

New information about pediatric foodborne infections: the view from FoodNet

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Purpose of review

Diarrheal illness is a significant burden to children and their parents. Recent studies describing the etiologic agents that cause diarrheal illness and examining the risk factors for the most common bacterial enteric pathogens are presented.

Recent findings

The most common bacterial causes of diarrheal illness among children are *Campylobacter* spp., *Salmonella* spp., *Shigella* spp. and Shiga toxin-producing *Escherichia coli*. The highest incidence of both *Campylobacter* and *Salmonella* is among infants. Risk factors for campylobacteriosis in this group include traveling outside the US, having a pet in the home with diarrhea and visiting or living on a farm. Risk factors for salmonellosis include traveling outside the US, exposure to reptiles and attending day-care with another child with diarrhea. Breastfeeding is a factor that protects against infection.

Summary

Despite a limited diet, infants are at risk of acquiring enteric pathogens that are commonly associated with consumption of contaminated food. Exposure to these pathogens may be through cross-contamination in the home or the environment. Educational measures that focus on improving prevention of exposure to infectious agents and an emphasis on eliminating cross-contamination are needed for parents and care-takers of this vulnerable population.

Keywords

diarrheal illness, foodborne illness, pediatrics, surveillance

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Introduction

Worldwide acute diarrheal illness accounts for an estimated 2.5 million childhood deaths annually [1]. Although diarrheal illness is less prevalent in developed than developing countries, its burden and impact can be substantial. An estimated 4% of hospitalizations and 2% of outpatient visits among children are due to diarrhea [2]. Diarrheal illness is often caused by enteric pathogens commonly transmitted through food. In the US, the Centers for Disease Control and Prevention's (CDC) Foodborne Diseases Active Surveillance Network (FoodNet) provides current, state-of-the-art research on the incidence and trends in foodborne pathogens, as well as epidemiologic studies of the risk factors associated with infection.

Background

In the US, Vernacchino *et al.* [3] found 2.2 episodes of diarrhea per person-year among a cohort of 604 healthy 6 to 36-month-old children. In this study, of the 611

diarrheal episodes reported, the most common bacterial pathogens found in diarrhea specimens were *Escherichia coli* genotypes, enteropathogenic *E. coli* (atypical) (12.9%) and enteroaggregative *E. coli* (4.1%), as well as *Clostridium perfringens* (2.3%) and *C. difficile* (1.9%). Numerous viral pathogens were also found including enteric adenovirus (5.7%), rotavirus (5.2%), astrovirus (3.5%), sapovirus (3.0%) and norovirus (1.9%). The mean duration of illness was 2 days; the median number of stools per episode was 6. The most common signs and symptoms of illness were loss of appetite (52.4%), cold symptoms (46.3%) and fever (28.3%); in 0.8% of episodes, blood was in the stool.

Population-based surveys conducted in FoodNet sites from 1996 to 2003 found the highest rates of self-reported acute diarrheal illness among those under 5 years of age [4•]. In an analysis of FoodNet data collected between 1996 and 1998, the authors found that children under the age of 5 years represented 21% of cases of all culture confirmed illness reported during those years. The incidence of bacterial enteric infections among the children

under 5 years of age was found to be the highest for *Campylobacter*, *Salmonella* and *Shigella* [5]. The highest incidence among children under 1 year of age was for *Salmonella* (122.2 per 100 000 population), *Campylobacter* (54.2) and *Yersinia enterocolitica* (24.7).

In the early 1990s, the National Academy of Science's Institute of Medicine publication [6] on the emergence of infectious diseases led the CDC to establish a plan for monitoring and preventing emerging infectious diseases. Among the issues of great concern was the change in the epidemiology of foodborne disease [7,8]. Specifically, there were new pathogens, such as *Cyclospora*, *E. coli* O157 and non-O157 Shiga toxin-producing *E. coli* (STEC), as well as multidrug resistant pathogens associated with food products. Moreover, there were changes in the nature of the food supply with an increase in production and distribution of foods from around the world. Locally, small agricultural businesses such as the family farm were giving way to large agribusinesses with fewer producers providing commodities to multiple distributors throughout the country. Consumers' habits were also changing; with an increase in the availability of 'fast-food' and an abundance of restaurants, people began to eat outside the home more frequently. Additionally, the proportion of the population that was susceptible to foodborne illness was growing, including the elderly, persons with immune compromising conditions, such as HIV infection, or those receiving immunosuppressive therapy, such as chemotherapy.

