JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 1991, p. 90–95
0095-1137/91/010090-06$02.00/0

Vol. 29, No. 1

Etiology of Childhood Diarrhea in Beijing, China

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Received 28 June 1990/Accepted 4 October 1990

To determine the role of recently recognized enteropathogens in childhood diarrhea in China, 221 children with diarrhea and 108 controls seen at the Beijing Children's Hospital were studied during April and May 1989. Stools were examined for ova, parasites, and rotavirus, cultured for bacterial pathogens, and probed for enterotoxigenic *Escherichia coli* (ETEC), enteroinvasive *E. coli* (EIEC), enterohemorrhagic *E. coli* (EHEC), and enteropathogenic adherence factor-positive (EAF+) *E. coli*. Pathogens were identified in 56.5% of children with diarrhea and 43.5% of controls ($P = 0.04$). Detection of enteropathogens was significantly greater in patients examined within 1 week of symptom onset (65%) than in patients examined later (39%; $P = 0.01$). ETEC was the most frequently detected pathogen in children with diarrhea, accounting for 20% of the cases. Other agents identified in patients included the following: salmonellae, 12%; rotavirus, 7%; EIEC, 7%; EHEC, 7%; members of the *Aeromonas hydrophila* group, 6%; EAF+ *E. coli*, 5%; *Ascaris lumbricoides*, 3%; shigellae, 3%; campylobacters, 2%; and *Vibrio* spp., 0.5%. The isolation rates of salmonellae ($P = 0.02$), EAF+ *E. coli* ($P = 0.04$), and mixed pathogens ($P = 0.05$) were significantly greater for diarrhea patients than for controls. Resistance to multiple antimicrobial agents occurred in 39% of the *Salmonella* isolates, 22% of the *Aeromonas* isolates, and 17% of the *Shigella* isolates. Multiresistant salmonellae ($P = 0.05$) and shigellae were recovered from diarrheal stools only. Ciprofloxacin, cefotaxime, and imipenem were the only agents tested to which all bacterial isolates were susceptible in vitro. These results suggest that both traditional and newly recognized agents are important causes of childhood diarrhea in Beijing and that therapy may be complicated by indigenous antimicrobial resistance.

Diarrheal disease is a major cause of morbidity and mortality among children in developing countries (29). It is estimated that worldwide, more than 4 million children under 1 year of age die each year of infectious diarrhea (26). In the last decade, laboratory advances have facilitated the detection of many newly recognized enteropathogens and improved recovery rates for a number of established etiologic agents. In particular, the development of sensitive and specific DNA probes for the detection of enterotoxigenic *Escherichia coli* (ETEC), (14), enterohemorrhagic *E. coli* (EHEC) (16), enteroinvasive *E. coli* (EIEC) (32), and the newly described enteropathogenic adherence factor-positive (EAF+) *E. coli* (22) has made it possible to examine large numbers of specimens for these agents.

Although gastroenteritis is recognized as a serious public health problem in the People's Republic of China, no comprehensive studies describing the enteric pathogens responsible for endemic diarrhea among China's 1.1 billion inhabitants have been reported in the English literature. The roles of agents such as EAF+ *E. coli*, EHEC, aeromonas, and cryptosporidia in childhood diarrheal illness are largely unknown.

To assess the roles of newly recognized and traditional enteropathogens in Beijing, we studied pediatric patients with and without diarrhea at the Beijing Children's Hospital.

