FRI Briefings

Campylobacter — Chronic Effects

first published July 1998
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Foodborne illness is typically short-lived and primarily involves gastrointestinal symptoms. However, certain pathogens cause more life-threatening disease and certain individuals — because of age or immune status — are more likely to experience severe symptoms. More serious effects are often associated with specific pathogens: *Clostridium botulinum* is often lethal; *E. coli* O157.H7 has become infamous for causing hemolytic uremic syndrome in children; *Listeria* can cause miscarriages and toxoplasmosis is an important cause of congenital malformations; septicemia may result from infections with *Salmonella* and *Listeria*.

Foodborne bacteria have also been shown to cause chronic effects (sequelae), including arthritis, ankylosing spondylitis, renal disease, cardiac and neurological disorders, and nutritional and malabsorptive disorders. Some data indicate that 2–3% of the population as a whole develop chronic effects after foodborne illness, but follow-up of some outbreaks of salmonellosis revealed that 15–16% of cases suffered reactive arthritis in the months following their initial illness (*19,20*). Persons positive for the major histocompatibility class antigen B27 have a significantly greater relative risk for developing some reactive diseases. As many as 20% of exposed, genetically susceptible persons may suffer these complications.

It can be difficult to identify specific foodborne pathogens as the causes of chronic illnesses because effects sometimes occur after a mild illness and may not be manifested until days or weeks after gastrointestinal symptoms have subsided. Such chronic disease may be caused by dispersal of the infective bacteria from the gastrointestinal tract to other locations in the body or by the induction of cross-reacting antibodies by some antigen or superantigen present in the infecting bacteria. These antigens may be similar to cell surface antigens normally present in the body, and therefore the antibodies raised against the bacteria react with and cause inflammation in healthy tissues.

According to USDA estimates, between 6 and 33 million cases of foodborne illness occur annually in the USA (*8*). *Campylobacter jejuni* has recently come to the fore as the major cause of foodborne disease. The most recent USDA data from FoodNet, an active foodborne disease surveillance project, indicated an incidence of 50.4 cases of foodborne illness caused by 7 known pathogens/100,000 population at the sentinel sites. *Campylobacter* accounted for nearly half of these cases while *Salmonella* sp. was identified in 27% of cases (*2*). According to data from the Economic Research Service (USDA), *Campylobacter jejuni* and *C. coli* cause approximately 1,375,000–1,750,000 cases of foodborne illness and 100–511 deaths annually in the USA (*3,6,8*). These figures are undoubtedly an underestimate because most cases of campylobacteriosis are relatively mild and are never seen in a clinic or hospital.

Poultry is the primary food vehicle for *Campylobacter*. Some case–control studies indicate that up to 70% of sporadic cases of campylobacteriosis are associated with eating chicken. Surveys by the USDA demonstrated that up to 88% of broiler chicken carcasses in the USA are contaminated with *Campylobacter* while a recent Consumer Reports study identified *Campylobacter* in 63% of more than 1000 chickens obtained in grocery stores (*1*). Other identified food vehicles include: milk, mushrooms, hamburger, cheese, pork, shellfish, and eggs. Most cases of campylobacteriosis are sporadic or involve small family groups, although some common-source outbreaks involving many people have been traced to contaminated water or milk. In 1996, fourteen people in Oklahoma were infected with *C. jejuni* after eating lettuce which had apparently been cross-contaminated by raw poultry in a restaurant kitchen (*10*).

Campylobacter jejuni is a Gram-negative, microaerophilic, thermophilic rod, growing best at 42°C and low oxygen concentrations. These characteristics are adaptations for growth in its normal habitat — the intestine of warm-blooded birds and mammals. Food, particularly the surface of meat, becomes contaminated by exposure to fecal material, but

generally *C. jejuni* does not multiply in food since it does not grow at temperatures lower than 28°C. *Campylobacter* can survive refrigeration temperatures but is sensitive to heat and, therefore, pasteurization of milk and adequate cooking of meat will destroy this organism. Freezing and exposure to salt concentrations >1% injure cells and may significantly reduce populations. (Illness most often occurs following consumption of raw or undercooked meat or other foods cross-contaminated by raw poultry.) *Campylobacter jejuni* produces a number of compounds which may be related to its pathogenicity. These include: cell surface molecules which facilitate adhesion to the small intestine; hemolysins which rupture red blood cells releasing iron which is essential for bacterial growth; and several cytotoxins which may damage epithelial cells and allow invasion (*16,29*).

