MAJOR ARTICLE

The Etiology of Severe Acute Gastroenteritis Among Adults Visiting Emergency Departments in the United States

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(See the editorial commentary by Jones, on pages 1334–5.)

Background. Acute gastroenteritis (AGE) remains a common cause of clinic visits and hospitalizations in the United States, but the etiology is rarely determined.

Methods. We performed a prospective, multicenter emergency department–based study of adults with AGE. Subjects were interviewed on presentation and 3–4 weeks later. Serum samples, rectal swab specimens, and/or whole stool specimens were collected at presentation, and serum was collected 3–4 weeks later. Fecal specimens were tested for a comprehensive panel of viral, bacterial, and parasitic pathogens; serum was tested for calicivirus antibodies.

Results. Pathogens were detected in 25% of 364 subjects, including 49% who provided a whole stool specimen. The most commonly detected pathogens were norovirus (26%), rotavirus (18%), and *Salmonella* species (5.3%). Pathogens were detected significantly more often from whole stool samples versus a rectal swab specimen alone. Nine percent of subjects who provided whole stool samples had >1 pathogen identified.

Conclusions. Viruses, especially noroviruses, play a major role as agents of severe diarrhea in adults. Further studies to confirm the unexpectedly high prevalence of rotaviruses and to explore the causes of illness among patients from whom a pathogen cannot be determined are needed. Studies of enteric pathogens should require the collection of whole stool samples.

Acute gastroenteritis (AGE) remains a common cause of clinic visits and hospitalizations in the United States. An estimated 179 million cases of AGE occur each year, resulting in millions of clinic visits, nearly 500 000 hospitalizations, and >5000 deaths [1, 2]. Although the burden of AGE in children has been described [3, 4], data on AGE in adults remain sparse. Between 1979 and 1995, 1.5% of all hospital discharges among adults had an *International Classification of Diseases, Ninth Revision, Clinical Modification* code for gastroenteritis, meaning that the lifetime risk of being discharged from the hospital with a diagnosis of gastroenteritis is approximately 1 in 8 among US adults [5].

Over the past 40 years, >20 new agents of gastroenteritis have been discovered [6]. Nevertheless,

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an etiologic agent is rarely identified in AGE cases, either because stool samples are infrequently collected or because many laboratories have a limited ability to detect the full range of pathogens, especially viruses [7, 8]. Less than 20% of AGE cases in the United States, including those requiring hospitalization, are attributed to specific pathogens [2]. In a study of >30 000 hospitalized adults with diarrhea, a bacterial agent was identified in <6% of cases [9]. Similarly, over half of foodborne disease outbreaks that occurred during 2006–2007 and were reported to the Centers for Disease Control and Prevention (CDC) had no confirmed etiologic diagnosis [10, 11].

The availability of new, more sensitive assays for detection of enteric pathogens may change this picture. Between 1993 and 1997, the proportion of all foodborne outbreaks reported to the CDC that were confirmed as outbreaks of norovirus infection increased from 0.3% to 27% because of wider availability of reverse-transcription polymerase chain reaction (RT-PCR) in public health laboratories [11, 12]. Noroviruses are now recognized as the leading cause of epidemic gastroenteritis in all age groups, accounting for >90% of viral gastroenteritis outbreaks and approximately 50% of all gastroenteritis outbreaks [13]. Data on norovirus prevalence among sporadic AGE cases, particularly among adults, have remained sparse because RT-PCR is generally not used for diagnostic purposes in clinical settings. Past reviews have found that norovirus was responsible for 12% of AGE cases among all age groups in community and outpatient settings [14] and 4.4%–8.7% of AGE cases among adults and elderly individuals admitted to the emergency department (ED) or hospitalized [15].

This study prospectively enrolled and tested adults with AGE presenting to EDs to determine the frequency, characteristics, and etiology of infectious AGE. We chose EDs as a study setting because the disease severity and economic burden associated with these cases are likely to be significant.

