID, et al. *Campylobacter*-associated diarrhoea in Southampton [letter]. Br Med J 1977;2:955–6.
8. Tiehan W, Vogt RL. Waterborne *Campylobacter* gastroenteritis. MMWR Morb Mortal Wkly Rep 1978;27:207.
9. Vogt RL, Sours HE, Barrett T, et al. *Campylobacter* enteritis associated with contaminated water. Ann Intern Med 1982;96:292–6.
10. Kornblatt AN, Barrett T, Morris GK, Tosh FE. Epidemiologic and laboratory investigation of an outbreak of *Campylobacter* enteritis associated with raw milk. Am J Epidemiol 1985;122:884–9.
11. Itoh T, Saito K, Maruyama T, et al. An outbreak of acute enteritis due to *Campylobacter fetus* subspecies *jejuni* at a nursery school of Tokyo. Microbiol Immunol 1980;24:371–9.
12. Blaser M, Allos BM. *Campylobacter jejuni* and related species. In: Mandell G, Bennet JE, Dolin R, editors. Principles and practice of infectious diseases. 6th ed. New York: Elsevier/Churchill Livingstone; 2005:2548–57.
13. Grant IH, Richardson NJ, Bokkenheuser VD. Broiler chickens as potential source of *Campylobacter* infections in humans. J Clin Microbiol 1980;11: 508–10.
14. Blaser MJ, LaForce FM, Wilson NA, Wang WL. Reservoirs for human campylobacteriosis. J Infect Dis 1980;141:665–9.
15. Zhao C, Ge B, De Villena J, et al. Prevalence of *Campylobacter spp., Escherichia coli,* and *Salmonella* serovars in retail chicken, turkey, pork, and beef from the Greater Washington, D.C., area. Appl Environ Microbiol 2001;67:5431–6.
16. Ghafir Y, China B, Dierick K, et al. A seven-year survey of *Campylobacter* contamination in meat at different production stages in Belgium. Int J Food Microbiol 2007;116:111–20.
17. Samuel MC, Vugia DJ, Shallow S, et al; Emerging Infections Program FoodNet Working Group. Epidemiology of sporadic *Campylobacter* infection in the United States and declining trend in incidence, FoodNet 1996–1999. Clin Infect Dis 2004;38 Suppl 3:S165–74.
18. Ruiz-Palacios GM. The health burden of *Campylobacter* infection and the impact of antimicrobial resistance: playing chicken [editorial]. Clin Infect Dis 2007;44:701–3.
19. Rees JR, Pannier MA, McNees A, et al. Persistent diarrhea, arthritis, and other complications of enteric infections: a pilot survey based on California FoodNet surveillance, 1998–1999. Clin Infect Dis 2004;38 Suppl 3:S311–7.
20. Friedman CR, Hoekstra RM, Samuel M, et al. Risk factors for sporadic *Campylobacter* infection in the United States: a case-control study in FoodNet sites. Clin Infect Dis 2004;38 Suppl 3:S285–96.
21. Kapperud G, Skjerve E, Bean NH, et al. Risk factors for sporadic *Campylobacter* infections: results of a case-control study in southeastern Norway. J Clin Microbiol 1992;30:3117–21.
22. Glass RI, Stoll BJ, Huq MI, et al. Epidemiologic and clinical features of endemic *Campylobacter jejuni* infection in Bangladesh. J Infect Dis 1983;148: 292–6.
23. Calva JJ, Ruiz-Palacios GM, Lopez-Vidal AB, et al. Cohort study of intestinal infection with *Campylobacter* in Mexican children. Lancet 1988;1:503–6.
24. Brooks JT, Ochieng JB, Kumar L, et al. Surveillance for bacterial diarrhea and antimicrobial resistance in rural western Kenya, 1997–2003. Clin Infect Dis 2006;43:393–401.