Acute effects of *Campylobacter* infections range from a day of diarrhea and lethargy to severe abdominal pain and diarrhea that lasts for several weeks. Most cases of campylobacteriosis are mild but up to 20% may last longer than a week and 2–10% of cases may be followed by chronic symptoms (*16,28*). Some chronic sequelae associated with *Campylobacter* infection include: appendicitis, arthritis, carditis, Reiter syndrome, Guillain-Barré syndrome (GBS), Miller Fisher syndrome, and urinary tract infections. Research on GBS from several areas of the world indicates that 20–40% of GBS cases were exposed to *C. jejuni* in the 1–3 weeks prior to the onset of neurological symptoms. This translates to 526–3830 cases associated with foodborne campylobacteriosis per year in the USA. Approximately 2% of GBS cases result in death (11–76 deaths/year related to foodborne campylobacteriosis).

Guillain-Barré syndrome has become the principal cause of acute neuromuscular paralysis in the USA since vaccination programs have nearly eliminated polio. GBS is an acute inflammatory disease affecting the peripheral nerves by removing the myelin sheath around the nerve cells. As the disease progresses, there is a loss of motor function (paralysis) and in many cases there is a loss of sensation as well. Even with prompt treatment, up to 20% of patients require mechanical ventilation. Usually only a small percentage of GBS patients die and of the survivors 80–85% recover totally. The remaining victims, however, may be left with severe neurological damage (*13*). *Campylobacter jejuni*–associated GBS more often has severe consequences than GBS associated with other causes (*5*).

Symptoms of GBS may be precipitated by numerous bacterial and viral infections but *C. jejuni* is recognized as the most common preceding infection. *Campylobacter* was first suggested to be a trigger for GBS in 1982 and since then numerous studies have documented a *C. jejuni* infection preceding GBS. Since symptoms of GBS may not be obvious until 2–3 weeks after infection with *C. jejuni,* analyses of stool samples may not be productive. However, serological analyses often demonstrate a high prevalence of antibodies to *C. jejuni* in serum of GBS patients (*22,27*).

There is evidence of antigenic similarity between some regions of the lipopolysaccharides of *C. jejuni* and the human gangliosides associated with nerve cells (*3*). Antibodies to human gangliosides, particularly the GM1 ganglioside, are known to be important in the pathogenesis of GBS (*11,12,14,15,17,24,31*). Therefore, it has been hypothesized that infection with *Campylobacter* induces formation of anti-ganglioside antibodies which then destroy or interfere with the function of peripheral nerves. Lipopolysaccharide structures in different strains of *C. jejuni* vary somewhat with some having more similarity to human gangliosides (*21,26*). This may make some strains more likely to cause GBS.

Only a small proportion of people infected with *C. jejuni* eventually develop GBS. It may be that some strains of *C. jejuni* are more likely to induce GBS and/or that some people are more susceptible. One *C. jejuni* strain, O:19, was found to be associated with 29% of *Campylobacter*-associated GBS in the USA and with 83% of cases in Japan (*4,25*). In South Africa, strain O:41 is associated with a high proportion of GBS cases (*9,18*). However, overall, these strains account for only 2–3% of *Campylobacter* infections in these countries. Genetically determined susceptibility may be a factor in some cases of GBS but it has not been demonstrated conclusively. One study from Japan indicated that characteristics of *C. jejuni* and of the infected persons interacted to determine the development of GBS (*25*).

Foodborne diseases in the USA have been estimated to cost in the billions of dollars each year. The Economic Research Service of the USDA estimates that seven foodborne pathogens induce illnesses costing $5.6 to 7.5 billion (*8*). Although little data on the economic effects of chronic sequelae to foodborne illness are available, the prolonged and debilitating effects of these complications may engender even greater costs than the immediate, acute symptoms. Costs (both medical and as a consequence of lost productivity) related to acute effects of foodborne campylobacteriosis have been estimated at $0.6–1.0 billion annually. Further analyses of *Campylobacter*-associated Guillain-Barré syndrome in the USA indicate that these cases may incur an additional $0.2–1.8 billion annually (*6,7*). Since only a

small proportion of patients with diarrhea seek medical attention and fecal testing is performed for only a small number of cases, the true incidence and cost of campylobacteriosis is probably significantly underestimated.

Based on 1995 data from Canterbury, New Zealand, a total of 65 hospital admissions and 977 outpatient cases with confirmed campylobacteriosis occurred during that year. Costs associated with these illnesses were estimated to total nearly $493,000: about 58% of this cost was due to time off work with the remainder attributed to medical tests, treatments, and consultations. In addition, two of eight patients diagnosed with Guillain-Barré syndrome were assumed to have had previous *Campylobacter* infections and these cases incurred additional costs of $89,522. Extrapolation of these figures to New Zealand as a whole indicated that the total national cost of campylobacteriosis was about $4.48 million in 1995 (*30*).

The incidence of chronic sequelae to campylobacteriosis is relatively small and is often overlooked. However, such chronic effects can be severe and involve long periods of hospitalization and time off from work. Therefore, the true cost of foodborne illness includes not only the acute effects experienced by about 2,000,000 people but also chronic effects like GBS which may affect up to 4,000 people/year in the USA.

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Last modified: 17 July 1998