Journal of the Formosan Medical Association (2011) 110, 611–612

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PERSPECTIVES

European *Escherichia coli* O104:H4 outbreak

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Received 25 June 2010; received in revised form 27 June 2011; accepted 5 July 2011

In May 2011, a large outbreak of bloody diarrhea and enteric infection-related hemolytic uremic syndrome occurred in numerous European countries as well as in Canada and the USA (Fig. 1).[1] As of 22 June 2011, a total of 3802 infections with Shiga toxin-producing *Escherichia coli* serotype O104:H4 had been confirmed. All of the infections were associated with the consumption of contaminated bean and seed sprouts.[1] Among the 3802 confirmed cases, 2938 (77.3%) involved cases of enterohaemorrhagic *E. coli* (EHEC) infection and 864 (22.7%) resulted in hemolytic uremic syndrome (HUS). This is the first and largest outbreak of infections due to serotype *E. coli* O104:H4.

E. coli are Gram-negative and rod-shaped bacteria that are part of the normal microflora in humans. Although most strains are harmless, certain serotypes can cause both intestinal and extraintestinal infections, with manifestations ranging from mild diarrhea to severe hemorrhagic colitis and HUS. Based on their virulence factors and pathogenesis, this group of bacteria has been divided into several pathotypes, including Shiga toxin-producing *E. coli* (STEC).[2] Although the most prevalent serotype of *E. coli* in previous outbreaks has been O157:H7, the number of outbreaks due to non-O157 *E. coli* has increased recently. Many kinds of foods have been reported to carry STEC, including raw beef, pork, poultry, fish, punch, and iceberg lettuce.[3] At least 150 STEC serotypes have been shown to be associated with sporadic or cluster illness.[3,4] The first documented outbreak of *E. coli* O104:H21 infection occurred in the US state of Montana in 1995,[5] and the first case of HUS caused by *E. coli* O104:H4 occurred in Korea in 2006.[6]

Compared to the O157 serotype, which is colorless and opaque-appearing on sorbitol-MacConkey agar, most non-O157 STECs appear as pink colonies and are not easily detectable on stool culture. [4] However, non-O157 STECs have accounted for up to 50% of all STEC infections in the USA.[4] In the United States, all stool cultures collected from patients with acute community-acquired diarrhea are tested for the presence of *E. coli* O157 and non-O157 STEC by detecting the genes or their products related to Shiga toxins, simultaneously.[7]

In this outbreak of HUS and EHEC in Europe and in North America, the majority of patients were 20 years of age or older (88%) and tended to be female (71%). However, in previous reports, adults only accounted for 1.5% to 10% of the infected population, and there was no gender difference.[4] In addition, more than 25% of the patients developed HUS during this outbreak, which is a much higher rate than occurred during previous outbreaks.[8,9] Epidemiological studies of the possibility of human-to-human transmission as well as the risk factors associated with HUS are currently being conducted by several institutes in Europe.

The *E. coli* strain O104:H4 has been shown to express only Shiga toxin 2 (stx_{2a}). In addition, the strain has been demonstrated to carry the *aatA* gene (ABC-transporter

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doi:10.1016/j.jfma.2011.08.001

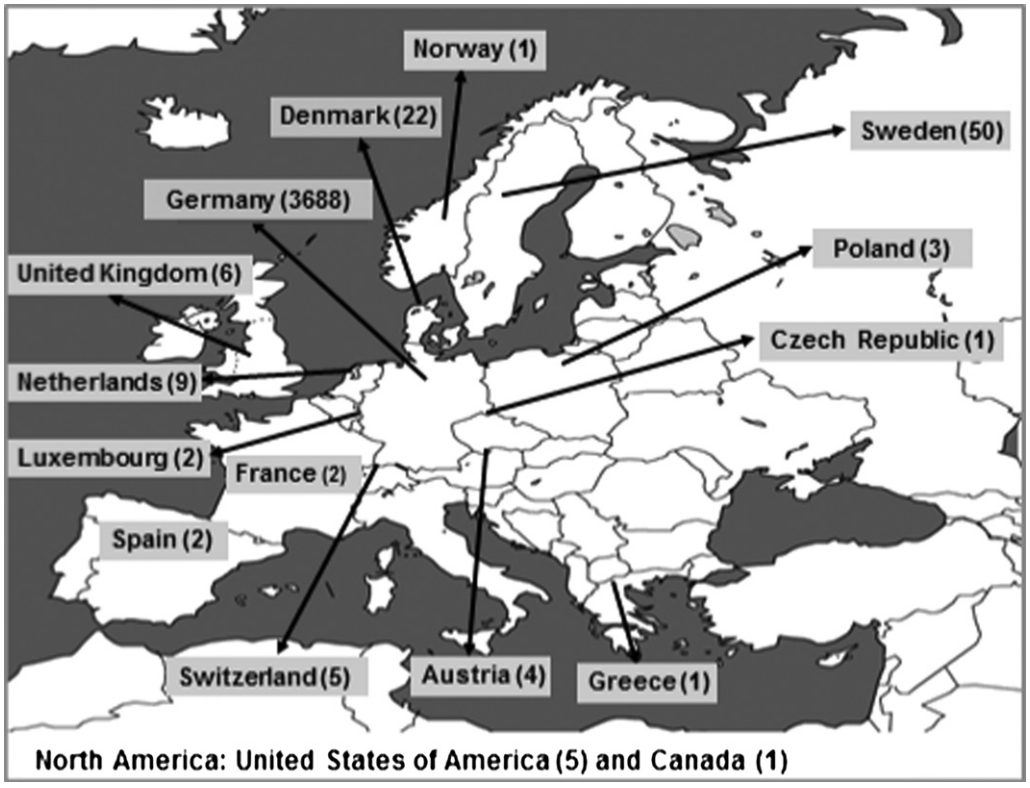

Figure 1 The geographical distribution and number of cases of *Escherichia coli* O104:H4 infection (in parenthesis) in countries in Europe and in North America.

protein gene), the *aggR* gene (master regulator gene of Vir-plasmids), the *aap* gene (secreted protein dispersin), the *aggA* gene (AAF/I-fimbral gene), and the *aggC* gene (AAF/I-fimbral operon-gene).[1] A recent comparative genomic study showed that several EHECs contained much larger genomes (5.5-5.9 Mb) and larger numbers of prophages, integrative elements, and virulence plasmids than non-EHEC strains. Furthermore, this strain showed multidrug resistance, including resistance to first and third generation cephalosporins (through extended-spectrum β-lactamase, CTX-M-type), tetracycline, nalidixic acid, streptomycin, and trimethoprim-sulfamethoxazole. These strains developed through distinct evolutionary tracts and obtained these mobile genetic elements independently.[10] The evolution of this unusual O104:H4 needs further study.

In Taiwan, physicians need to be aware that patients who have recently traveled in regions endemic for *E. coli* O104:H4 and who present with diarrhea and HUS might be carriers of non-O157 STECs.

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