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HOSPITAL OUTBREAK OF *ESCHERICHIA COLI* O157:H7 ASSOCIATED WITH A RARE PHAGE TYPE — ONTARIO

Introduction

Since the early 1980s, verotoxigenic *Escherichia coli* serotype O157:H7 has emerged as a major cause of both sporadic and epidemic disease in North America and other regions of the world. Most infections result in mild diarrhea but more serious illnesses include hemorrhagic colitis, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura[1]. Outbreaks of *E. coli* O157:H7 infection have occurred in various settings including schools, day-care centres, and nursing homes[2]. Most outbreaks and sporadic cases have been associated with the consumption of foods of bovine origin, particularly undercooked ground beef. This report presents findings of the investigation of an unusual outbreak involving the patients and staff members of a suburban acute-care hospital in southern Ontario.

Epidemiologic and Laboratory Investigation

Peel Memorial Hospital is a 360-bed community hospital located in Brampton, Ontario. Between 1 November and 7 November 1995, 21 individuals associated with the hospital including eight patients, 10 staff members and three volunteers met the suspect case definition: bloody diarrhea and abdominal cramping consistent with acute hemorrhagic colitis. All patients recovered from their illnesses and none progressed to the hemolytic uremic syndrome. Of the 19 cases who submitted stool specimens for culture, 15 were positive for *E. coli* O157:H7. The four individuals with negative cultures had been on antimicrobial therapy prior to obtaining stool specimens. There were two instances of secondary transmission to family members in the community.

All primary cases had eaten food prepared in the hospital between 30 October and 1 November 1995. A case-control study was done with three to four diarrhea-free controls per case matched by status (patient, staff member or volunteer), ward, and department. The results of this study indicated that green salad served on 30 October was a significant risk factor (matched odds ratio = 16.62, $p < 0.00042$).

Patients and staff had been served salads and dressing; one lot of iceberg lettuce was common to both salads. One individual's only meal in the hospital was a sandwich containing lettuce from the implicated lot. Two of the three volunteers consumed only green salad on 30 October, their only day in the hospital complex. A kitchen inspection revealed no opportunity for contamination of lettuce from raw or undercooked meat. The implicated lettuce was a single box of imported iceberg lettuce; the kitchen staff had filed an incident report upon its receipt because of heavy soilage.

Samples of pre-cooked, cooked, and raw ingredients from the hospital's kitchen were obtained for bacteriologic analyses. All samples were culture negative. No samples of food served between 30 October and 1 November were available. Isolates from suspect cases were obtained from the hospital laboratory and from various private laboratories. They were confirmed as *E. coli* O157:H7 at the Enteric Reference Laboratory, Central Public Health Laboratory, Toronto, by standard methods[3]. Each of the isolates was tested for the production of verotoxin by using the Vero cell monolayer assay[4] and the genetic identification of verotoxins was performed at the National Laboratory for Enteric Pathogens, Ottawa, by using a polymerase chain reaction–based method[5]. Subtyping of the isolates was performed by phage typing at the Laboratory Centre for Disease Control, Ottawa[6], and by large-fragment genomic fingerprinting using pulsed-field gel electrophoresis (PFGE) at the Central Public Health Laboratory. All isolates from suspect cases produced VT_1 and VT_2, belonged to phage type 10, and had identical PFGE patterns that were

distinguishable from epidemiologically unrelated clinical strains of *E. coli* O157:H7 isolated during the same period in Ontario.

Discussion

This outbreak of verotoxigenic *E. coli* (VTEC) was characterized by several unusual aspects including the vehicle of transmission, the phage type, and the setting. Most outbreaks and sporadic cases of *E. coli* O157:H7 have been associated with the consumption of foods of bovine origin including ground beef, roast beef, and raw milk. The transmission of this organism by contaminated water supplies, person-to-person transmission, as well as direct animal-to-human transmission, have also been documented[1,2,7]. In recent years, there have been infrequent reports of its transmission by raw vegetables. In one community outbreak in the United Kingdom, the risk of illness was found to be associated with the handling of raw potatoes possibly contaminated by cow manure[8]. An investigation of a cluster of *E. coli* O157:H7 infections in the United States identified the consumption of raw vegetables grown in a garden fertilized with cow manure as the source of infection[9]. The results of the present investigation indicate that iceberg lettuce may represent a previously unrecognized food vehicle for VTEC. A recent European study, which reported that iceberg lettuce can act as a vehicle of transmission for other bacterial enteropathogens, supports this finding [10]. Each of the isolates associated with this outbreak belonged to phage type 10. Currently, a total of 82 phage types are recognized in the phage typing scheme for *E. coli* O157:H7. Strains belonging to phage type 10 have been rarely isolated in Canada. In 1994, only three of these strains were isolated; between 1990 and 1995, phage type 10 strains accounted for less than 1% of all *E. coli* O157:H7 strains isolated in Canada.

