Multidrug-Resistant Enteroaggregative *Escherichia coli* Associated with Persistent Diarrhea in Kenyan Children

To study the association of multidrug-resistant enteroaggregative *Escherichia coli* with persistent diarrhea in Kenyan children, stool specimens were obtained from 862 outpatients under 5 years of age from July 1991 to June 1993. *E. coli* O44 was identified as the sole bacterial pathogen in four patients experiencing at least 14 days of fever, vomiting, and diarrhea. Disk diffusion testing showed *E. coli* O44 resistance to tetracycline, ampicillin, erythromycin, trimethoprim-sulphamethoxazole, and amoxicillin/clavulanate and sensitivity to chloramphenicol, nalidixic acid, azithromycin, and cefuroxime. Further studies are needed to clarify the epidemiology, clinical spectrum, and pathogenesis of enteroaggregative *E. coli* infection.

Escherichia coli infection is an important cause of illness and death in infants in developing countries (1). On the basis of patterns of adherence to tissue culture cells (HEp-2 or HeLa), *E. coli* strains can be classified into three groups: localized, diffuse, and aggregative (2). Much remains unknown about these strains. Enteroaggregative *E. coli* (EAggEC), which exhibits aggregative adherence, has been associated with diarrhea in children in Chile (3) and with persistent diarrhea in children in India (4). We report the first evidence of multidrug-resistant EAggEC associated with persistent diarrhea in Kenyan children.

From July 1991 to June 1993, stool specimens from 862 outpatients under 5 years of age at Malindi Hospital were examined for pathogenic organisms. Standard methods for isolating enteric pathogens were used. Laboratory tests to detect pathogenic factors, e.g., verotoxins (VT) in cultures of all *E. coli* isolates, were done by applying the conventional tissue culture method (which uses the Vero cell line [5] and the VT1 or VT2 genes [6]) and polymerase chain reaction (7). The genes for heat-labile enterotoxin and heat-stable enterotoxin, VT, and invasiveness were tested by DNA probes on all *E. coli* strains. The strains were further examined for adherence to HEp-2 cells (8) and tested by the disk diffusion method (9) for susceptibility to the antibiotics chloramphenicol, erythromycin, ampicillin, nalidixic acid, cefuroxime, trimethoprimsulphamethoxazole, amoxicillin/clavulanate, tetracycline, and azithromycin.

Bacterial pathogens were found in 27.7% of the samples; 119 *E. coli* isolates were obtained. The results indicated that many of the bacteria, e.g., pathogenic *E. coli* , *Salmonella* spp., and *Shigella* spp. (Table), had been transmitted by the fecal-oral route. *E. coli* O44 was isolated from four patients; the isolates occurred in an aggregative adherence pattern as chains and nearly random aggregates on HEp-2 cells.

The case descriptions of the four patients from whom the O44 strains were isolated are as

Table. Identification of enteric pathogens in children with diarrhea.

Pathogens (number tested)	Number	Percentage %
Bacteria (862)	239	28.0
Escherichia coli		
enteropathogenic *E. coli* (EPEC)	71	8.0
EAgg *E. coli (ETEC)*	4	0.5
enterotoxigenic *E. coli*	43	5.0
enterohemorrhagic *E. coli*	1	0.1
Salmonella spp.	63	7.3
Shigella spp.	56	6.5
Campylobacter spp.	42	4.9
Vibrio parahaemolyticus	4	0.5
Parasites (862)	109	12.6
Entamoeba histolytica	67	7.8
Giardia lamblia	42	4.9
Viruses (427)		
Rotavirus	69	16.2

Mixed infections: ETEC/EPEC = 12, EPEC/ *Campylobacter* = 8, *Salmonella/* ETEC = *7, Salmonella/* EPEC = *3, Shigella/ Campylobacter* = *2, Vibrio/Shigella* = 2, *Shigella/ Salmonella* = 1, EPEC */Shigella* = 6, ETEC/ *Shigella* = 4.

follows: Patient 1, age 28 months, had fever, gross blood in stool, vomiting, and diarrhea lasting 14 days; Patient 2, age 35 months, had fever, abdominal pain, nausea, vomiting, and diarrhea lasting 15 days; Patient 3, age 24 months, had fever, gross blood in stool, vomiting, and diarrhea lasting 14 days; and Patient 4, age 26 months, had fever, abdominal pain, vomiting, and diarrhea lasting 14 days. The patients were not related and lived in different communities. These particular strains of *E. coli* O44 had similar patterns of resistance to tetracycline, ampicillin, erythromycin, trimethoprimsulphamethoxazole, and amoxicillin/clavulanate; they were all sensitive to chloramphenicol, nalidixic acid, azithromycin, and cefuroxime.

Persistent diarrhea is increasingly recognized as an important public health problem among children in developing countries (10) and is a research priority of the Diarrhoeal Diseases Control Programme of the World Health Organization (11). In the four patients from whom it was isolated, EAggEC was the sole bacterial pathogen recovered. However, tests for parasitic causes of persistent diarrhea, such as *Cyclospora* and *Cryptosporidium*, were not available at the time of our study and were not performed. The association of EAggEC with persistent diarrhea will be strengthened by extending this kind of study to other areas in Kenya and identifying all causes of persistent diarrhea.

Tetracycline, ampillicin, and trimethoprim-sulphamethoxazole are recommended by the Kenyan Ministry of Health for the empiric treatment of diarrhea. These drugs were largely ineffective against *Shigella* spp. and EAggEC. Our results are consistent with the findings of Yamamoto et al., who found multidrug resistance in EAggEC strains from Thailand, Mexico, Chile, and Peru (12), and suggest that monitoring sensitivity to antibiotics in Kenya is necessary for optimum selection of effective antibiotics and elimination of antibiotics with little therapeutic value. Similarly, the epidemiology, clinical spectrum, and pathogenesis of EAggEC infection and the reservoir of the putative etiologic agent are still poorly understood or unknown. Further clinical, epidemiologic, and laboratory studies are needed to clarify these issues.

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