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Shigatoxigenic *Escherichia coli* (STEC) infections in Finland during 1998–2002: a population-based surveillance study

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SUMMARY

During 1998–2002, 124 microbiologically confirmed infections caused by shigatoxigenic *Escherichia coli* (STEC) were reported in Finland. Of these, 25 (20%) were associated with recent foreign travel. Temporal, geographical and type distribution of the domestically acquired infections ($n=99$) caused by strains of serogroup O157 ($n=52$) and non-O157 ($n=47$) were analysed further. The median age of the patients was 6·8 years (range 0·2–73·1 years). Of the index cases within 26 families, 71% were <5 years old. Family-related infections accounted for 49%, sporadic infections 39%, and 11% were associated with three clusters. Only strains of serogroup O157 carrying *eae* and stx_2 or its variants caused separate clusters. The incidence of STEC infections was at its highest (0·64/100 000) in 1998. Since 1999 it has declined considerably (0·17/100 000 in 2002). STEC infections occurred in 14 hospital districts, mostly (28%) in the Helsinki region. However, the incidence was highest (10·3) in northwest Finland.

INTRODUCTION

Shiga toxin-producing *Escherichia coli* (STEC), especially serogroup O157, but also numerous other serogroups, have caused severe foodborne outbreaks, sporadic illnesses and deaths worldwide [1]. In Europe, the highest incidence of O157 infections ranging from 1·3 to 2·1/100 000 population per year was found in England and Wales during 1995–1998 [1, 2], and more than 500 cases with 21 deaths occurred in an outbreak in central Scotland in 1997 [3]. In addition, an international outbreak caused by STEC O157 occurred among tourists of five nationalities holidaying in Spain [4], where the prevalence of STEC infections has also risen from 0% in 1992 to 4·4% in 1999 [5]. Moreover, outbreaks caused by strains of several other serogroups, especially of O26, O103, O111 and O145 in continental Europe and Australia, underline the capability of STEC to be widespread [1, 6, 7]. In Scandinavia, the first recognized outbreak of STEC O157 infection affecting 110 subjects occurred in Sweden in 1995 [8], and by 1999 around 520 human cases had been identified [9]. In Norway, during the past 10 years less than 100 STEC cases have been reported, the highest number being 17 cases in 2003 (0·4/100 000 population) [10]. In Finland between 1990 and 1999, 105 STEC O157 infections have been diagnosed, the annual incidence ranging from 0·06 to 1·0/100 000 population [11, 12]. In addition, almost 60 STEC infections caused by non-O157 serogroups have occurred in Finland during 1990–2000 [13], with annual incidence ranging from 0·02 to 0·4.

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The transmission of STEC commonly occurs by the faecal–oral route through zoonotic or environmental spread or by person-to-person contact [14]. Vehicles for STEC infection include under-cooked or cross-contaminated food products, especially cattle meat, vegetables, unpasteurized milk products or beverages and water [3, 14]. However, the sources and vehicles of STEC infections are not always identified, even when the number of cases in a country has been substantial [15]. This is the case in Finland where more than 80% of STEC infections have been of domestic origin [12, 13]. The O157 infections were traced to cattle in only a few cases [16, 17] and non-O157 infections only once [18].

This study was undertaken to determine temporal trends, geographical distribution, and the distribution of known exposure factors for domestically acquired STEC infections in Finland between 1998 and 2002, and to describe the phenotypic and genotypic characteristics of the infecting STEC strains.

MATERIALS AND METHODS

Surveillance system

The Finnish clinical microbiology laboratories are mandated to report their STEC findings to the National Infectious Disease Register (NIDR) maintained at the Department of Infectious Disease Epidemiology, the National Public Health Institute (KTL) and to send the corresponding cultures to the Enteric Bacteria Laboratory (EBL), the Department of Bacterial and Inflammatory Diseases of KTL, for verification of the STEC strains.

Microbiological investigations

The bacterial cultures were examined by PCR for the presence of the stx_1, stx_2 and *eae* genes [11, 13]. The specific colonies were isolated and the purified strains possessing the *stx* gene(s) were identified biochemically with API 20E (bioMérieux SA, Marcy l'Etoile, France). The STEC strains were further assayed for their O:H serotype, and phage type (PT) [12, 13]. In addition, possession of the *stx* variants was determined [19]. The strains were also genotyped by nationally standardized pulsed-field gel electrophoresis (PFGE) using *Xba*I restriction of their DNA [20]. One band difference was marked as significant in the comparison of PFGE profiles. The subtypes of the isolates were named according to their phenotypic (serotype [O:H] and PT) and genotypic (*stx*, *eae* and PFGE) results [12, 19]; the final subtype being for example O157:H7:PT2:stx_2:stx_{2c}:*eae*:1.1.

