



# Microbiology of Community-Acquired Diarrhea in Infants and Young Children in the United States: The National Pediatric Diarrhea Surveillance Study

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## ABSTRACT

**Background:** The microbiology of community-acquired pediatric diarrhea in the U.S. is not well described. **Objective:** To define the microbiology of community-acquired diarrhea in young U.S. children. **Design/Methods:** Healthy children 6-36 months old were enrolled by their primary care physicians and followed for 6 months. Stool samples obtained at baseline and during diarrhea episodes were assayed for 20 potentially-causative bacteria, parasites, and viruses. **Results:** 604 children from 34 states were enrolled. Baseline specimens were obtained from 485 (80.3%), 611 diarrhea episodes were reported, and specimens obtained for 447 (73.2%). The following were at least as prevalent at baseline as during diarrhea: enteroadherent *E. coli* (12.2% baseline, 12.9% diarrhea), enteroaggregative *E. coli* (3.7%, 4.1%), *C. difficile* (3.5%, 1.9%), *C. perfringens* (2.9%, 2.3%), and *Giardia* (0.4%, 0.2%). Other bacteria and parasites were rare: *Aeromonas* (0.3% baseline, 1.0% diarrhea), *Campylobacter* (0.2%, 0.7%), *Cryptosporidium* (0%, 0.5%), enterohemorrhagic *E. coli* (0%, 0.2%), *Yersinia* (0%, 0.2%), ST1-producing *E. coli* (0%, 0.2%), *Salmonella* (0.2%, 0%), LT1-producing *E. coli* (0%, 0%), *Shigella* (0%, 0%), and *Vibrio* (0%, 0%). Viruses were found in some baseline specimens but all were more common in diarrhea specimens: enteric adenovirus (1.5% baseline, 5.7% diarrhea;  $p=0.0004$ ), rotavirus (1.5%, 5.2%;  $p=0.001$ ), astrovirus (1.4%, 3.5%;  $p=0.05$ ), Sapporo-like virus (0.8%, 3.0%;  $p=0.01$ ), and Norwalk-like virus (0.8%, 1.9%;  $p=0.17$ ). Of note, 77.9% of diarrhea specimens yielded no likely pathogen. The presence of vomiting was highly predictive of isolating a likely pathogen in the stool ( $p=0.0001$ ), while fever, abdominal pain and blood or mucus in the stool were not. **Conclusions:** *C. difficile*, *C. perfringens*, enteroadherent *E. coli*, and enteroaggregative *E. coli* are common in the stool of healthy young children and are not associated with diarrhea. Pathogenic bacteria and parasites are rare in this age group. Enteric adenovirus, rotavirus, astrovirus, Sapporo-like virus, and Norwalk-like virus are present at baseline in a small percentage of children (about 1% each) and are associated with diarrhea. In over three-quarters of diarrhea episodes, no likely pathogen is identifiable. Vomiting is the best clinical predictor of isolating a pathogen.

### OBJECTIVE

To describe the microbiology of community-acquired diarrhea in infants and young children in the U.S.

### BACKGROUND

The microbiology of diarrhea in hospitalized children in the U.S. has been studied extensively, but little is known about the microbiology of diarrhea not severe enough to require hospitalization. Among children hospitalized with diarrhea, the vast majority of cases are infectious and approximately 25% of cases are due to rotavirus which dwarfs the contribution of any other single etiologic agent. Studies of the microbiology of outpatient diarrhea in children have often lacked control groups and thus have not been able to differentiate true infection from incidental carriage.

### METHODS

#### NATIONAL PEDIATRIC DIARRHEA SURVEILLANCE STUDY

- Prospective cohort study
- Subjects recruited and enrolled by SCOR Network primary care physicians throughout U.S.
- Inclusion criteria: healthy children ages 6-36 months without history of intestinal malabsorption, IBD, CF
- Baseline interview and stool specimen
- Active surveillance for all episodes of diarrhea during 6-month study period
- Diarrhea defined as "change in bowel habits involving more frequent and/or more watery stools"
- For each diarrhea episode, interview conducted and stool specimen obtained

#### SCOR NETWORK

- National office-based research network of pediatricians and family practitioners administered by Slone Epidemiology Center at Boston University
- Currently 479 participating physicians
- Past/current projects include:
  - Boston University Fever Study (RCT of safety of ibuprofen for children)
  - Study of NSAID use and invasive Group A Streptococcal infections complicating varicella (case-control study)
  - National Pediatric Diarrhea Surveillance Study (cohort study)
  - Xylitol for prevention of acute otitis media (pilot RCT)

### RESULTS

TABLE 1. MICROBIOLOGY OF BASELINE AND DIARRHEA STOOL SPECIMENS

	Baseline specimens No. positive/No. tested (%)	Diarrhea specimens No. positive/No. tested (%)
<b>Bacteria</b>		
<i>Aeromonas</i>	1/375 (0.3)	4/394 (1.0)
<i>Campylobacter</i>	1/484 (0.2)	3/431 (0.7)
<i>C. difficile</i>	17/484 (3.5)	8/431 (1.9)
<i>C. perfringens</i>	15/484 (2.9)	10/431 (2.3)
<i>E. coli</i> —enteroadherent	59/482 (12.2)	57/442 (12.9)
<i>E. coli</i> —enteroaggregative	18/482 (3.7)	18/442 (4.1)
<i>E. coli</i> —enterohemorrhagic	0/482 (0.0)	1/444 (0.2)
<i>E. coli</i> —enterotoxigenic (LT-1)	0/442 (0.0)	0/442 (0.0)
<i>E. coli</i> —enterotoxigenic (ST-1)	0/481 (0.0)	1/442 (0.2)
<i>Salmonella</i>	1/482 (0.2)	0/443 (0.0)
<i>Shigella</i>	0/482 (0.0)	0/443 (0.0)
<i>Yersinia</i>	1/482 (0.2)	1/443 (0.2)
<i>Vibrio</i>	0/482 (0.0)	0/443 (0.0)
<b>Parasites</b>		
<i>Cryptosporidium</i>	0/484 (0.0)	2/435 (0.5)
<i>Giardia</i>	2/484 (0.4)	1/435 (0.2)
<b>Viruses</b>		
Astrovirus	7/483 (1.4)	15/431 (3.5)
Enteric adenovirus	7/482 (1.5)	25/442 (5.7)
Norwalk-like virus	4/484 (0.8)	8/431 (1.9)
Rotavirus	7/482 (1.5)	23/442 (5.2)
Sapporo-like virus	4/484 (0.8)	13/431 (3.0)