To better understand the effects of these changes and to monitor the safety of the food supply from farm to fork, the CDC initiated FoodNet in 1996 as the primary foodborne component of the CDC Emerging Infections Program [9]. FoodNet is a collaborative effort between the CDC, the US Food and Drug Administration, the US Department of Agriculture and 10 State Health Departments. In the decade since FoodNet was initiated, the population under surveillance increased from 14.2 million persons (5% of the US population) in five states to 44.9 million persons (15% of the US population) in 10 states [10^{*}]. FoodNet sites are located in the states of Connecticut, Georgia, Maryland, Minnesota, New Mexico, Oregon and Tennessee, and selected counties in California, Colorado and New York. The goals of FoodNet are to determine the burden of foodborne illness in the US, monitor trends in the burden of specific foodborne illnesses over time, attribute the burden of foodborne illness to specific foods and settings, and develop and assess interventions to reduce the burden of foodborne illness.

FoodNet overview

FoodNet conducts active laboratory-based surveillance for seven bacterial and two parasitic organisms. Bacterial

pathogens include *Campylobacter* spp., *Salmonella* spp., *Shigella* spp., *E. coli* O157 and other non-O157 Shiga toxin-producing *E. coli* (STEC), *Listeria monocytogenes*, *Vibrio* spp. and *Yersinia* spp. Parasitic pathogens under surveillance include *Cyclospora* and *Cryptosporidium*. Active surveillance is also conducted for hemolytic uremic syndrome (HUS) through pediatric nephrologists' offices, for children 18 years of age or under. On a monthly or quarterly basis, staff in each FoodNet site contact clinical laboratories to assure complete ascertainment of cases. Surveillance data are maintained in databases at each site and forwarded to the CDC to be aggregated and analyzed. Incidence rates are calculated based on the estimated census population in each site.

Common enteric bacterial infections of children

There are a number of common enteric bacterial infections of children.

Campylobacteriosis

Illness caused by *Campylobacter* spp. is the most common cause of bacterial enteric infections in the US, causing an estimated 2 million infections annually [11]. Most cases of campylobacteriosis are sporadic and not associated with outbreaks. Numerous outbreaks have occurred, however, including those caused by ingestion of untreated water, raw milk, undercooked chicken and cross-contaminated foods [12^{**}]. Additional studies of sporadic illness have identified contact with pets, specifically kittens and puppies. Chickens are a risk factor, as well as exposure to the farm environment. Limited studies have been conducted among children and even fewer among infants. These groups are generally not involved in outbreaks yet they represent a substantial burden of illness in the population. Two case-control studies have been conducted among infants and young children in Sweden and Australia. In a matched case-control study in Queensland, Tenkate and Stafford [13] found risk factors for sporadic campylobacteriosis among children under 36 months of age to be ownership of pet chickens or a puppy and consumption of mayonnaise. Carrique-Mas *et al.* [14] identified having a well in the household and drinking water from a lake/river, having a dog, and eating grilled meats as risks for children under the age of 6 years.

Salmonellosis

Salmonella spp. is estimated to cause 1.4 million infections annually in the US [15]. Unlike *Campylobacter*, *Salmonella* has been identified in numerous outbreaks associated with a wide range of risk factors. Moreover, the over 2500 *Salmonella* serotypes are found in a variety of sources, including food, animals and the environment. The most common serotypes of *Salmonella* found in

infants are Typhimurium, Newport, Javiana, Enteritidis and Heidelberg. Although generally self-limited, invasive *Salmonella* can cause serious morbidity, especially among infants [16].