The PFGE genomic fingerprints of the outbreak-associated isolates were indistinguishable from each other, but they were clearly different from those of epidemiologically unrelated *E. coli* O157:H7 strains isolated in Ontario during the same period as the outbreak. Taken together, the subtyping results indicate that the outbreak was caused by a distinct strain that was not previously circulating in the community; this provides further evidence that the outbreak was linked to the consumption of an imported foodstuff. The results of the present study also demonstrate the value of prospective subtyping of *E.coli* O157:H7 for monitoring the prevalence of different subtypes within the community. Recent studies have indicated that the combined use of phage typing and PFGE analysis may provide for optimal discrimination between strains[11].

Previous outbreaks of VTEC have occurred in various settings including schools, day-care centres, nursing homes, and custodial institutions[2]. Widespread community outbreaks associated with consumption of undercooked foods at fast-food restaurants and familial clusters of infection have also been described[2]. Nosocomial person-to-person transmission of this organism has been described previously[8,12] but, to the authors' knowledge, the present report represents the first description of a foodborne outbreak in an acute-care hospital. The potentially serious consequences of VTEC infections in health-care institutions have been previously documented[13] and, therefore, this study should alert such institutions to the newly recognized hazards associated with contaminated lettuce and other raw vegetables.

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Editorial Comment: *Escherichia coli* O157:H7 remains the most common VTEC identified in humans in Canada and the most commonly identified cause of hemolytic-uremic syndrome in Canadian children[1]. National notifications for VTEC have ranged from approximately 1,100 to 1,600 per year (3.5 to 6 per 100,000) since 1990, down from the peak of 2,432 notifications in the late 1980s[2,3]. (Not all provinces have contributed to the national data each year.) Provisional data suggest the total for 1996 will be close to 1,100.

This report serves to emphasize a number of points. First, the implicated food was not one usually suspected of transmitting VTEC. Although the majority of outbreak reports have implicated ground beef or hamburgers, including the largest known North American outbreak[4], other fresh foods have been important sources of infection[5]. It is interesting to note that at the time of this outbreak, a number of North American outbreaks potentially linked to lettuce were being investigated, including a restaurant outbreak in Calgary, Alberta. Phage typing at the National Enteric Reference Laboratory, LCDC, quickly determined that the restaurant and hospital outbreaks were not related; the strains from Calgary were the more common phage type 2.

The epidemiologic investigation of the Calgary outbreak went on to implicate a component of salad other than lettuce[6]. The considerable effort that might have been undertaken to link the two outbreaks to a single source of lettuce was avoided through this combination of laboratory and field investigation. Phage typing provides a rapid, inexpensive method of screening strains to determine which may be related to an outbreak. When the more common phage types are identified and strains cannot be related on the basis of epidemiologic data, then additional molecular typing methods may be used to refine the case definition for an outbreak investigation[7]. However, molecular typing methods are costly and labour-intensive and generally are not performed on routine isolates[8].

Finally, this was a point source outbreak in which a suspected vehicle was readily identified with standard investigation methods. Rapid action to identify a food source of a hospital outbreak is an important adjunct to infection control. This is even more important when there is an ongoing source in any institution with a population at risk of serious complications, since secondary transmission poses a serious threat.