Patients and data collection

All microbiologically confirmed STEC infections detected between 1998 and 2002 were included in the study. The information of residence, age, gender and recent foreign travel of all subjects was collected on a standard form accompanying the isolate or the data received from the hospital by telephone. Patients were interviewed comprehensively, by telephone, by a trained member of staff to determine the consumption of cooked, undercooked or unpasteurized food items, contact with cattle or other animals, contact with persons with diarrhoea or exposure to the environment.

Definitions

Domestic case. A STEC case with no history of foreign travel during the 2 weeks prior to the finding of STEC.

Family-related case. A STEC case with a link to another case in the same family.

Cluster (*denoted C1–C3 in the text*). Two or more epidemiologically linked STEC cases caused by strains of identical subtype and not limited to one family.

Index case. A first detected STEC case in a cluster or in a family.

Non-sporadic case. A STEC case in a cluster or in a family.

Sporadic case. A STEC case with no link to any other STEC cases.

Statistical methods

Epi-Info 6 software [21] was used for statistical analyses. Fisher's exact test was used to compare proportions and to test the statistical significance ($P < 0{\cdot}05$).

RESULTS

STEC cases

Between 1998 and 2002, 124 microbiologically confirmed cases of STEC infection were reported in Finland. Of these, 25 cases (20%) were associated with recent foreign travel. These cases were excluded

Table 1. *Age and gender distribution of patients with microbiologically confirmed STEC infection*

Category	*n*	Age (years)		Age <5 years	Gender (%)	
		Median	Range	No. of cases (%)	Males	Females
All cases	99	6·8	0·2–73·1	38 (38)	43 (43)	56 (57)
Sporadic cases	39	8·9	0·6–73·1	11 (28)	19 (49)	20 (51)
Non-sporadic cases	60	5·0	0·2–50·8	27 (45)	24 (40)	36 (60)
All cluster-related cases	11	15·6	3·0–28·2	3 (27)	5 (45)	6 (55)
Index cases	3	15·6	3·0–19·0	1 (33)	2 (67)	1 (33)
Other cases	8	16·5	1·9–28·2	2 (25)	3 (38)	5 (62)
All family-related cases	49*	5·0	0·2–50·8	24 (49)	19 (39)	30 (61)
Index cases	17	2·4	0·9–50·8	12 (71)	4 (24)	13 (76)
Other cases	32	6·8	0·2–43·0	12 (38)	15 (47)	17 (53)

* In 26 families.

Table 2. *Distribution of STEC O157 and non-O157 strains and strains with* stx *and* eae *genes among 99 microbiologically confirmed cases* (*% in parentheses*)

Category of cases	*n*	Serogroup of the strains		Virulence gene(s) of the strains		
		O157	Non-O157	stx_1	stx_2, stx_{2c} alone or with other *stx*	*eae*
All cases	99	52 (53)	47 (47)*	21 (21)	78 (79)†	85 (86)
Sporadic cases	39	20 (51)	19 (49)	8 (21)	31 (79)	33 (85)
Non-sporadic cases	60	32 (53)	28 (47)	13 (22)	47 (78)	52 (87)
All cluster-related cases	11	11 (100)	0 (0)	0 (0)	11 (100)	11 (100)
Index cases	3	3 (100)	0 (0)	0 (0)	3 (100)	3 (100)
Other cases	8	8 (100)	0 (0)	0 (0)	8 (100)	8 (100)
All family-related cases	49	21 (43)‡	28 (57)§	13 (27)	36 (73)	41 (84)
Index cases	17	7 (41)	10 (59)	6 (35)	11 (65)	15 (88)
Other cases	32	14 (44)	18 (56)	7 (22)	25 (78)	26 (81)

* O103:H2 (18 strains), O145:H28/H$^-$ (6 strains), 12 other non-O157 serotypes (23 strains).
† stx_2 or stx_{2c} alone (37 strains), stx_2:stx_{2c} (23 strains), stx_1:stx_2 (6 strains), seven other *stx* types (12 strains) according to Lin et al. [45] and Bastian et al. [46].
‡ In 11 families.
§ In 15 families.

from further analysis, leaving 99 domestically acquired cases of STEC infection: 52 were caused by strains of O157 and 47 of serogroup non-O157. Sixty (61%) of the cases were non-sporadic, including 49 family-related cases in 26 families and 11 cases in clusters C1–C3. The remaining 39 STEC infections were sporadic.

The age of the 99 patients ranged from 0·2 to 73·1 years (median 6·8 years) (Table 1). The median age was lowest (2·4 years) among family-related index cases. Of all patients 38%, but of the family-related index cases, 71% were <5 years old. Only five patients (5%) were aged ⩾45 years. The proportion of females was highest (76%) among family-related index cases but among all cases STEC infection was nearly as common in both sexes. The age distribution was similar among patients with an O157 or non-O157 infection (data not shown).

