Editorials

Do You Have a *Campylobacter* in Your Future?

A SHORT TIME AGO, *Campylobacter jejuni* was not a well-recognized pathogen. This curved, gram-negative rod was considered an esoteric microbe associated with veterinary diseases and occasional human cases of bacteremia or septic abortion. As culture methods for campylobacters improved, the recognition of the important role of these microorganisms in causing human disease also increased. In the article by Peterson elsewhere in this issue of the journal, the impressive scope and magnitude of clinical disease produced by *C jejuni* are reviewed.[1] In addition to its major role in the causation of commonly acquired infectious diarrhea among persons in developed countries, several important observations have emerged. *Campylobacter jejuni* is now appreciated as an important cause of morbidity and mortality in young children in developing countries and in immunocompromised persons in developed countries, and it also may be the most important trigger of the Guillain-Barré syndrome in this country and in others.[2-4] Most recently, *C jejuni* has been implicated as a cause of acute motor axonal neuropathy, a paralytic disease that has affected thousands of Chinese children.[5,6]

Despite the substantial burden of illness imposed by *C jejuni* infections, many clinical microbiology laboratories still do not look for campylobacters in stool specimens submitted for routine culture. Furthermore, a growing number of "atypical" campylobacters—other *Campylobacter* species and species within the *Arcobacter, Helicobacter,* and *Wolinella* genera—are increasingly implicated in human disease,[7-9] but they are fastidious organisms and difficult to culture. Identifying these organisms requires special culture media or filtration methods; unless they are specifically searched for, they will not be found. Consequently, new associations of disease with these unusual or difficult-to-grow microorganisms may be missed. When a new pathogen is identified, such as *C jejuni* or *Legionella pneumophila* serogroup 1, an explosion of discoveries of other related species frequently ensues. In the current medical cost-containing environment, however, filtration techniques for campylobacters may seem frivolous when the yield often is low.

A brief consideration of the epidemiology of *Campylobacter* infections narrows the group of patients with diarrhea in whom a search for campylobacters is indicated. Persons in whom diarrhea develops after they have been in a hospital more than 72 hours are unlikely to be infected with *C jejuni*—or *Salmonella* or *Shigella* species, for that matter[10]—and routine cultures should not be done. In contrast, *Campylobacter* cultures should be done on persons who are at high risk for being infected with these organisms. These high-risk persons include outpatients who present with fever and diarrhea (especially diarrhea that is bloody or contains leukocytes) and who are far more likely to have a bacterial cause of their illness. Infections with *Campylobacter* species may mimic appendicitis in some patients; identification of campylobacters in stool specimens could eliminate the need for surgical intervention in some of these patients, although culture results may not be available in time to prevent many laparotomies. Similarly, persons infected with the human immunodeficiency virus (HIV) or other immunocompromised persons with diarrhea may be infected with campylobacters and related organisms, even if the symptoms are chronic.[11] Other persons at high risk for *C jejuni* infection include travelers to developing countries and persons with possible occupational or recreational exposures to campylobacters in whom diarrhea develops. Persons suspected of having inflammatory bowel diseases should have stool cultures for campylobacters and related organisms as a routine part of their diagnostic workup. The cost of campylobacter cultures is minimal when compared with the medical and social costs associated with a false diagnosis of idiopathic inflammatory bowel disease.

Campylobacter jejuni infections are most likely prevented by adhering to basic food safety rules. As highlighted by Peterson, *C jejuni* usually is not transmitted from person to person, but is acquired from foods of animal origin. Although unpasteurized milk is the most common cause of outbreaks of *C jejuni* infections,[12] sporadic cases—which account for the lion's share of disease—are most often associated with the consumption of poultry and poultry products.[13,14] Reducing *Campylobacter* species contamination of poultry and poultry products will diminish the burden of human disease. For consumers, because *C jejuni* is easily killed by heat, thorough cooking and avoidance of cross-contamination of utensils (such as cutting boards) probably could reduce the rate of *C jejuni* infections. Special vigilance for preventing *C jejuni* exposure is warranted in patients with HIV infection in whom more severe and chronic infections with *C jejuni* may develop than in immunocompetent persons.[15,16] *Campylobacter jejuni* infections among patients infected with HIV are clinically apparent more than 30 times more frequently than in the general population.[11] This implies that *C jejuni* is in wide circulation but that the inoculum usually encountered is insufficient to cause illness in a normal host.

Despite the ubiquity of *C jejuni* and the frequency of both symptomatic and asymptomatic infections, the pathogenesis of *C jejuni* enteritis remains poorly understood. Because many patients with *C jejuni* infections experience watery diarrhea and because *C jejuni* isolates have been reported to be enterotoxigenic,[17,18] this mechanism was thought to be important. More recently, however, the role of enterotoxins in the pathogenesis of *C jejuni* enteritis has been called into question for the following reasons:

- Enterotoxin production cannot be detected in vivo;
- Patients with *C jejuni* infection do not have a serologic response to cholera toxin[19]; and
- Most patients have fever, bloody stools, and fecal leukocytes, which are not caused by choleralike enterotoxins.

The pathogenesis of *C jejuni* infection more likely involves cytotoxin production or direct bacterial invasion and proliferation within the intestinal epithelium. Both natural and experimentally induced infections typically induce serum- and mucosal-specific antibody responses,[20] and the increased frequency of *C jejuni* bacteremia in persons with hypogammaglobulinemia[21,22] suggests that humoral responses play a key role in limiting the scope of infection. The increased frequency of chronic *C jejuni* infections in HIV-positive persons suggests, however, that cell-mediated immunity also may play a protective role.

Humoral immune responses also may have deleterious effects. Cross-reactivity between antibodies to *C jejuni* and host structures may be responsible for a number of other postinfectious illnesses including Reiter's syndrome and Guillain-Barré syndrome. Identifying particular serotypes or other strain characteristics capable of triggering this type of immune response is necessary so that control and prevention strategies may be devised.

In the past 20 years, *C jejuni* has become established as an important cause of enteric infection; the rheumatologic and neurologic sequelae of *C jejuni* infections also are becoming increasingly well publicized. But *C jejuni* infections continue to be underconsidered by physicians and underdiagnosed by microbiology laboratories, and cases are underreported. Despite the fact that campylobacters are detected in stool specimens of patients with diarrhea more frequently than *Salmonella* and *Shigella* species combined when they are looked for,[10] states continue to report cases of *C jejuni* infections at a far lower rate.[23,24] Further efforts are needed to increase campylobacter surveillance and to investigate the pathogenesis of the sequelae of campylobacter infections. Such studies are likely to shed light on the expanding roles these organisms play in causing human disease.

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Are We Plumb Crazy?

LEAD (in Latin, *plumbum*) was used in some of the earliest inventions, including the forging of rigid metal implements, in medicinals, and in cosmetics. Its use was a key to the advancement of some civilizations and perhaps contributed to the demise of others.[1] Today lead lingers in the environment as an inauspicious consequence of human achievement. Had we known, in the making of that first leaded utensil, what poisonous course would be weaved for humankind, we may have tended our progress more cautiously. Yet in 1990, more than 1,275,000 metric tons of lead were used annually in the United States.

The toxicity of lead has been known since antiquity and was described by Nikander and other ancient writers. Premodern descriptions of lead toxicity focused only on occupational exposure. The classical clinical effects of lead and other metals were recognized in potters, painters, and miners. That it could afflict persons outside the trades was not reported until the late 1800s, however. The original cases of childhood lead poisoning due to lead-based paint were uncovered in Queensland, Australia, when paralysis, colic, convulsions, and optic neuritis were de-