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International Notes

OUTBREAKS OF *ESCHERICHIA COLI* O157:H7 INFECTION AND CRYPTOSPORIDIOSIS ASSOCIATED WITH DRINKING UNPASTEURIZED APPLE CIDER — CONNECTICUT AND NEW YORK, OCTOBER 1996

In October 1996, unpasteurized apple cider or juice was associated with three outbreaks of gastrointestinal illness. In the Western United States, an outbreak of *Escherichia coli* O157:H7 infections associated with unpasteurized commercial apple juice caused illness in 66 persons and one death[1]. In addition, one outbreak of apple cider-related *E. coli* O157:H7 infections and another of cider-related *Cryptosporidium parvum* infections occurred in the Northeast. Apple cider is a traditional beverage produced and consumed in the fall. Cider often is manufactured locally at small cider mills where apples are crushed in presses, and the cider frequently is not pasteurized before sale. This report summarizes the clinical and epidemiologic features of the two apple cider-related outbreaks, which suggest that current practices for producing apple cider may not be adequate to prevent microbial contamination.

Connecticut

On 11 October, the Connecticut Department of Public Health (DPH) was notified by staff of the Connecticut site of United States Centers for Disease Control and Prevention (CDC)

Foodborne Diseases Active Surveillance Network, of four reported cases of *E. coli* O157:H7 infection in residents of New Haven County (1995 population: 794,785). An investigation of this cluster was initiated by DPH. A case was defined as onset of diarrhea (i.e. three or more loose stools per day) during 1 to 11 October in a Connecticut resident and laboratory-confirmed infection with *E. coli* O157:H7. Additional case-finding was conducted by notifying all Connecticut clinical laboratories of a possible outbreak of *E. coli* O157:H7 infection and requesting that cases be reported immediately to DPH. As a result of active case-finding, DPH initially identified eight cases with onset during 3 to 11 October.

Of the eight case-patients, the mean age was 25 years (range: 2 to 73 years), and six were female. Case-patients resided in six towns within New Haven County. Manifestations included bloody diarrhea and abdominal pain (eight patients), vomiting (five), and fever (four). The median duration of illness was 7 days (range: 3 to 11 days). Five patients were hospitalized, including one with hemolytic uremic syndrome (HUS) and one with thrombotic thrombocytopenic purpura.

On 17 October, DPH conducted a matched case-control study to determine probable sources for the outbreak. Controls were selected from telephone-exchange lists and were matched to cases by sex, town of residence, and age group. Controls reported no diarrhea during the 20-day period beginning 10 days before illness onset in their matched cases. Case-patients were asked about food consumption during the 7 days preceding illness, and controls were asked about consumption during the same 7 days as their matched cases. Based on interviews with the first eight case-patients and 21 controls, increased risk for illness was associated with drinking fresh apple cider during the 7 days preceding onset of illness [matched odds ratio (OR) = 12.0, 95% confidence interval (CI) = 1.3-111.3, $p < 0.01$]. Specifically, illness was associated with drinking brand A cider (matched OR = undefined, 95% CI = 3.5-∞, $p < 0.01$). No other food item (including ground beef, unpasteurized milk or lettuce) or common event was significantly associated with increased risk of illness. Of the eight patients, seven reported drinking brand A cider during the 7 days preceding illness.

After completion of the case-control study, six additional patients were identified; of these, four had culture-confirmed infection, and two had been hospitalized with HUS but did not have culture-confirmed *E. coli* O157:H7 infection. All six had a history of drinking brand A cider. Ten of the 12 outbreak-associated isolates of *E. coli* O157:H7 were sent to CDC for pulsed-field gel electrophoresis typing; all 10 were determined to be closely related.

On 18 October, DPH and the Connecticut Department of Consumer Protection (DCP) advised Connecticut residents to discard or boil before drinking all brand A cider purchased since the beginning of the cider season in September. DCP coordinated a recall of brand A cider from all retail outlets. Approximately 9,000 gallons of the cider had been distributed throughout Connecticut and three neighboring states. DCP and the regional office of the Food and Drug Administration notified regulatory agency and state health department personnel in the three neighboring states of the recall.

Brand A cider was pressed at a mill in a residential area from apples purchased from multiple sources. Some of the apples used were "drop" apples (i.e. apples picked up from the ground). All apples were brushed and washed in potable municipal water in a flow-through wash system before pressing in a wooden press. Potassium sorbate 0.1% was added as a preservative; the cider was not pasteurized.

New York

During 10 to 15 October, a local hospital laboratory notified the Cortland County Health Department (CCHD) about 10 cases of laboratory-confirmed cryptosporidiosis with recent onset among county residents (1990 population: 48,963). During the same period in 1995, one case of cryptosporidiosis was reported to CCHD. All case-patients had onset of symptoms during 28 September to 10 October and reported drinking apple cider produced at a local cider mill (mill A). CCHD, the New York State Department of Health (NYSDOH), and the New York State Department of Agriculture and Markets (NYS A&M) initiated an investigation of this cluster.