MATERIALS AND METHODS

Subjects

Subjects were enrolled from the EDs in 3 major medical centers that also serve as Foodborne Diseases Active Surveillance Network sites [16, 17] in the United States: Yale–New Haven Hospital, New Haven, Connecticut; Albany Medical Center, Albany, New York; and Oregon Health and Science University, Portland, Oregon. Yale–New Haven Hospital is a 944-bed tertiary referral center where staff in the adult-specific ED treat approximately 60 000 patients per year. Albany Medical Center is a 631-bed tertiary referral center with approximately 55 000 ED visits a year. Oregon Health and Science University is a 420-bed urban university teaching hospital with an annual ED census of 46 000 visits.

Subjects were enrolled 5 days per week at each site during the following periods: at Yale–New Haven Hospital, between 1 September 1999 and 31 August 2001; at Albany Medical Center, between 22 January 2000 and 20 April 2001; and at Oregon Health and Science University, between 25 August 2000 and 24 August 2001. All persons aged ≥18 years who presented to a participating ED with AGE were asked to participate. AGE was defined as the occurrence of ≥1 episode of vomiting and or ≥3 episodes of diarrhea within a 24-hour period. Subjects were excluded if (1) they had onset of AGE symptoms ≥7 days prior to the ED visit, (2) their reason for care was unrelated to treatment for AGE, or (3) they had a known noninfectious or chronic cause of their symptoms, such as a inflammatory bowel disease or medication overdose. All enrolled subjects gave written informed consent. The study was approved by institutional review boards at the CDC and at each of the participating institutions.

Data Collection

After subjects provided informed consent, they were administered a standardized questionnaire on their illness characteristics, medical history, and specific exposures. Some data were extracted from the subject's ED records, including illness signs and treatment details. Each subject was contacted 3–6 weeks after the ED visit, to assess illness duration, outcome, and possible secondary spread of illness.

Specimen Collection and Testing

Whole stool samples were collected from each subject during the ED visit. If whole stool specimens were not available, 2 rectal swab specimens at minimum were collected.

Viruses

Viral RNA was extracted from a 10% clarified stool or rectal swab specimen suspension, using a NucliSens Extractor (BioMerieux, Durham, NC), and was amplified by conventional RT-PCR for norovirus [18] and astrovirus [19]. Positive results were confirmed by sequencing [20]. Stool samples were tested for rotavirus, using Pathfinder Rotavirus Kit (BioRad) and RT-PCR [21].

Bacteria

A swab of each whole stool specimen or the original rectal swab specimen was examined for *Shigella* species, *Salmonella* species, *Yersinia enterocolitica*, *Vibrio* species, *Escherichia coli* O157:H7 and other Shiga toxin–producing *E. coli*, *Campylobacter* species, and enterotoxigenic *E. coli*. Stool samples were tested for *Clostridium difficile* toxins A and B by the diagnostic assays routinely used in each hospital.

Parasites

Two aliquots of stool were fixed in 10% formalin (1 aliquot) or polyvinyl alcohol (1 aliquot) and stored at room temperature. Stool specimens preserved in 10% formalin were concentrated using a formol-ethyl acetate procedure and examined by microscopy for *Giardia* species and *Entamoeba histolytica* (wet mount), *Cyclospora* and *Isospora* species (wet mount with epifluorescence, safranin staining), and *Microsporidia* species

(chromotrope stain). Formol-ethyl acetate–fixed specimens were also tested for *Cryptosporidium* and *Giardia* species by direct fluorescent antibody assay [22, 23]. Smears from some polyvinyl alcohol–preserved stool specimens were examined for *E. histolytica* and *Blastocystis* species. Formalin-fixed material from rectal swab specimens was tested on Alexon-Trend's *Giardia intestinalis* and *Cryptosporidium parvum* microplate assay, and results were read visually. Polyvinyl alcohol–preserved slides were stained using Trend's Trichrome Stain Set and examined by light microscopy.