Shigellosis

Shigella spp. affects an estimated 450 000 persons annually in the US [15]. Outbreaks of shigellosis have been associated with consumption of food products, such as parsley [17], tomatoes [18], water [19,20] or with person-to-person transmission among day-care center attendees and workers [21,22]. More recently, *Shigella* cases have been identified among men who have sex with men [23]. In 2005, FoodNet staff in the 10 sites interviewed all cases of culture-confirmed *Shigella* to better understand the risk factors for sporadic shigellosis and to estimate the proportion of shigellosis potentially transmitted by food [24]. Risk exposures for cases included international travel in the week prior to symptom onset (26%), attending or working in day-care or contact with a child or household member with diarrheal illness (38%), using untreated drinking water or recreational water (12%), or sexual contact with someone with diarrhea (2%). Multiple risk exposures were reported by 9% of patients who did not travel internationally. Twenty-seven percent of the patients denied all risk exposures and are most likely to have acquired their infection through consumption of contaminated food.

Shiga toxin-producing *E. coli*

The most common STEC serogroup identified by clinical laboratories in the US is O157, causing an estimated 73 000 infections per year [15]; however, the increased use of nonculture based methods, such as shiga toxin enzyme-immunoassays (Stx EIAs), to identify all Shiga toxin-producing *E. coli* including O157 and other non-O157 STEC has resulted in a dramatic increase of reports of non-O157 serogroups. During 2000–2005, the percentage of clinical laboratories conducting Stx EIAs in Connecticut increased from 11 to 31% [25**]. Since 2000, clinical laboratories in Connecticut are required to submit the toxin-positive broths to the State Public Health Laboratory for culture and further characterization. Stx EIA-positive infections (Shiga toxin-related disease) are reportable to the Connecticut Department of Public Health. The percentage of STEC isolates initially identified by Stx EIA testing increased significantly from 33% in 2000 to 59% in 2005 ($P < 0.001$). Reports of Shiga toxin-related disease have caused confusion among clinicians who may incorrectly believe that the patient has shigellosis and order inappropriate therapy for the non-O157 STEC infection.

The incidence of non-O157 STEC has increased as more laboratories conduct Stx EIAs. National surveillance for non-O157 STEC conducted by the CDC between 1983

and 2002 [26] has shown the most common serogroups to be STEC O26 (22%), O111 (16%), O103 (12%), O121 (8%) and O45 (7%). As identification of non-O157 serogroups is relatively new, little is known about clinical and epidemiologic factors associated with infection. Nevertheless, Johnson *et al.* [27] provide guidance on the clinical approach to these emerging pathogens.

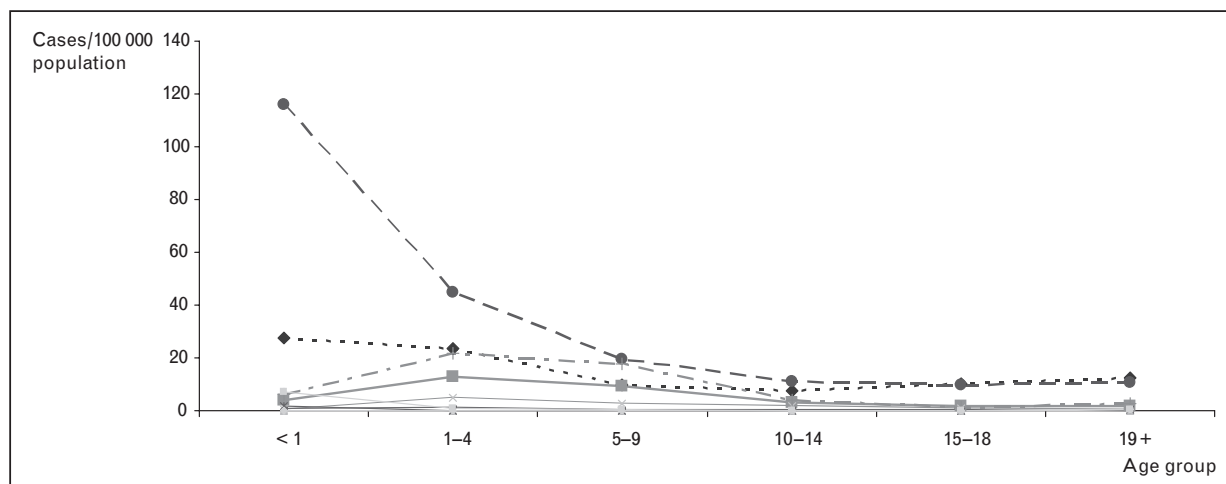
Case-control studies and outbreak investigations of STEC O157 have repeatedly been associated with exposure to bovine sources, including ground beef and contact with cattle on farms [28,29]. Foods contaminated by bovine feces (e.g. lettuce, spinach and apple cider) have also been associated with outbreaks. Nonfoodborne outbreaks have been associated with attending child day-care [30], drinking contaminated water [31] and swimming in unchlorinated water [19,32,33]. In a case-control study of *E. coli* O157 conducted by FoodNet in 1996, Kassenborg *et al.* [28] conducted a separate analysis of patients under 6 years old. Multivariable analysis found living on, or visiting a farm, and having a child under 2 years old in the household to be five times higher in cases than controls. A more recent case-control study of *E. coli* O157 conducted by the same group in 1999–2000 found illness among all case-patients to be associated with eating undercooked (pink) hamburgers, drinking untreated surface water and contact with cattle [29].