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MATERIALS AND METHODS

Patient population. During April and May 1989, all children presenting to the outpatient department or admitted to the Beijing Children's Hospital with diarrhea were eligible for the study. Diarrhea was defined as the passage of three or more loose stools (able to conform to a container) in the preceding 24 h. During this same period, children seen at the same hospital for reasons other than gastrointestinal illness were selected as controls. Controls had not had diarrhea during the previous 2 weeks. Neither patients nor controls had received antibiotics during the preceding 2 weeks. Patients were examined and a standard questionnaire was completed to define the history of the current diarrheal illness, clinical and epidemiologic features, and possible risk factors for infection. Stool samples from patients and controls were obtained by a nurse, who noted the consistency of the specimen and the presence or absence of gross blood or mucus. Specimens were examined microscopically for the presence of erythrocytes (RBCs) and leukocytes and then transported to the microbiology laboratory in stool cups or enteric pathogen transport media (Prepared Media Laboratories, Tualatin, Oreg.) for microbiologic examination. All specimens were processed within 4 h of collection.

The study period was designed to fall between the peaks of winter viral gastrointestinal disease and summer bacterial diarrheal illness.

Microbiologic methods. Stool samples were processed at the Sino-Canadian Research Laboratory at Beijing You An Hospital. Stool specimens were cultured for *E. coli* O157:H7, salmonellae, shigellae, aeromonas, plesiomonas, campylobacters, and vibrios. A portion of each sample was plated onto MacConkey, MacConkey-sorbitol, Hektoen en-

teric, yersinia-selective (cefsulodin-Irgasan-novobiocin [CIN]), and aeromonas-selective agars (Prepared Media Laboratories) and onto blood-free campylobacter-selective agar with cefoperazone (Oxoid Ltd., Basingstoke, England). Fecal specimens were also added to Selenite-F broth (Prepared Media Laboratories), incubated overnight, and subcultured to bismuth sulfite agar (Difco Laboratories, Detroit, Mich.). Cold enrichment in Dulbecco's phosphate-buffered saline (Oxoid) at 4°C was performed on all specimens and was followed by subculture to yersinia-selective agar at 10 days. Isolates were identified by standard methods (12). Salmonellae and shigellae were serotyped by using API Salmonella and Shigella Serimmsure antiserum strips (Analytab Products, Plainview, N.Y.) and later confirmed by the Enteric Reference Laboratory, British Columbia Center for Disease Control. Sorbitol-negative *E. coli* strains were screened with a latex agglutination test (Pro-Lab Inc., Toronto, Ontario, Canada) and later confirmed as *E. coli* O157:H7 by the British Columbia Center for Disease Control.

Pathogenic *E. coli* infections were detected by DNA hybridization of stool blots by using a modification of the method of Echeverria et al. (8). Briefly, specimens were diluted with phosphate-buffered saline and replicate blotted with a Steers replicator onto six different nitrocellulose filters overlying MacConkey agar. Following overnight incubation at 37°C, filters were dried and processed as previously described (20). Stool blots were then hybridized with radiolabeled probes that detect the enteropathogenic adherence factor (EAF+ or localized adherence of *E. coli*) described by Nataro et al. (1-kb *Bam*HI-*Sal*I fragment of pJPN16) (22), EHEC adherence plasmid (3.4-kb *Hin*dIII fragment of pCVD419) described by Levine et al. (16), EIEC plasmid (2.5-kb *Hin*dIII fragment of pPS2.5) (32), heat-labile enterotoxin (LT) (1.2-kb *Hin*cII fragment of pCVD403), and human (216-bp *Eco*RI fragment of pCVD427) and porcine (157-bp *Pst*I fragment of pCVD426) heat-stable enterotoxins (ST) of ETEC (14).

Antimicrobial susceptibility testing was performed by using a standard agar dilution technique (23) and the following antimicrobial agents: co-trimoxazole (trimethoprim-sulfamethoxazole), ampicillin, piperacillin, cefazolin, cefoxitin, cefotaxime, tobramycin, gentamicin, imipenem, and ciprofloxacin. Current National Committee for Clinical Laboratory Standards guidelines (M7-A-S2) for MIC interpretation standards were followed.

Rotavirus was identified with a monoclonal latex agglutination test (Meridian Diagnostics Inc., Cincinnati, Ohio).