Serum specimens from the acute phase (during the first 5 days of symptoms) and the convalescent phase (during 3–6 weeks after resolution of symptoms) were collected from each subject. Serum samples were tested for immunoglobulin G antibodies to norovirus by use of a recombinant virus-like particle (VLP)–based enzyme immunosorbant assay [18, 24], using the following VLPs: GI.1 Norwalk Virus, GII.1 Hawaii Virus, GII.2 Chesterfield Virus, GII.3 Toronto Virus, GII.4 Burwash Landing Virus, GII.5 White River Virus, GII.6 Florida Virus, GII.7 Gwynedd Virus, and GII.8 Idaho Falls Virus. Seroconversion for an individual patient was defined as a ≥4-fold increase in antibody units between acute-phase and convalescent-phase sera.

Data Handling and Statistical Analyses

All questionnaire and laboratory results were collated at each participating site. At the CDC, data were merged and analyzed. Proportional outcomes were compared using χ^2 tests, and continuous variables were compared using nonparametric tests (ie, the Wilcoxon rank-sum test). Stratified analyses were performed using the Cochran-Mantel-Haenszel test.

RESULTS

During the study period, 389 subjects were enrolled. Of these, 25 did not meet eligibility criteria (24 had had symptoms for >7 days before their ED visit, and 1 was <18 years of age) (Table 1). Of 364 subjects, 180 (49%) were from Yale–New Haven Hospital, 138 (38%) were from Albany Medical Center, and 46 (13%) were from Oregon Health and Science University. Median age was 34 years (range, 18–91 years). Fewer than 5% of patients were ≥65 years of age. One-third (32%) reported an underlying or chronic disease, and 6.4% lived in a chronic care facility or nursing home. No differences in the characteristics of the subjects between the 3 study sites were observed.

Etiology From Testing of Stool Samples

Of 364 subjects, 330 (91%) provided stool specimens; 133 (40%) had a whole stool specimen, 197 (60%) had a rectal swab specimen, and 34 provided both (Table 2). Overall, norovirus was detected in 16% of whole stool and rectal swab specimens (42 of 264) combined, and rotavirus was detected in 14% (20 of 140). Although rotavirus was identified in all sites in each year of the study, it was the predominant agent identified at Oregon Health and Science University, where 13 of the 20 rotavirus-positive subjects were enrolled. All rotavirus-positive specimens were confirmed by RT-PCR. Bacterial agents were detected in 29 of 316 cases (9%), with *Salmonella* being most common. Parasitic agents were detected in 2 patients during the study.

Whole stool specimens were significantly more likely to yield positive results than rectal swab specimens, both for viral and bacterial agents (Table 2). Overall, a pathogen was detected in 25% of all patients, but the detection rate was higher (49%) for subjects who provided whole stool samples, compared with subjects who had only rectal swab specimens (8.7%; $P < .0001$). Detection rates for norovirus, rotavirus, and any bacterial agent were 4–6-fold higher when testing was performed on whole stool samples, compared with rectal swab specimens.

Mixed infections were detected in whole stool samples from 12 subjects (9%) but in none from rectal swab specimens (Table 3). Norovirus was the most commonly detected pathogen in mixed infections. Samples from most (5 of 7) subjects positive for *C. difficile* also tested positive for other pathogens. Five of the 19 rotavirus-positive stool specimens (26%) also tested positive for norovirus. No specific demographic characteristics or clinical risk factors were found to be associated with having a mixed infection.

Table 1. Characteristics and Potential Risk Factors for Illness Among Study Subjects, Multicenter Gastrointestinal Disease Study, 1999–2001

Characteristic	Value (n = 364)
Age, years	
Median (range)	34 (18–91)
18–35	201 (55)
36–64	145 (40)
65–74	6 (1.6)
≥75	12 (3.3)
Female sex	213 (59)
Chronic diseases[a]	116 (32)
Illness duration before presentation, days, median (range)	1 (1–7)
Possible risk factors for illness	
Member of known outbreak	31 (9)
Exposed to ill person in household	55 (15)
Exposure to ill person outside household	46 (13)
Recent international travel	12 (3)
Resident of long-term care facility	23 (6)
Any possible risk factor[b]	110 (30)

Data are no. (%) of subjects, unless otherwise indicated.