Surveillance

Incidences of *Campylobacter* and *Salmonella* have been consistently higher among infants than among other age groups (Fig. 1). In FoodNet sites in 2005, the incidence of infections of salmonellosis among under 1-year-olds was 115.9 per 100 000 persons compared with 10.6 per 100 000 among those over the age of 19 years [34]. The incidence of campylobacteriosis among under 1-year-olds was 27.4 per 100 000 compared with 12.5 per 100 000 population among those 19 years and older. Likewise incidence of *Yersinia enterocolitica* was also highest among under 1-year-olds (6.9 per 100 000) compared with rates of less than one per 100 000 for all other age groups. Incidence of shigellosis, on the other hand, was highest among 1 to 4-year-olds (22.0 per 100 000) and 5 to 9-year-olds (17.6), demonstrating its concentration among preschool and school-aged children. Of the 2095 cases of shigellosis ascertained by FoodNet in 2005, 60 (3%) were outbreak-associated and 2035 (97%) were sporadic cases. The overall incidence was 4.5 cases per 100 000 population. Of the isolates that were serotyped, 75% were *S. sonnei* and 18% were *S. flexneri*.

FoodNet sites also conduct surveillance for HUS, a life-threatening illness primarily affecting children, generally caused by infection with STEC. In the 10 FoodNet sites in 2004 (the last year data were available), there were

Figure 1 Incidence of infections by pathogen and age group, FoodNet, 2005



STEC, Shiga toxin-producing *E. coli*; -◆-, *Campylobacter*; -▲-, *Cyclospora*; -✕-, *Listeria*; -+ -, *Shigella*; -◇-, *Vibrio*; -■-, *Cryptosporidium*; -○-, *E. coli*O157; -●-, *Salmonella*; -□-, *STE nonO157*; -■-, *Yersinia*.

63 cases reported among children under the age of 18 years; two (3%) children died. Of these, 41 (62%) were among children under the age of 5 years (rate: 1.47 per 100 000 children aged under 5 years). Sixty-seven percent of HUS cases were diagnosed between June and September.

Epidemiologic studies

Few studies have been conducted to identify risk factors for diarrheal illness among infants. Bruce *et al.* [33] reported that '[s]ome studies have demonstrated that infants infected with *Salmonella* are less likely to be breastfed, more likely to be fed high-iron formula, and more likely to have a household member with diarrhea than healthy infants'. To further explore these factors among sporadic cases of illness, in 2002–2004, FoodNet conducted a population-based case-control study of *Salmonella* infection among infants less than 1 year of age [35**]. The purpose of the study was to identify dietary and environmental risk factors for *Salmonella*. Any infant under 1 year old who had a laboratory-confirmed diagnosis of *Salmonella* residing in Connecticut, Minnesota and Oregon, and selected counties in California, Colorado, Georgia, New York and Tennessee, was eligible for enrollment in the study. Healthy controls were frequency matched by age and identified through birth registries or published birth announcements. Parents or guardians of cases and controls were interviewed by telephone. The questionnaire included information on demographic characteristics, general health status and medications, symptoms of illness, food exposures, and potential social and environmental risk factors. Cases and controls were interviewed about exposures in the 5 days before illness onset or interview date.

