Heat-Stable Enterotoxin-Producing *Escherichia coli* O169:H41 in Japan

To the Editor: Enterotoxigenic *Escherichia coli* (ETEC) cause diarrhea by producing either a heat-labile enterotoxin, a heat-stable enterotoxin (ST), or both. Consequently, ETEC can be identified either by detecting the enterotoxin in the culture fluid by immunologic assays or by detecting enterotoxin-coding genes with DNA probes or polymerase chain reaction (PCR) amplification. For many clinical laboratories, however, serologic typing is the most common test used to determine if isolates are members of known pathogenic groups.

Although *E. coli* serotype O169:H8 has been recognized as one of the ETEC strains (1), serotype O169:H41 is not established worldwide as one of the diarrheagenic *E. coli* of the ETEC group. Ando et al. first reported that an outbreak at a school for physiologically handicapped children in Saitama Prefecture was due to ST-producing *E. coli* serotype O169:H41 (2). We report an outbreak of diarrhea caused by *E. coli* O169:H41 that predates the outbreak reported by Ando et al. and information about additional outbreaks in Japan since 1991.

In June 1991, we is olated toxigenic *E. coli* from the stool of two of three ill members of an eight-member family during an outbreak of diarrheal illness in Osaka, Japan. An epidemiologic investigation implicated pickles (kimchi) purchased during a visit to Korea; only the three members of the family who ate the pickles became ill. The major symptoms were diarrhea (3/3), abdominal pain (2/3), and fever (2/3) of 38° C. The incubation period was estimated at 33 hours. The serotype of these ST-producing *E. coli* isolates was not recognized immediately because the cultures were non-typable by the lot of *E. coli* antiserum available when the cultures were first is olated. The cultures were identified as *E. coli* O169:H41 when a new lot of antiserum became available.

In another outbreak investigated by the Osaka City Department of Environment and Health and the Osaka Prefecture Department of Environment and Health, food poisoning occurred among 776 of 1,242 guests of wedding receptions held at a wedding facility during September 1993. The main symptoms were diarrhea (98%) and abdominal cramps (74%), and the mean incubation period was 40.5 hours. *E. coli* O169:H41 was isolated from the stool specimens of 7 of 14 patients. A strain of *E. coli* O169:H41 was isolated from frozen, ready-to-eat seafood recovered from a distributor who provided foods to the wedding facility.

In addition to the outbreaks mentioned above, Japanese surveillance reports describe foodborne outbreaks in different prefectures between January 1991 and September 1994. In addition to being cultured for *E. coli* , stools were also routinely cultured for *Shigella, Salmonella* (including *typhi* and *paratyphi*), *Vibrio, Clostridium, Aeromonas, Plesiomonas, Bacillus cereus,* and *Staphylococcus aureus* . Stools were also examined for rotaviruses and small round viruses by electron microscopy. *E. coli* serotype O169:H41 was isolated from patients' stools in 11 of 40 outbreaks; recovery rates were 10%-100%. In 7 of the 11 outbreaks, recovery rates of serotype O169:H41 exceeded 75%. PCR was used to examine the diarrheagenicity of 31 *E. coli* isolates selected from reported outbreaks that occurred from 1991 to 1994 (3). ST production of the 31 isolates was also examined by COLI ST EIA (Denka Seiken Co., Ltd., Tokyo, Japan), a competitive enzyme-linked immunosorbent assay (ELISA) for toxigenic and invasive strains of *E. coli* . Strains were grown in Casamino Acids-Yeast Extract broth shaken at 37° C for 18 hours. The supernatant obtained after the centrifugation of cells was used for the test according to the manufacturer's instructions.

Thirty of the 31 *E. coli* O169:H41 isolates tested demonstrated toxigenicity by both PCR and ELISA. Collaborative studies are in progress to further characterize these isolates and to study the relationships between different isolates by molecular epidemiologic methods. Five cultures of *E. coli* O169:H41 have been ribotyped by a digoxigenin-labeled (Genius System, Boehringer Mannheim) probe prepared from pKK3535 ac cording to the manufacturer's instructions. The resulting patterns were indistinguishable when the restriction enzymes *Eco* RI, *Sma* I, *Bg* lII, *Bam* HI, *Sal* I, *Pst* I, or *Hind* III were used to digest chromosomal DNA.

We suggest that this comparatively new serotype of ETEC may be spreading across Japan and urge that studies be conducted to determine its distribution and association with gastroenteritis worldwide.

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The GAP Project in Southeastern Turkey: The Potential for Emergence of Diseases

To the Editor : The undersigned, representing interested scientists from both T urkey and the United States, recently visited the water development projects in southeastern Anatolia, Turkey. This letter describes our observations and projections on the possible health-related consequences of these projects with specific emphasis on infectious diseases.

When new irrigation schemes are introduced into previously dry areas, disease frequently follows the new water. The Southeastern Anatolia Irrigation Project or GAP (its Turkish acronym) is one of the largest projects ever undertaken in Turkey. This water resources development program includes the construction of 22 dams and 19 hydroelectric plants on the Euphrates and Tigris rivers in southeastern Turkey. Upon completion, the project will also include an irrigation network for 1.7 million hectares of land, covering eight provinces corresponding to approximately 10% of Turkey's total population and surface area (1). In its entirety, GAP comprises investments in development projects linked to agriculture, energy, transportation, telecommunications, health care, education, and urban and rural infrastructures. To ensure the success of the project, an agency has been established (the Republic of Turkey Prime Ministry Southeastern Anatolia Project Regional Development Administration) to oversee and implement all of these projects.