[a] Chronic diseases queried included diabetes, Crohn disease, hyperthyroidism, ulcerative colitis, systemic lupus erythrematosis, history of bowel surgery, irritable bowel syndrome, cancer, human immunodeficiency virus infection or AIDS, history of organ transplantation, immunodeficient state, gastric ulcers, renal disease, or other.

[b] Subjects with any of the 5 potential risk factors listed in the table.

Table 2. Distribution of Pathogens by Type of Stool Specimen, Multicenter Gastrointestinal Illness Study, 1999–2001

Pathogen	Whole Stool, % (No. Positive/ No. Tested)	Rectal Swab, % (No. Positive/ No. Tested)	*P*
Viral			
Norovirus	26 (33/127)	6.6 (9/137)	.00002
Rotavirus	18 (19/106)	2.9 (1/34)	.04
Astrovirus	1 (1/106)	Not tested	
Bacterial			
Total	17 (22/133)	3.8 (7/183)	.003[a]
*Salmonella*species[b]	5.3 (7/133)	2.2 (4/183)	.21
Clostridium difficile	5.3 (7/133)	Not tested	
Campylobacter species[c]	3 (4/133)	0 (0/183)	.03
Other[d]	3 (4/133)	1.6 (3/183)	.46
Parasitic			
Total	3 (3/102)	0 (0/87)	.25
Giardia intestinalis	1 (1/102)	0 (0/87)	1.0
Blastocystis hominis	2 (2/102)	0 (0/87)	.25
Endolimax nana	1 (1/102)	0 (0/87)	1.0
Mixed infections	9 (12/133)	0 (0/197)	.00001
Any documented enteric pathogen[e]	49 (65/133)	8.7 (17/197)	<.00001

The number of infections is greater than the number of subjects who tested positive (12 subjects had mixed infections, and all pathogens are accounted for in the table).

[a] Comparison performed for all subjects with any bacterial pathogens detected except *Clostridium difficile*, since only those persons with whole stool were tested for this pathogen.

[b] Includes *S. enterica* serovar Enteritidis (5), *S. enterica* serovar Typhimurium (2), group B *Salmonella* organisms (1), *S. enterica* serotype Berta (1), *S. enterica* serotype Newport (1), *S. enterica* serotype Thompson.

[c] Includes *C. jejuni* (3) and *C. coli* (1).

[d] Includes *Vibrio parahaemolyticus* (2); *Shigella sonnei* (2); enterotoxigenic *Escherichia coli* O148:H28 LT, ST; Shiga toxin–producing *E. coli* O157:H7; and Shiga toxin–producing *E. coli* O Rough:H34 stx1.

[e] Denominators are total number of eligible subjects. Because not all subjects' specimens were tested for all pathogens, this proportion is assumed to be a lower limit of the true proportion in this population.

Table 3. Characteristics of Subjects With Mixed Infections, Multicenter Gastrointestinal Infection Study, 1999–2001

Subject Age/Sex	Pathogens
25/F	Norovirus, rotavirus
27/M	Norovirus, rotavirus
25/M	Norovirus, rotavirus
48/M	Norovirus, rotavirus
47/F	Norovirus, rotavirus, *Salmonella enterica* serovar Enteritidis
35/M	Norovirus, *Clostridium difficile*
20/M	Norovirus, *C. difficile*
23/F	Norovirus, *C. difficile*
52/F	Norovirus, *Campylobacter coli*, *Vibrio* species
39/F	*Shigella sonnei, C. difficile*
26/M	*S. enterica* serotype Newport, *C. difficile*
38/F	*Endolimax nana, Blastocystis hominis*