TABLE 2. CHARACTERISTICS OF DIARRHEA EPISODES BY PATHOGEN

	Rotavirus n=23	Adenovirus n=25	Astrovirus n=15	Norwalk-like virus n=8	Sapporo- like virus n=13	Any pathogenic bacteria n=10
Median duration in days (25 <sup>th</sup> , 75 <sup>th</sup> percentiles)	6.0 (2.0-8.0)	4.0 (1.0-5.5)	3.0 (2.0-4.0)	14.0 (4.0-18.5)	4.0 (2.0-7.0)	2.0 (1.75-5.75)
Median number of stools per episode (25 <sup>th</sup> , 75 <sup>th</sup> percentiles)	10.0 (5.0-20.0)	8.5 (3.5-22.0)	6.5 (5.0-25.0)	TNTC (19.0-TNTC)	12.0 (5.0-32.5)	11.0 (3.75-20.25)
Associated signs and symptoms, No. (%)						
Loss of appetite	18 (78.3)	14 (56.0)	6 (40.0)	0 (0.0)	10 (76.9)	7 (70.0)
Cold symptoms	7 (30.4)	14 (56.0)	9 (60.0)	5 (62.5)	6 (46.2)	6 (60.0)
Fever	13 (56.5)	5 (20.0)	5 (33.3)	4 (50.0)	4 (30.8)	3 (30.0)
Abdominal pain	8 (34.8)	5 (20.0)	4 (26.7)	2 (25.0)	0 (0.0)	1 (10.0)
Vomiting	14 (60.9)	6 (24.0)	2 (13.3)	5 (62.5)	4 (30.8)	1 (10.0)
Mucus in stool	7 (30.4)	1 (4.0)	4 (26.7)	3 (37.5)	3 (23.1)	3 (30.0)
Blood in stool	0 (0.0)	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)
Another person in home with diarrhea	6 (26.1)	5 (20.0)	4 (26.7)	2 (25.0)	4 (30.8)	4 (40.0)
Physician/ER visit, No. (%)	5 (21.7)	3 (12.0)	0 (0.0)	1 (12.5)	1 (7.7)	2 (20.0)

### CONCLUSIONS

- Enteroadherent *E. coli*, Enteroaggregative *E. coli*, *C. difficile*, and *C. perfringens* are common in the stool of healthy infants and young children and appear not to be associated with community-acquired diarrhea
- Bacteria and parasites are rare causes of community-acquired diarrhea in this age group
- Viruses are the most common infectious cause of diarrhea in young children, with enteric adenovirus, rotavirus, astrovirus, and the caliciviruses (Norwalk and Sapporo) all being fairly common

- Rotavirus and Norwalk-like virus cause the most severe and most prolonged diarrhea
- Rotavirus and, to a lesser extent, enteric adenovirus and astrovirus have a seasonal pattern with higher prevalence in the winter and spring
- Overall, only 22% of diarrhea episodes yielded a likely pathogen; the other 78% were negative for all pathogens tested
- Vomiting is the only clinical symptom that is predictive of isolating a pathogen from the stool

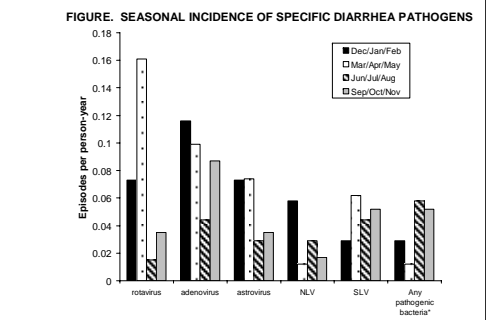


TABLE 3. CHANCE OF ISOLATING A LIKELY PATHOGEN\* FROM DIARRHEA EPISODES ACCORDING TO PRESENCE OR ABSENCE OF VARIOUS ASSOCIATED SIGNS AND SYMPTOMS

Associated sign/symptom		No. with likely pathogen / No. tested (%)	p	Crude RR (95% CI)
Loss of appetite	Present	57/222 (25.7)	0.08	1.42 (0.96-2.11)
	Absent	30/166 (18.1)		
Cold symptoms	Present	43/189 (22.8)	0.9	1.03 (0.71-1.49)
	Absent	44/199 (22.1)		
Fever	Present	31/115 (27.0)	0.19	1.29 (0.88-1.89)
	Absent	55/264 (20.8)		
Abdominal pain	Present	19/77 (24.7)	0.47	1.19 (0.75-1.89)
	Absent	48/231 (20.8)		
Vomiting	Present	28/65 (43.1)	0.0001	2.39 (1.66-3.42)
	Absent	58/321 (18.1)		
Blood or mucus in stool	Present	20/69 (29.0)	0.11	1.44 (0.93-2.22)
	Absent	59/293 (20.1)		