25. Steffen R, Collard F, Tornieporth N, et al. Epidemiology, etiology, and impact of traveler's diarrhea in Jamaica. JAMA 1999;281:811–7.
26. Taylor DN, Houston R, Shlim DR, et al. Etiology of diarrhea among travelers and foreign residents in Nepal. JAMA 1988;260:1245–8.
27. Tribble DR, Sanders JW, Pang LW, et al. Traveler's diarrhea in Thailand: randomized, double-blind trial comparing single-dose and 3-day azithromycin-based regimens with a 3-day levofloxacin regimen. Clin Infect Dis 2007;44: 338–46.
28. Laughon BE, Druckman DA, Vernon A, et al. Prevalence of enteric pathogens in homosexual men with and without acquired immunodeficiency syndrome. Gastroenterology 1988;94:984–93.
29. Fujihara N, Takakura S, Saito T, et al. A case of perinatal sepsis by *Campylobacter fetus subsp. fetus* infection successfully treated with carbapenem—case report and literature review. J Infect 2006;53:e199–202.
30. Goossens H, Henocque G, Kremp L, et al. Nosocomial outbreak of *Campylobacter jejuni* meningitis in newborn infants. Lancet 1986;2:146–9.
31. Lopman BA, Reacher MH, Vipond IB, et al. Epidemiology and cost of nosocomial gastroenteritis, Avon, England, 2002–2003. Emerg Infect Dis 2004;10: 1827–34.
32. van Spreeuwel JP, Duursma GC, Meijer CJ, et al. *Campylobacter colitis:* histological immunohistochemical and ultrastructural findings. Gut 1985;26:945–51.
33. Young KT, Davis LM, Dirita VJ. *Campylobacter jejuni*: molecular biology and pathogenesis. Nat Rev Microbiol 2007;5:665–79.
34. Ketley JM. Pathogenesis of enteric infection by *Campylobacter.* Microbiology 1997;143(Pt 1):5–21.
35. Robinson DA. Infective dose of *Campylobacter jejuni* in milk. Br Med J (Clin Res Ed) 1981;282:1584.
36. Black RE, Levine MM, Clements ML, et al. Experimental *Campylobacter jejuni* infection in humans. J Infect Dis 1988;157:472–9.
37. Bereswill S, Kist M. Recent developments in *Campylobacter* pathogenesis. Curr Opin Infect Dis 2003;16:487–91.
38. Nataro JP, Mai V, Johnson J, et al. Diarrheagenic *Escherichia coli* infection in Baltimore, Maryland, and New Haven, Connecticut. Clin Infect Dis 2006;43:402–7.

39. Svenungsson B, Lagergren A, Ekwall E, et al. Enteropathogens in adult patients with diarrhea and healthy control subjects: a 1-year prospective study in a Swedish clinic for infectious diseases. Clin Infect Dis 2000;30:770–8.
40. Blaser MJ, Reller LB, Luechtefeld NW, Wang WL. *Campylobacter* enteritis in Denver. West J Med 1982;136:287–90.
41. Pitkanen T, Ponka A, Pettersson T, Kosunen TU. *Campylobacter* enteritis in 188 hospitalized patients. Arch Intern Med 1983;143:215–9.
42. Ponka A, Pitkanen T, Sarna S, Kosunen TU. Infection due to *Campylobacter jejuni*: a report of 524 outpatients. Infection 1984;12:175–8.
43. Molina J, Casin I, Hausfater P, et al. *Campylobacter* infections in HIV-infected patients: clinical and bacteriological features. AIDS 1995;9:881–5.
44. Bokkenheuser V. *Vibrio fetus* infection in man. I. Ten new cases and some epidemiologic observations. Am J Epidemiol 1970;91:400–9.
45. Guerrant RL, Lahita RG, Winn WC Jr, Roberts RB. Campylobacteriosis in man: pathogenic mechanisms and review of 91 bloodstream infections. Am J Med 1978;65:584–92.