Comparison of Norovirus Diagnosis From Stool and Sera Samples

Serum pairs were obtained from 133 of the subjects with stool specimens (Table 4). Subjects from whom paired sera were obtained were similar to those without paired sera with respect to illness characteristics, sex, age, exposure history, and outcomes. Evidence of acute norovirus infection was observed in 29 (22%) of these subjects. The incidence of serologically confirmed norovirus infection was similar among subjects for whom rectal swab specimens versus whole stool specimens were obtained (21% vs 22%; $P = .96$). While the sensitivity of RT-PCR for norovirus detection was slightly better than that for serology when whole stool specimens were available (26% vs 22%), serology significantly increased the rate of norovirus detection among subjects for whom only rectal swab specimens were available (21% vs 6.6%; $P = .004$). Subjects with a longer duration of illness prior to ED visit and sample collection had lower rates of norovirus detection in stool and sera samples (Figure 1). Almost 90% of all norovirus-positive subjects presented ≤3 days after illness onset. All norovirus-positive subjects presented ≤5 days after illness onset. In samples collected ≤3 days after onset, norovirus was detected in 35 of the 157 stool samples (23%), and seroconversion was confirmed in 22 of the 83 serum pairs (27%), compared with 4 of the 70 stool samples (5.7%; $P = .003$) and 4 of 39 sera (10%; $P = .04$), respectively, collected >3 days after onset of illness. No significant differences in detection of bacterial pathogens or rotavirus by the duration of symptoms prior to presentation were observed.

Epidemiologic Features

No differences were observed in age distribution or presence of underlying chronic disease, by pathogen type. Gastroenteritis-associated ED admissions and confirmed norovirus cases occurred throughout the year, and no clear seasonality was noted. Seasonal peaks were difficult to discern for rotavirus and bacterial pathogens because of the small numbers of cases.

The probable sources of the illnesses were usually not known to the subject. Only 30% subjects had known prior contact with another person with AGE, most commonly a household member, during the week before their ED visit; 9% reported that, before their illness, they attended a group event after which other people also became ill. Norovirus-positive subjects were more likely to have known exposures to someone with AGE prior to their onset of illness, compared with subjects without norovirus infection (46% vs 26%; $P = .006$). Neither recent international travel nor residence in a long-term care facility was associated with any particular pathogen.

Table 4. Comparison of Stool and Serum Testing for Norovirus Infection, Multicenter Gastrointestinal Infection Study, 1999–2001

Test(s)	Stool Specimen Type, % Positive (No. Positive/No. Tested)	
	Swab	Whole stool
Only stool RT-PCR	6.6 (9/137)	26 (33/127)
Only serology	21 (14/66)	22 (15/67)
Stool RT-PCR or serology[a]	24 (11/46)	27 (18/66)

Abbreviation: RT-PCR, reverse-transcription polymerase chain reaction.

[a] From patients with both types of specimens.

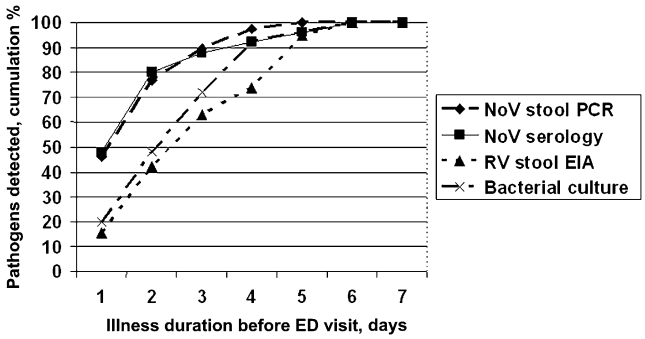

Figure 1. Cumulative proportion of pathogens detected, by duration of illness prior to presentation. Abbreviations: ED, emergency department; EIA, enzyme immunosorbant assay; NoV, norovirus; PCR, reverse-transcription polymerase chain reaction; RV, rotavirus.

Clinical Features

Subjects reported becoming ill 1 day (interquartile range, 1–3 days) before presentation to the ED. Nausea (93%), vomiting (81%) or diarrhea (89%), and abdominal pain (76%) were reported by most subjects. Signs of moderate-to-severe dehydration, such as dry mucous membranes, decreased skin turgor, or altered mental status, were present in <10% of subjects on examination. A temperature >37.8°C at admission (14%) and blood in stool (15%) was uncommon, and there was no difference between subjects with confirmed viral infection versus those with bacterial infection. Respiratory symptoms, including sore throat, cough, and rhinorrhea, were reported in approximately 10% of the subjects.