Formalin-ether concentrates and smears stained with iron hematoxylin were prepared from each of the specimens and examined microscopically for intestinal parasites. Smears stained by modified acid-fast stain were examined for cryptosporidia.

Statistical analysis. Clinical and numeric data were analyzed with a two-tailed chi-square test with Yates' correction, Fisher's exact test, or the Mann-Whitney test (two-tailed) as appropriate.

RESULTS

Children. During April and May 1989, fecal specimens from 221 children referred to the outpatient department or admitted to Beijing Children's Hospital with diarrhea were examined for enteric pathogens. The median age was 1 year. The sex distribution (male/female) was 1.9:1. The urban/rural ratio was 3.1:1. Of these children, 65% sought medical attention within 1 week of symptom onset, 38% were febrile (>37.5°C), 7% were dehydrated (≥5%), 40% had nausea and/or vomiting, 6% had grossly bloody stools, and 18% had RBCs detected on microscopic examination of fresh feces.

TABLE 1. Enteropathogens isolated from children with diarrhea and controls

Enteropathogen	No. (%) of isolates in:		*P* value[a]
	Diarrheal group (*n* = 221)	Control group (*n* = 108)	
Rotavirus	15 (6.8)	3 (2.8)	NS
A. hydrophila	13 (5.9)	10 (9.3)	NS
Campylobacter sp.[b]	5 (2.3)	1 (0.9)	NS
Salmonella spp.	27 (12.2)	4 (3.7)	0.02
Shigella spp.	6 (2.7)	0 (0)	NS
Vibrio spp.	1 (0.5)	0 (0)	NS
Y. enterocolitica	0 (0)	2 (1.8)	NS
ETEC[c,d]	41 (19.8)	18 (16.7)	NS
LT	40 (19.3)	18 (16.7)	NS
ST	1 (0.5)	0 (0)	NS
LT and ST	0 (0)	0 (0)	NS
EIEC[c]	15 (6.8)	4 (3.7)	NS
EHEC[c]	15 (6.8)	6 (5.6)	NS
EAF+ *E. coli*[c]	11 (5)	0 (0)	0.04
Hookworm	0 (0)	1 (0.5)	NS
A. lumbricoides	7 (3.2)	6 (5.6)	NS
Multiple[d]	33 (16)	8 (7)	0.05
None found[d]	90 (43.5)	61 (56.5)	0.04

[a] Statistical evaluation by chi-square test with Yates' correction or two-tailed Fisher's exact test. NS, Not significant.
[b] *Campylobacter jejuni* or *Campylobacter coli*.
[c] As determined by DNA probes.
[d] Excludes 14 patients who did not have ETEC LT or ST tests performed.

During the same period, 108 controls (median age, 1.5 years; sex ratio [male/female], 1.8:1) from socioeconomic and residential areas similar to those of the patients were studied.

Etiologic agents. Of patients with diarrhea, a single enteric pathogen was identified in stool samples from 40.5%, multiple pathogens were identified in 16%, and none were identified in 43.5% (Table 1). Detection of enteropathogens was significantly greater for patients that had stools examined within 1 week of onset of symptoms than for those who presented later (85 of 142 versus 32 of 77; $P = 0.01$).

ETEC was the most frequently identified pathogen in children with diarrhea but was detected with comparable frequency in controls. Most ETEC strains detected by hybridization were positive with the LT probe only, and none were positive with both ST and LT probes. The mean age of patients infected with ETEC was 25 months. In contrast, the mean age of controls carrying ETEC was 50.7 months ($P = 0.03$). EAF+ *E. coli* was identified in 11 patients (5%) but in none of the controls. The mean age of patients with EAF+ *E. coli* (33.4 months) was higher than that of patients with ETEC (25 months), EHEC (22.6 months), and EIEC (21.3 months), but this difference was not statistically significant. EHEC was detected in stool samples from 15 patients (6.8%). In one case, EHEC was isolated on MacConkey-sorbitol agar and serotyped as O157:H7, and the remainder were detected by stool blot hybridization. In all 15 cases of EIEC, the pathogen was identified by hybridization.