A confirmed case was defined as onset of diarrhea during 28 September to 19 October in a Cortland County resident and laboratory evidence of *Cryptosporidium* in a stool specimen. A suspected case was defined as onset of diarrhea during the outbreak period in a household member of a person with confirmed cryptosporidiosis. CCHD conducted active surveillance for additional cases by contacting area clinicians, hospitals, and laboratories.

A total of 20 confirmed and 11 suspected cases were identified from 19 households. The median age was 27 years (range: 1 to 62 years), and 17 were female. Symptoms included diarrhea (100%), abdominal cramping (55%), vomiting (39%), fever (36%), and bloody diarrhea (10%). The median duration of symptoms was 6 days (range: 1 to 21 days).

CCHD and NYSDOH conducted a matched case-control study to assess probable sources of the outbreak. One neighborhood-matched control-household was contacted for each household with a laboratory-confirmed case. In each control-household, an adult (age ≥ 18 years) member was asked about history of illness, whether anyone in the household had drank apple cider since 28 September, which brand of cider was consumed, and the date it was purchased.

Eighteen case-households were included in the matched case-control study. A history of drinking cider from mill A was reported for at least one member of the 18 households, compared with only one of the 18 control-households (matched OR = undefined, $p < 0.01$). Specifically, cider pressed during 28 to 29 September (i.e. opening weekend) was associated with illness: 15 of 17 case-households in which the purchase date was known compared with none of the control-households reported drinking cider pressed on opening weekend (matched OR = undefined, $p < 0.01$).

Mill A purchased all apples for cider pressing from one New York orchard. Local and state health departments and NYS A&M inspected the cider mill and apple orchard. The owner of the orchard reported that only picked apples were sold to the cider mill, and drop apples were sold for use in processed or pasteurized foods. Before pressing, the mill washed and brushed the apples

using water from a 45-foot drilled well; preservatives were not added to the cider. Although diary livestock were not maintained by the orchard, the cider mill was located across the road from a dairy farm. Testing of remaining cider samples from opening weekend, swabs of equipment surfaces, and water obtained on 21 October from the drilled well did not yield *Cryptosporidium*. However, coliform bacteria were detected in four water samples obtained from the well, and *E. coli* was detected in one sample.

MMWR Editorial Note: Unpasteurized apple cider and juice have been associated with outbreaks of *E. coli* O157:H7 infection, cryptosporidiosis, and salmonellosis[1-4]. Animals are the primary reservoir for the pathogenic organisms associated with these outbreaks. In particular, cattle, deer, and sheep can asymptomatically carry *E. coli* O157:H7 and *Cryptosporidium*, and many animals, including cattle, chickens, and pigs, can asymptomatically carry *Salmonella*. Although the exact mechanisms of contamination for these previous outbreaks were not clearly determined, in three of the outbreaks, manure was suspected to have contaminated the apples.

These previous outbreaks prompted recommendations to reduce the risk for producing contaminated cider, including 1) preventing the introduction of animal manure into orchards, 2) avoiding the use of apples that have fallen to the ground, 3) washing and brushing apples before pressing, 4) using a preservative such as sodium benzoate, and 5) routine pasteurization[3,5]. At least two factors complicate efforts to reduce the risk for transmission of enteric pathogens through unpasteurized apple cider and juice. First, a small number of pathogenic organisms can result in infection — ingestion of as few as 30 *Cryptosporidium*[6] and < 1,000 *E. coli* O157:H7[7] have caused symptomatic infection in humans. Second, although apple cider and juice usually are acidic (pH of 3-4)[5], both *Cryptosporidium* and *E. coli* O157:H7 are acid-tolerant, and both organisms can survive in apple cider for up to 4 weeks[3,5]. The addition of preservatives to apple cider containing *E. coli* O157:H7 does not consistently kill the organism[5], and *Cryptosporidium* oocysts are resistant to most common disinfectants (e.g., bleach, iodine, and sodium hydroxide)[8]. Pasteurization and boiling kill *E. coli* O157:H7 and *Cryptosporidium*, and other methods that might increase the safety of cider are under investigation.

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