46. Michalak DM, Perrault J, Gilchrist MJ, et al. *Campylobacter fetus ss. jejuni:* a cause of massive lower gastrointestinal hemorrhage. Gastroenterology 1980; 79:742–5.
47. McKinley MJ, Taylor M, Sangree MH. Toxic megacolon with *Campylobacter* colitis. Conn Med 1980;44:496–7.
48. Blaser MJ. Extraintestinal *Campylobacter* infections [editorial]. West J Med 1986;144:353–4.
49. Allos BM. Association between *Campylobacter* infection and Guillain-Barre syndrome. J Infect Dis 1997;176 Suppl 2:S125–8.
50. Rhodes KM, Tattersfield AE. Guillain-Barre syndrome associated with *Campylobacter* infection. Br Med J (Clin Res Ed) 1982;285:173–4.
51. Mishu B, Ilyas AA, Koski CL, et al. Serologic evidence of previous *Campylobacter jejuni* infection in patients with the Guillain-Barre syndrome. Ann Intern Med 1993;118:947–53.
52. Kaldor J, Speed BR. Guillain-Barre syndrome and *Campylobacter jejuni*: a serological study. Br Med J (Clin Res Ed) 1984;288:1867–70.
53. Rees JH, Soudain SE, Gregson NA, Hughes RA. *Campylobacter jejuni* infection and Guillain-Barre syndrome. N Engl J Med 1995;333:1374–9.
54. Kuroki S, Saida T, Nukina M, et al. *Campylobacter jejuni* strains from patients with Guillain-Barre syndrome belong mostly to Penner serogroup 19 and contain beta-N-acetylglucosamine residues. Ann Neurol 1993;33:243–7.
55. Yuki N, Taki T, Takahashi M, et al. Molecular mimicry between GQ1b ganglioside and lipopolysaccharides of *Campylobacter jejuni* isolated from patients with Fisher's syndrome. Ann Neurol 1994;36:791–3.
56. Salloway S, Mermel LA, Seamans M, et al. Miller-Fisher syndrome associated with *Campylobacter jejuni* bearing lipopolysaccharide molecules that mimic human ganglioside GD3. Infect Immun 1996;64:2945–9.
57. Hannu T, Kauppi M, Tuomala M, et al. Reactive arthritis following an outbreak of *Campylobacter jejuni* infection. J Rheumatol 2004;31:528–30.
58. Hannu T, Mattila L, Rautelin H, et al. *Campylobacter*-triggered reactive arthritis: a population-based study. Rheumatology (Oxford) 2002;41:312–8.
59. Yu D, Kuipers JG. Role of bacteria and HLA-B27 in the pathogenesis of reactive arthritis. Rheum Dis Clin North Am 2003;29:21–36, v–vi.
60. Petersel DL, Sigal LH. Reactive arthritis. Infect Dis Clin North Am 2005;19: 863–83.
61. Locht H, Krogfelt KA. Comparison of rheumatological and gastrointestinal symptoms after infection with *Campylobacter jejuni/coli* and enterotoxigenic *Escherichia coli*. Ann Rheum Dis 2002;61:448–52.
62. Howard RS, Sarkies NJ, Sanders MD. Anterior uveitis associated with *Campylobacter jejuni* infection [letter]. J Infect 1987;14:186–7.
63. Thornley JP, Jenkins D, Neal K, et al. Relationship of *Campylobacter* toxigenicity in vitro to the development of postinfectious irritable bowel syndrome. J Infect Dis 2001;184:606–9.
64. Spiller RC. Postinfectious irritable bowel syndrome. Gastroenterology 2003; 124:1662–71.
65. Spiller RC, Jenkins D, Thornley JP, et al. Increased rectal mucosal enteroendocrine cells, T lymphocytes, and increased gut permeability following acute *Campylobacter* enteritis and in post-dysenteric irritable bowel syndrome. Gut 2000;47:804–11.
