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EDITORIAL

Importance of *Escherichia coli* Strains Producing Verotoxins

The production of a heat-labile protein unrelated to cholera toxin was described in the 1960s in studies of *Escherichia coli* isolated from animals (1,2). However, it was not until 1982 when Riley *et al*. reported an outbreak of haemorrhagic colitis associated with an *E. coli* that produced the same heat-labile toxin, and that these strains were considered hazardous to humans (3). A second interesting outcome of the study by Riley *et al*. was that *E. coli* strains isolated during this outbreak belonged to a serotype that had not been previously associated with human disease. Over the subsequent years, this 'new' serotype, O157:H7, became the predominant causal pathogen worldwide for both haemorrhagic colitis and haemolytic-uraemic syndrome. Outbreaks of haemorrhagic colitis and haemolytic-uraemic syndrome associated with O157:H7 *E. coli* strains have been reported in Canada, the United States, Europe, and Japan (4).

The production of heat-labile cytotoxin is not restricted to *E. coli* O157:H7, with studies showing that other *E. coli* strains have this character (5), and the common trait among these bacteria is the ability to produce heat-labile cytotoxin. Such strains have been grouped according to specific characteristics: Verocytotoxin-producing *E. coli*, which relates to the capacity to destroy monolayers of vero cells in culture; enterohaemorrhagic *E. coli* for their capacity to cause haemorrhagic colitis and haemolytic-uraemic syndrome; and more recently, Shiga-toxin (Stx)-producing *E. coli* (STEC) for the similarity of the toxin produced by these *E. coli* strains with that produced by *Shigella dysenteriae* type 1 (4).

Given the severity of the diseases associated with infection by these strains and their importance as the leading cause of acute renal failure in children aged less than five years in developed countries, an international network of interested laboratories has been established to conduct surveillance and determine the burden of disease associated with these infections. Concerned laboratories in less-developed areas of the world have also joined this international endeavour to determine the importance of such strains as part of the spectrum of diarrhoeal diseases in their own environments.

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Studies conducted in less-developed areas of the world have already shown little participation of STEC strains as causal agents of diarrhoeal disease in these countries (4). What is interesting is that the conditions for transmission of these strains from animals to humans exist, as do the inherent problems relating to basic sanitation and safe drinking-water. Therefore, the question that remains to be answered is why there has been such a lack of isolation of STEC in these areas.

The reason is not due to a lack of technical capacity in participating laboratories or to inadequate surveillance systems in these areas. Active surveillance at the community level has been conducted in several longitudinal surveys of diarrhoeal disease in less-developed countries in which other types of pathogenic strains of *E. coli* have been properly identified and characterized by state-of-the-art methods (4). Therefore, there has to be another explanation for the lack of participation of STEC as a cause of major outbreaks of disease in these areas of the world.

In this issue of JHPN, Voravuthikunchai *et al*. report the results of a study conducted in Thailand to determine whether the presence of a humoral immune response to O157 lipopolysaccharide (LPS) could be a reason for the lack of disease associated with infection by these strains in people with diarrhoea in that country (6). An IgM response to the O157 LPS was found by these authors in 12% of 332 serum samples obtained from healthy blood donors and patients with diseases unrelated to diarrhoea. In the case of an IgG response, 23% of these same samples showed a positive response to O157 LPS. The authors conclude that possible exposure to cross-reacting antigens in these subjects could be the reason for finding this response in their sera, and a possible protection against colonization and disease associated with O157:H7 strains.

Similar findings have been reported in previous studies conducted in serum samples obtained from humans

in other less-developed areas of the world. Navarro *et al*. (7) showed that serum samples obtained from Mexican adults and children aged less than one year not only responded to the O157 LPS, but also to two other cross-reacting LPSs: O7 and O116. They concluded that colonization by any of these strains could have a protective immune response against infection by O157 strains, which could explain why strains belonging to this serotype are seldom isolated from the Mexican population, especially when a similar immune response to these LPSs was also found in breastmilk samples obtained by the authors. In the same study (7), Navarro *et al*. reported that rabbit antiserum raised against O6, O114, and O157 LPSs has a homologous and a heterologous bactericidal capacity against strains with these LPSs, and that serum samples obtained from herds of cattle in different parts of Mexico showed a similar response to that found in humans, which explains why the local animals are seldom shown to be colonized by O157:H7 strains (8,9).

The presence of anti-LPS antibodies in serum could also reflect the presence of a similar response in the intestine. In this case, the presence of specific IgA antibodies against cross-reacting non-O157 bacterial antigens could inhibit the pathogenic capacity of O157:H7 strains through the temporal loss of critical virulence factors used by these strains to cause disease in humans, as shown recently by Mellmann *et al*. (10).

The lack of isolation of O157:H7 strains in less-developed areas of the world does not mean, however, that STEC strains are not part of the burden of diarrhoeal disease in children from these areas. *E. coli* belonging to serotypes other than O157:H7 have been associated with both outbreaks and sporadic diseases in animals and humans (5,11). Given these findings, it seems necessary to determine the epidemiological importance of all *E. coli* strains producing verocytotoxin isolated in these areas, regardless of their serotype, to determine the real participation of these pathogens in the burden of diarrhoeal disease in humans living in different parts of the world.

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