Salmonellae were isolated from 27 (12.2%) children with diarrhea. Eight serotypes of *Salmonella* were identified, with *Salmonella typhimurium* (9 of 27), *S. infanti* (7 of 27), and *S. agona* (5 of 27) accounting for the majority of cases. Other

TABLE 2. Clinical features associated with single-agent *E. coli* versus other enteropathogens

Enteropathogen (no. of patients)	% of patients					
	Presentation at ≤1 wk[a]	Fever	Nausea, vomiting	Dehydration	Fecal leukocytes	Fecal RBCs
EAF+ *E. coli* (9)	78	56	22[b]	11	33[b]	33
EHEC (11)	64	27[b]	27[b]	0	18[b]	18[b]
EIEC (9)	75	62	25	12	50	12[b]
ETEC (29)	57	36[b]	33	4	34[b]	17[b]
Salmonella spp. (26)	69	44[b]	38	19	41[b]	26[b]
S. typhimurium (9)	89	56	67[c]	22	44	22[b]
S. infanti (6)	33[d]	67	17	50	67	17
Shigella spp. (6)	100	100	83	17	100	83

[a] Presentation within 1 week of onset of symptoms.
[b] $P < 0.05$ versus value for *Shigella* spp. All statistical evaluations derived by chi-square test with Yates' correction or two-tailed Fisher's exact test.
[c] $P = 0.05$ for *S. typhimurium* value versus values for other *Salmonella* serotypes.
[d] $P = 0.05$ for *S. infanti* value versus values for other *Salmonella* serotypes.

serotypes identified included *S. derby*, *S. thompson*, *S. chailey*, *S. manhattan*, and *S. meleagridis*. The mean age of patients infected with *S. infanti* was 6.3 months, which was significantly lower than that observed with *S. typhimurium* (mean age, 14.0 months; $P = 0.01$) or other *Salmonella* serotypes (mean age, 14.0 months; $P = 0.01$).

Shigellae were recovered only from diarrheal stools and only from children older than 21 months. Children with shigellosis were significantly older (mean age, 39.8 months) than patients with salmonellosis ($P = 0.00$), ETEC ($P = 0.04$), and EHEC ($P = 0.03$) but not EIEC or EAF+ *E. coli*. Of the six isolates of *Shigella*, four were *Shigella flexneri* and two were *S. sonnei*.

Members of the *Aeromonas hydrophila* group were isolated with equal frequency from both patients and controls. However, for the first month of the study, they were recovered primarily from diarrheal stools (10 of 150 patients [7%] versus 2 of 83 controls [2%]; $P = 0.27$).

Many of the control subjects also carried enteropathogens (Table 1). With the exception of *A. hydrophila*, *Yersinia enterocolitica*, and *Ascaris lumbricoides*, all pathogens were isolated more frequently from children with diarrhea than from controls. This difference was significant for salmonellae and EAF+ *E. coli*. Eight of 108 controls (7.4%) carried mixed enteric pathogens, but they were significantly less likely to have multiple pathogens than were children with diarrhea.