Of the 674 cases of infant salmonellosis reported in FoodNet sites during the study period, 442 were enrolled in the study. A total of 928 controls were interviewed. Of the 442 cases, 98% experienced diarrhea (median duration 7 days), 73% had fever, 33% had vomiting, 52% were treated with an antibiotic, 30% received intravenous hydration therapy and 25% were hospitalized (median duration 3 days). Two of the infants died. The multiple regression analysis found that case-patients were more likely than controls to have traveled outside of the US [odds ratio (OR) 8.9; 95% confidence interval (CI) 2.6–31.0], to have attended day-care with a child with diarrhea (OR 4.4; 95% CI 1.8–10.7), to have ridden in a shopping cart next to meat or poultry (OR 3.2; 95% CI 2.1–5.1), or to have had exposure to reptiles (OR 5.2; 95% CI 3.4–7.9). Cases were also more likely to have consumed meat (OR 1.2; 95% CI 1.1–2.7) or concentrated liquid infant formula (OR 2.0; 95% CI 1.4–2.8). Breastfeeding was found to be protective (OR 0.5; 95% CI 0.3–0.6).

The authors of this study concluded that some risk factors associated with infant salmonellosis were potentially preventable. Specifically, promoting breastfeeding, which is known to prevent a wide range of infectious diseases, would be prudent [36]. In this study, breastfeeding was protective particularly among children under the age of 6 months. The finding of illness risk among infants riding in shopping carts next to meat and poultry was unexpected. Studies in the UK [37] demonstrated bacterial contamination on the outside of packages of meat and poultry sold at the retail level. It is possible that this finding plays a role in the exposure of infants to these pathogens. The risk of *Salmonella* associated with

exposure to reptiles is well documented [38]. Although some of the older infants may have had direct contact with the reptile in their homes, it is also likely that the infants were indirectly infected through exposure in the environment or through contaminated hands of caregivers.

Concurrent with the infant salmonellosis case-control study was a study of sporadic *Campylobacter* infections among infants in FoodNet sites [12^{••}]. The study methodology was identical for both studies and the same controls were used for comparison. Of the 123 enrolled cases, 99% reported diarrhea, 67% had fever and 44% reported vomiting. Eighty-nine (72%) cases were treated with an antibiotic; 90% of those who could remember the name of the antibiotic had taken a macrolide. Eleven percent of the cases were hospitalized (mean length of stay 3 days); no cases died.

Risk factors for campylobacteriosis were drinking well water (OR 2.6; 95% CI 1.3–5.3), eating fruits and vegetables prepared in the home (OR 2.0; 95% CI 1.1–3.6), having a pet in the home with diarrhea (OR 5.3; 95% CI 1.8–15.5), visiting or living on a farm (OR 4.1; 95% CI 1.9–8.9), riding in a shopping cart next to meat or poultry (OR 2.2; 95% CI 1.1–4.6), and traveling outside the US (OR 19.3; 95% CI 4.5–82.1). Infants with campylobacteriosis were less likely to be breastfed (OR 0.3; 95% CI 0.2–0.6) or to be in a household where hamburger was prepared (OR 0.6; 95% CI 0.3–0.9).

Conclusion

Diarrheal illness continues to be a burden to infants and young children. Guidelines for clinical management of children with diarrhea are well established [39]; however, these should be updated as additional information on the epidemiology of acute diarrheal illness in children becomes available. Despite their limited diet, infants remain at risk of acquiring enteric pathogens that are commonly associated with consumption of contaminated food. Recent epidemiologic studies and surveillance have found the highest incidence of campylobacteriosis, salmonellosis and yersiniosis among infants. Exposure to these pathogens may be through cross-contamination in the home or the environment. Comprehensive surveillance to monitor trends in infection and for detection of outbreaks is a necessary component of any public health program. As children with diarrhea pose a risk of transmission to others in the household and at day-care centers, good personal hygiene and exclusion of ill children from day-care are prudent preventive measures. Educational measures that focus on improving prevention of exposure to infectious agents and an emphasis on eliminating cross-contamination are needed for parents and care takers of this vulnerable population.

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 114).

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