Few differences in clinical features were observed that could distinguish subjects with AGE due to viral infection from those with bacterial infection. Norovirus-positive subjects were slightly more likely to present with vomiting (89%), compared with subjects with either rotavirus infection (70%) or bacterial infection (69%) ($P = .06$).

Treatment and Outcome

While few subjects had documented clinical signs of dehydration, 81% were treated with intravenous rehydration. Overall, 45 of the 350 subjects (13%) for whom follow-up was available were admitted to the hospital. No subject died. While 53 of 171 subjects (31%) continued to have gastrointestinal symptoms 1–2 weeks following discharge and 20% of 108 subjects required medical follow-up after discharge because of continuing symptoms, none were readmitted to the hospital during the follow-up period. No differences were identified in outcomes or treatments by pathogen type, except that norovirus-positive subjects were less likely to report continued symptoms 2 weeks following ED discharge, compared with those who were norovirus negative (16% vs 38%; $P = .02$)

DISCUSSION

This study provides unique data on the infectious causes of AGE in adults treated in EDs. An etiologic agent was identified in almost 50% of cases when whole stool specimens were collected and tested using all available laboratory assays for known enteric pathogens. Norovirus was the most frequently identified cause of ED visits for AGE, with detection in 27% of subjects for whom stool and serum specimens were available. While no other data are available on adults presenting to EDs, studies of AGE etiology conducted in outpatient settings in other industrialized countries also identified norovirus as the leading cause [19, 25–28]. A study of general practitioner visits for AGE in England identified norovirus in 30% of adult cases and 9% of adult controls, using a combination of electron microscopy and RT-PCR [25]. Noroviruses were detected in 16% of cases and 3% of controls in outpatient clinics in Germany across all age groups [26]. Other studies have generally detected that ≤10% of stool specimens from adults with AGE were positive for norovirus in community or outpatient settings [19, 27–29]. Hospital-based studies among adults in Ireland [30] and South Africa [31] also found relatively lower rates of norovirus infection (11% and 10%, respectively). The relatively high rates of norovirus detection in our study may represent the use of both serologic and RT-PCR methods, the appropriate collection and handling of specimens, and/or the exclusion of subjects with onset >1 week before presentation. In a previous study in which serologic testing was used, evidence of norovirus infection was found in 33% of adults followed for 1 year [32].

The finding of rotavirus in 18% of adult cases for which whole stool specimens were available was surprising. While most rotavirus-positive subjects were enrolled from one of the 3 sites, cases were confirmed in all 3 sites during the study. Rotaviruses are the most common cause of severe gastroenteritis among young children, but adult cases are thought to be uncommon [31, 33, 34]. Adults who work in child-care settings or who care for young children have been reported to develop rotavirus gastroenteritis following exposure to sick children [35]. Data on these exposures were not available in our study, but the lack of rotavirus detection in elderly

subjects may indicate that these infections are more common among those more likely to be exposed to young children (eg, parents and child-care workers). This study was conducted prior to the introduction of universal childhood rotavirus vaccination. Rotavirus vaccine appears to confer herd protection in older children, and it may do so in parents of vaccinated children as well [36].

Salmonella and *Campylobacter* species were the most common bacterial pathogens identified. *C. difficile* was identified relatively frequently in the small number of samples available for testing but in most cases was detected in association with another pathogen. Of the 2 subjects for whom *C. difficile* was detected as the sole pathogen, neither reported use of antibiotics in the month prior to their illness.