The largest of the completed dams on the Euphrates River is the Ataturk Dam. It is the sixth-largest rock-filled dam in the world; its hydroelectric systems have already produced more than seven billion kilowatt hours of power since 1992 (2). Water from the Ataturk Dam reservoir is diverted to the plains of upper Mesopotamia through the Sanliurfa Irrigation Tunnel System. This system consists of two parallel tunnels, each 26.5-km long and 7.62 m in diameter, and numerous other irrigation networks and canal systems. The first water started to flow to the plains of Harran in November 1994. Additional lands will be incorporated into the irrigation scheme as the canals are completed. (The year 2020 is the target date for completion.) When fully operational, GAP is expected to double Turkey's hydroelectric production, increase irrigated areas by 50%, more than double the per capita income in the region, more than quadruple the gross national product, and create two million new jobs in the coming decade (3). The total surface area affected by the irrigation scheme is about 75,000 km^2; of this, 46.2% is cultivated (36% semiarid rain-fed farmland), 33.3% is dry pastures, 20.5% is forest and bush.

One of GAP's major goals is to remove the socioeconomic disparity between the country's more developed regions and the project area. For GAP to reach its targeted and sustainable economic aims, projects in various other sectors also need to be considered and integrated. In this context, the public health consequences of emerging diseases in this setting must be anticipated so that appropriate health education and disease prevention measures can be implemented.

To anticipate changing patterns in disease associated with microclimatic and other environmental changes, knowledge of existing diseases in the region is vital. Since arthropods, reservoir animals, and other intermediate hosts are involved in the trans mission of many wa terborne parasitic diseases, a clear understanding of the existing species—especially of insect vectors—is equally important.

Historically, occasional cases of malaria have occurred in the region; however, limited records show that this disease is clearly on the rise. Cutaneous leishmaniasis is also endemic and on the rise, but few data are available on the prevalence of the visceral form of the disease. Other common diseases in the region include bacterial and helminthic gastrointestinal infections as well as trachoma.

According to data from the Malaria Division of the Turkish Health Ministry, the reported cases of *Plasmodium vivax* malaria rose from 8,680 in 1990 to 18,676 in 1992 (4). The province of Sanliurfa (population one million in 1990), which is at the heart of the irrigated plains in GAP, has reported that malaria cases increased from 785 in 1990 to 5,125 in 1993. The numbers of cases in the first 9 months of 1994 alone were already significantly higher than those reported in 1993 (S. Aksoy, unpublished data). Although presumably *P. vivax* malaria is most common, cases of *P. falciparum* malaria have also been reported in the country. Three cases of *P. falciparum* malaria were recently documented in Izmir, which is on the Aegean Sea coast of Turkey (4). No cases of drug-resistant malaria have been reported.

Another endemic disease on the rise in the southeastern region is leishmaniasis, transmitted by biting sand flies. In Sanliurfa the number of documented cases of the cutaneous form of this disease has risen from 552 in 1990 to 1,955 in 1993. In the first 9 months of 1994 alone, the number of reported cases was more than 3,000 (S. Aksoy, unpublished data). At Sanliurfa's Diyarbakir Hospital, in 1991, in addition to cases of the cutaneous forms of the disease, there were 80 potential cases of visceral leishmaniasis (kala-azar) in children ages 2 to 10 (5). *Leishmania donovani* is often the causative agent of kala-azar, but both *L. tropica* and *L. infantum* may also be involved (6). As the economic oppor-

tunities in the GAP provinces attract populations to the region, visceral leishmaniasis may become a greater threat. The prevalence of the sand-fly species in the region, their habitats, and the future implications of the microclimatic changes for these habitats must be studied to anticipate future disease patterns.

Other prevalent pathogens in the region include *Entamoeba histolytica, Giardia lamblia , and Ascaris lumbricoides.* Of 22,468 stool samples examined in one study, over 90% carried intestinal parasites; in children from infancy to 5 years of age, 60% contained *Giardia intestinalis* (7). In a second study in Diyarbakir involving 4,670 patients (ages <1–65 years), the incidence of protozoan and helminthic infection was approximately 16% (53%, *E. histolytica* ; 31%, *G. lamblia* ; and 10%, *A. lumbricoides*) (8). In both studies, the incidence of amebiasis was approximately 8% to 9%. In 1989, a sur vey conducted among 1,001 children in four elementary schools in Sanliurfa found parasites in 88% of the stool samples examined (50% *Ascaris* , 53% *Trichuris trichiura,* 22% *Giardia* , 11% *Entamoeba coli)* (9). Ancylostomiasis, which occurs in the eastern Mediterranean, is a potential danger for the region (10).

The emergence of schistosomi asis, which can quickly reach epidemic proportions in water-related projects unless measures are taken, should not be ignored. A recent study in Sanliurfa has identified *Bulinus truncatus* , the snail vector of *Schistosoma haematobium* in the region (11). Whether other regions in GAP also harbor this species is not known, although there have been reports of these s nails in the Nusaybin and Mardin regions (12). A few decades ago, sporadic cases of disease were also reported from southeastern regions (13). As microclimatic changes occur in the GAP area, the presence of these snails and the potential emergence of schistosomiasis should be closely monitored.

The costs of combating epidemic diseases can be very large, whereas the costs of prevention are much lower. Large national projects that anticipate economic benefits may sometimes overlook the distant prospects of disease. Ideally, health planning should be built into a project from its inception for small funds invested for prevalence studies early on can bring high returns later. Earlier dam projects in Senegal, Lake Volta, and Egypt have shown that unless effective measures are taken early, infections can quickly reach epidemic levels (14). The establishment of good surveillance and recording systems is an important first step.

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