Epidemiologic features. The sex distribution (male/female) was 1.9:1 for patients and 1.8:1 for controls. Female patients were significantly more likely to be infected with ETEC than were male patients (20 of 76 females versus 19 of 145 males; $P = 0.02$). The urban/rural ratio was 3.1:1 for children with diarrhea and 4.7:1 for controls (P, not significant). Ten of the thirteen cases of ascaris infection (77%) were identified in children from rural areas (10 of 73 rural children versus 3 of 256 urban children; $P = 0.00$). Recovery of other agents was not significantly different between rural and urban environments. Overall, 68% of patients less than 18 months old had been breast-fed. However, patients were significantly more likely to have been bottle-fed than controls (70 of 220 versus 12 of 94; $P = 0.00$). Rotavirus infection occurred more commonly in bottle-fed infants than in breast-fed infants (9% versus 4%), but this difference was not statistically significant. Identification of other pathogens was not significantly different between breast- and formula-fed infants. Fifty-one children with diarrhea (23%) had a history of consumption of uncooked food or untreated water. This was observed in 50% of *Campylobacter*, *Shigella*, and *S. infanti* infections. Overall, 58 (27%) of the patients had a history of recent (within 1 week) animal exposure. Acquisition of campylobacters was significantly associated with animal exposure (4 of 58 versus 1 of 159; $P = 0.03$). Close contact with animals was also common among children with EAF+ *E. coli* infections (6 of 58 versus 5 of 159; $P = 0.07$).

Clinical features. Clinical data from patients with single-agent infections due to EHEC, EIEC, ETEC, and EAF+ *E. coli* were analyzed and compared with data for other enteropathogens (Table 2).

Most patients presented to the hospital within 1 week of onset of symptoms. However, only two of six patients with *S. infanti* infection sought medical attention during the first week of illness, compared with 80% (16 of 20) of patients with other serotypes ($P = 0.05$ by Fisher's exact test).

The clinical features of *Salmonella* infections were not significantly different from those of infections with other agents, except for shigellosis. Different serotypes of *Salmonella* were, however, associated with different clinical presentations. Patients with *S. typhimurium* tended to present acutely ($P = 0.19$) and were significantly more likely to experience nausea or vomiting than were patients infected with other serotypes of *Salmonella*. In contrast, children with *S. infanti* were seen significantly later in the course of illness, were significantly younger and more often malnourished (3 of 6 versus 0 of 20; $P = 0.01$), and were more likely to be febrile (67% versus 37%; $P = 0.35$) and dehydrated (50% versus 10%; $P = 0.06$) than children infected with other serotypes.

EAF+ *E. coli* infections were generally associated with moderate numbers of loose stools, fever in over one-half of the cases, and fecal leukocytes and RBCs in one-third of the cases. Frank blood in fecal specimens was not observed.

EHEC infections were usually associated with frequent, watery stools, with one patient (7%) developing grossly bloody stools. Fever, nausea, vomiting, and fecal leukocytes were seen in fewer than one-third of the cases.

Clinical features of EIEC infections were similar to those of shigellosis, with frequent stools, fever, and abdominal pain. There were no significant differences between these agents in the incidence of fever or number of patients with fecal pus cells, but children with *Shigella* infections were significantly more likely to have RBCs detected in stool specimens than were those with EIEC infections (83 versus 12%; $P = 0.03$).

Rotavirus infections were frequently associated with watery diarrhea and vomiting but not significantly more so than infections with other agents. Two of twelve patients infected

with rotavirus alone had >10 leukocytes per high-power field, and in addition, one had small numbers of fecal RBCs.

Eighty percent of patients with *Aeromonas* infection presented with acute, watery diarrhea. Fever, vomiting, and fecal leukocytes and RBCs were noted in fewer than one-third of the cases.

Patients with shigellosis were significantly more likely to have fever and pus cells and RBCs identified in stools than were children infected with EHEC, ETEC, salmonellae, aeromonas, and rotavirus.