66. Lecuit M, Abachin E, Martin A, et al. Immunoproliferative small intestinal disease associated with *Campylobacter jejuni*. N Engl J Med 2004;350:239–48.
67. Parsonnet J, Isaacson PG. Bacterial infection and MALT lymphoma. N Engl J Med 2004;350:213–5.
68. Wang H, Murdoch DR. Detection of *Campylobacter* species in faecal samples by direct Gram stain microscopy. Pathology 2004;36:343–4.
69. Paisley JW, Mirrett S, Lauer BA, et al. Dark-field microscopy of human feces for presumptive diagnosis of *Campylobacter fetus* subsp. jejuni enteritis. J Clin Microbiol 1982;15:61–3.
70. Ternhag A, Asikainen T, Giesecke J, Ekdahl K. A meta-analysis on the effects of antibiotic treatment on duration of symptoms caused by infection with *Campylobacter* species. Clin Infect Dis 2007;44:696–700.
71. Guerrant RL, Van Gilder T, Steiner TS, et al; Infectious Diseases Society of America. Practice guidelines for the management of infectious diarrhea. Clin Infect Dis 2001;32:331–51.
72. Anders BJ, Lauer BA, Paisley JW, Reller LB. Double-blind placebo controlled trial of erythromycin for treatment of *Campylobacter* enteritis. Lancet 1982;1: 131–2.
73. Mandal BK, Ellis ME, Dunbar EM, Whale K. Double-blind placebo-controlled trial of erythromycin in the treatment of clinical *Campylobacter* infection. J Antimicrob Chemother 1984;13:619–23.
74. Allos BM. *Campylobacter jejuni* infections: update on emerging issues and trends. Clin Infect Dis 2001;32:1201–6.
75. Pai CH, Gillis F, Tuomanen E, Marks MI. Erythromycin in treatment of *Campylobacter* enteritis in children. Am J Dis Child 1983;137:286–8.
76. Dryden MS, Gabb RJ, Wright SK. Empirical treatment of severe acute community-acquired gastroenteritis with ciprofloxacin. Clin Infect Dis 1996;22:1019–25.
77. Adachi JA, Ostrosky-Zeichner L, DuPont HL, Ericsson CD. Empirical antimicrobial therapy for traveler's diarrhea. Clin Infect Dis 2000;31:1079–83.
78. Endtz HP, Ruijs GJ, van Klingeren B, et al. Quinolone resistance in campylobacter isolated from man and poultry following the introduction of fluoroquinolones in veterinary medicine. J Antimicrob Chemother 1991;27:199–208.
79. Bodhidatta L, Vithayasai N, Eimpokalarp B, et al. Bacterial enteric pathogens in children with acute dysentery in Thailand: increasing importance of quinolone-resistant *Campylobacter*. Southeast Asian J Trop Med Public Health 2002;33:752–7.
80. Gupta A, Nelson JM, Barrett TJ, et al; NARMS Working Group. Antimicrobial resistance among *Campylobacter* strains, United States, 1997–2001. Emerg Infect Dis 2004;10:1102–9.
81. McDermott PF, Bodeis SM, English LL, et al. Ciprofloxacin resistance in *Campylobacter jejuni* evolves rapidly in chickens treated with fluoroquinolones. J Infect Dis 2002;185:837–40.
82. Kuschner R, Trofa AF, Thomas RJ, et al. Use of azithromycin for the treatment of *Campylobacter* enteritis in travelers to Thailand, an area where ciprofloxacin resistance is prevalent. Clin Infect Dis 1995;21:536–41.
83. Harris NV, Weiss NS, Nolan CM. The role of poultry and meats in the etiology of *Campylobacter jejuni/ coli* enteritis. Am J Public Health 1986;76:407–11.
84. Adak GK, Cowden JM, Nicholas S, Evans HS. The Public Health Laboratory Service national case-control study of primary indigenous sporadic cases of campylobacter infection. Epidemiol Infect 1995;115:15–22.