An important finding of this study was the high rate of pathogen detection in whole stool specimens, compared with rectal swab specimens. Historically, rectal swab specimens placed in transport media have been the recommended specimens for diagnosis of bacterial infection. This study clearly indicates that testing only rectal swab specimen significantly reduces the chance of establishing an etiologic diagnosis, for both viral and bacterial infections. For noroviruses, the addition of serologic testing of subjects for whom only rectal swab specimens were available increased the detection rate to levels equal to those of testing whole stool samples by RT-PCR. Since testing of paired sera is impractical for clinical diagnosis, whole stool specimens should be collected for viral testing. Few studies have compared bacterial detection rates for whole stool specimens and rectal swab specimen in the same study, and those that have performed such comparison produced mixed results [37–40]. Even so, use of rectal swab specimens alone for diagnosis may significantly reduce sensitivity for detection and is not supported by this study. Finally, while only 12% of subjects presented with vomiting without diarrhea, these persons were less likely to have a whole stool sample collected than were subjects with diarrhea. Pathogen detection in these patients may therefore be a particular challenge.

The likelihood of detecting norovirus depended on the duration of symptoms that were observed. While one previous study found no such differences [41], subjects in our study who presented earlier in their illness were more likely to test positive for norovirus by either seroconversion or by RT-PCR than were those who presented later. This finding supports CDC recommendations to collect specimens early during illness from patients with AGE [42]. However, no apparent decline in rates of detection for rotavirus or bacterial agents during this window was observed, so this variable alone might not dissuade a clinician from testing a person with AGE.

One objective of this study was to identify epidemiologic or clinical variables that could be used to identify patients most likely to have an infectious pathogen, thus making testing more efficient and directed. Most of the subjects were young and healthy and had no obvious risk factors for illness. While previous studies found higher rates of norovirus among elderly individuals [25] or during winter and spring seasons [26, 28, 43], our study failed to confirm these findings. While subjects with norovirus and rotavirus infections were more likely to report exposure to other ill people, most positive subjects did not report any exposure. Similarly, while subjects with viral infections were more likely to report exposure to a known outbreak of AGE, this exposure was noted in <15% of all subjects. From these data, we were unable to determine variables that would help clinicians or public health investigators target certain people for testing.

This study has several important limitations. The number of sites and subjects, weekly period of enrollment, and the duration of the study were necessarily limited. Therefore, these data may not be representative of all cases presenting to EDs in the United States each year. Even so, this study provides the most comprehensive data to date on the etiology of AGE in adults, and the finding that the distribution of pathogens was similar in both years and in all 3 geographically distinct sites provides some reassurance that the findings are reasonably representative. Because of the complexity of the specimen handling and testing algorithm and the variable amount of stool available for testing, some patients were not tested for all pathogens. This may have biased the results; however, no demographic or clinical differences were observed for the various subsets of patients for whom testing was performed, nor for subjects who were not tested at all because of ineligibility or lack of any specimens. Finally, the lack of healthy controls limits conclusions about the relative importance of each pathogen.

The high prevalence of viral agents and the superiority of whole stool specimens collected early in illness for detection of bacterial and viral pathogens may have important implications for development of simple, efficient algorithms for testing patients with AGE. Timely and sensitive detection of viral pathogens may help avoid unnecessary antibiotic use and further diagnostic testing. Parasitic agents were rare in these subjects, possibly as a result of the case definition requiring that the illness duration was <7 days before the ED visit. Parasitic tests might be limited to patients with consistent clinical and epidemiologic characteristics. Vaccines against rotavirus are used widely in infants in the United States and other countries [44, 45], and the impact of noted disease reductions among infants may result in fewer infections among adults [46]. Vaccines against noroviruses are in early development stages [47, 48] but offer the promise of preventing the most common cause of outbreaks and sporadic gastroenteritis among adults. Finally, simpler, economical diagnostics for the variety of enteric pathogens are needed. New diagnostics that would allow for detection of multiple enteric pathogens could support

better understanding of the true impact of these agents, enhance syndromic surveillance systems, and spur interest in development of novel therapeutics and vaccines for these agents. Progress in treatment, prevention, and diagnosis, however, will always rely on the appropriate collection, testing, and interpretation of clinical samples.

Notes

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