Antimicrobial susceptibility. Antimicrobial resistance, as determined by agar dilution susceptibility testing, was observed in 13 (42%) of 31 *Salmonella* isolates, 6 (100%) of 6 *Shigella* isolates, and 21 (91%) of 23 *Aeromonas* isolates. Resistant salmonellae and shigellae were recovered from children with diarrhea only. Twelve (39%) of the *Salmonella* isolates were resistant to multiple antimicrobial agents including 11 (35%) resistant to aminoglycosides, 12 (39%) resistant to ampicillin and piperacillin, 6 (19%) resistant to co-trimoxazole, and 4 (13%) resistant to cefazolin. Patients were significantly more likely to have multiresistant salmonellae than were controls (12 of 221 versus 0 of 108; $P = 0.03$). Of six shigella isolates, 89% (five) were resistant to co-trimoxazole, 33% were resistant to ampicillin, and 17% were resistant to aminoglycosides and piperacillin. Plasmid analysis of *Salmonella* and *Shigella* strains did not reveal a common pattern among resistant isolates. All 23 *Aeromonas* isolates were resistant to ampicillin, 22% were resistant to co-trimoxazole, and another 65% were resistant to cefazolin, cefoxitin, or piperacillin. Ciprofloxacin, imipenem, and cefotaxime were the only agents tested to which all bacterial isolates were susceptible in vitro.

DISCUSSION

Reports in the English literature on diarrheal illness in China, with the exception of rotavirus infection, are rare. There have been, to our knowledge, no previously published studies in English or Chinese of newly recognized agents such as enteroadherent *E. coli* or EHEC in China, and only limited information on traditional etiologic agents is available. The findings of the present study indicate that both newly recognized and established agents are important causes of childhood diarrhea in China. In addition to cases attributed to agents classically associated with diarrheal illness in the developing world, such as ETEC, salmonella, and rotavirus, a number of cases in this study were attributable to EHEC, EIEC, and EAF+ *E. coli* infections.

As has been found in studies from developing nations (2, 7), interpreting the etiology of diarrheal illness in this study was complicated by frequent mixed infections and by the high carriage rate of enteropathogens by controls. Despite this, salmonellae and EAF+ *E. coli* were both significantly associated with diarrhea in Chinese children.

In agreement with other reports about nonepidemic diarrheal illness in China (18, 19, 31), we found that ETEC was the bacterial agent most frequently isolated from children with diarrhea. Most of the ETEC strains identified were LT-positive only, and as in other studies in the developing world, carriage of these strains was not statistically associated with diarrhea (7, 13). ST-positive ETEC strains are more clearly associated with diarrhea, and recent studies from China indicate seasonal peaks of ST-positive ETEC in the summer (18, 19), a period not included in the present study.

Salmonellae were the second most commonly isolated pathogens, and the incidence of *Salmonella* infections was significantly greater in children with diarrhea than in controls. Different serotypes were associated with different clinical profiles, with *S. typhimurium* infection occurring as a more acute illness associated with significantly more nausea and vomiting than infections with other serotypes. In contrast, *S. infanti* infections occurred as more chronic illnesses in younger, more debilitated children than did infections with other serotypes. Whether these differences reflect variations in host susceptibility or in organism virulence or just socioeconomic differences is not clear.

The rate of identification of EIEC in children with diarrhea in this study (6.8%) is similar to that reported in Thailand (4 to 9%) (27, 28) and greater than that reported in Korea (0.4%) (13). EIEC, like shigellae, was found in older children and was most commonly associated with a dysenteric illness.

E. coli strains that produce Shiga-like toxins I and II (verotoxins), often referred to as EHEC, have been associated with a spectrum of illness that includes watery diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome (11, 24, 25). In Asia, EHEC has been isolated from 7% of children with bloody diarrhea in Thailand (3) and from 1.3% of children with of nonbloody diarrhea in Korea (13). In the present study, EHEC was identified in 6.8% of diarrheal stools either by isolation or by hybridization with an EHEC probe (15, 16). The recovery of one strain of O157:H7 on MacConkey-sorbitol agar represents, to our knowledge, the first EHEC serotype reported from China. However, the frequent occurrence of sorbitol-negative non-O157 colonies made this an impractical screening method for this population. The rarity of O157:H7 identified in this study and in one other study from northeast Asia (13) and the recognition of additional serotypes associated with EHEC (1, 16) suggest that EHEC may occur as serotypes other than O157:H7 in China. The EHEC probe described by Levine et al. (16) detects an EHEC fimbrial gene and is sensitive and specific for the detection of O157:H7 and approximately 80% of verotoxin-producing serotypes other than O157:H7. With this probe, 14 additional cases of EHEC were identified. One of these cases was associated with bloody diarrhea. These findings suggest that both O157:H7 and other verotoxin-positive *E. coli* serotypes occur in China. In addition, as has recently been described in Thailand (1), serotypes other than O157:H7 may be more common. However, further controlled studies are needed in this area.

E. coli strains exhibiting localized adherence to HEp-2 or HeLa cells in an in vitro assay originally described by Cravioto et al. (5) have consistently been associated with diarrhea around the world (4, 10, 21). The DNA probe for detecting genes conferring localized adherence developed by Nataro et al. (22) has been shown to be a sensitive and specific method for identifying EAF+ *E. coli*. We used this probe to identify EAF+ *E. coli* infections in our patients. As in studies from several developing nations, EAF+ *E coli* infections were significantly associated with diarrhea in this study, and this represents the first time that EAF+ *E. coli* has been identified in China. A number of patients infected with EAF+ *E. coli* in this study and one other study (13) either had fever or had fecal leukocytes and RBCs, features more frequently associated with invasive diarrheal agents. These findings lend support to recent in vitro observations that in addition to demonstrating adherence, EAF+ *E. coli* may also invade epithelial cells (6).

Except for ascaris, the yield from examination for ova and parasites was low. This may be explained in part by the

limitation of a single stool sample, the small stool quantity available from some children, and the brief duration and the timing of the study. Cryptosporidia were looked for in all specimens but were not found. Limited information suggests that both giardias and cryptosporidia are infrequent pathogens in China, accounting for 2 and 1%, respectively, of cases of diarrhea in children (9, 30). In addition, as in other temperate areas, incidence of cryptosporidium and giardia infections may be seasonal.

Antimicrobial susceptibility testing by standardized methods is not widely available in many clinical laboratories in China. For this reason, results of susceptibility testing of enteric pathogens are scarce and published results must be interpreted with caution. In this study, 42% of *Salmonella* and 100% of *Shigella* isolates were resistant to aminoglycosides, co-trimoxazole, or ampicillin. Patients with diarrhea were significantly more likely to have multiresistant salmonellae than controls were. Although multiresistant salmonellae have been previously described in the Chinese literature, these infections were primarily in hospitilized patients (17). As the majority of our patients were outpatients and none had recently received antibiotics, the observation of frequent multiresistance was unexpected. The reasons for the resistance patterns observed are presently unclear. Extended-spectrum cephalosporins, quinolones, and imipenem were the only agents tested to which all bacterial isolates were susceptible in vitro. None of these antimicrobial agents are widely available in China, limiting therapeutic options for children infected with multiresistant salmonellae and shigellae.

In summary, the present study documents the roles of newly recognized and traditional agents as important causes of diarrheal illness in Beijing and indicates that therapy may be complicated by indigenous antimicrobial resistance. *Salmonella* serotypes, EAF+ *E. coli*, and mixed pathogens were significantly associated with diarrhea in children, and *E. coli* strains associated with hemorrhagic colitis and hemolytic uremic syndrome were identified for the first time in China. It should be emphasized that this study was conducted during April and May and that additional studies are required to define the relative frequency of specific pathogens during other seasons.

ACKNOWLEDGMENTS

This work was supported in part by a grant from the Canadian International Development Agency (project number 908-282/14218) under the Canada/China University Linkage program and by kind donations from Prepared Media Laboratories, Oxoid Ltd., and Metro-McNair Laboratories, Vancouver, Canada.

The DNA probes used in this study were kindly provided by J. B. Kaper (Center for Vaccine Development, University of Maryland School of Medicine). Bacterial pathogens were serotyped by J. Jessop, Enteric Section, British Columbia Center for Disease Control.

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