STEC findings

The distribution of STEC infections caused by strains of serogroup O157 and non-O157 was almost even in each category studied (Table 2). The only exception was among the cluster-related cases where all 11 infections were caused by strains of serogroup O157. The most common virulence characteristic in 99 strains was stx_2, stx_{2c} alone or with other *stx* (79%). The stx_1 gene alone was present in only 21% of the strains. There was no difference in the distribution of

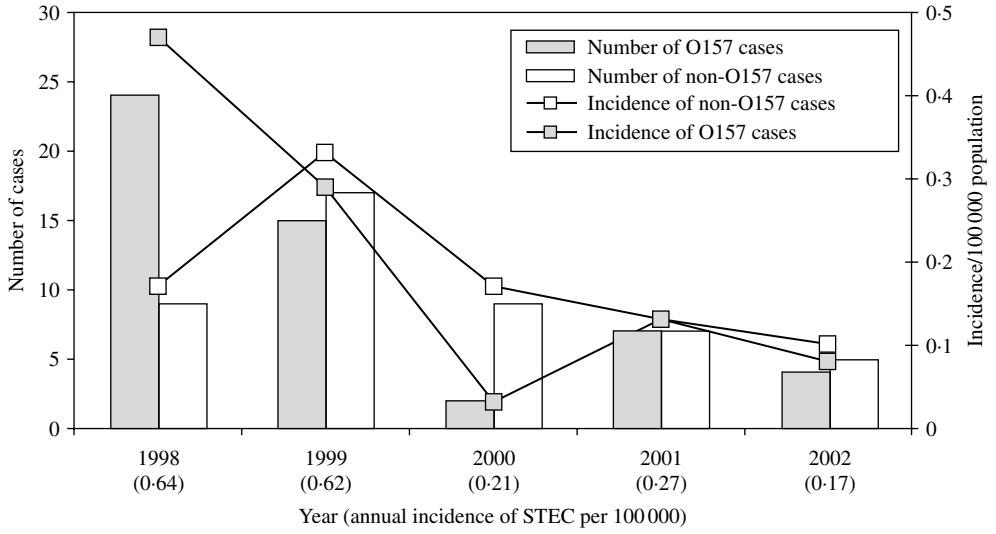

Fig. 1. Annual occurrence of 99 domestic STEC O157 ($n=52$) and non-O157 ($n=47$) infections in Finland during 1998–2002.

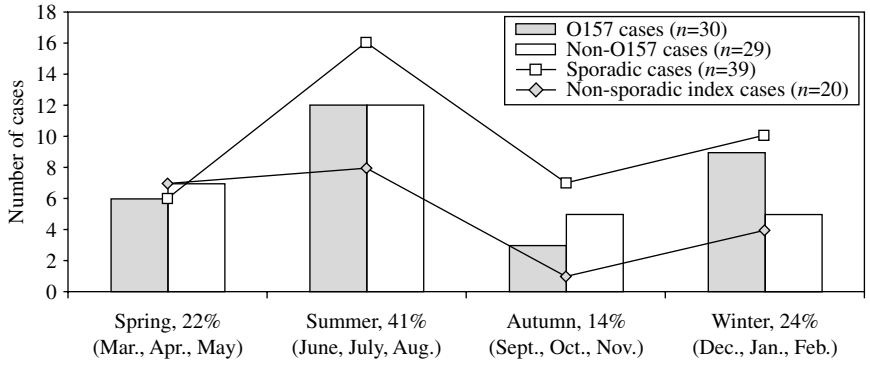

Fig. 2. Seasonal occurrence of 59 domestic STEC O157 ($n=30$) and non-O157 ($n=29$) index ($n=20$) and sporadic ($n=39$) infections in Finland during 1998–2002.

the strains carrying these genes (stx_1 or other) between sporadic and non-sporadic infections. However, strains carrying stx_1 only caused family-related infections (27%) but not cluster-related infections (0%; Table 2). Correspondingly, 86% of the strains carried *eae*, and the distribution of the *eae*-positive strains was equal between sporadic (85%) and non-sporadic (87%) infections. However, all strains associated with clusters were positive for *eae*. The most common (11 isolates) single subtype was O157:H7:PT2:stx_2:stx_{2c}:*eae*:1.1. Also in C1, strains of this subtype caused three out of four infections. The remaining strain (subtype O157:H$^-$:PT88:stx_2:*eae*:1.13) was isolated from a child whose mother was infected with a strain of the former C1 type. In C2, a two-band difference was observed in the PFGE patterns among the isolates [O157:H7:PT4:stx_2:*eae*:1.57 (3 strains), O157:H7:PT4:stx_2:*eae*:1.58 (1 strain)]. In C3, an identical strain of subtype O157:H7:PT14:$stx_{1,2}$:*eae*:1.67 caused all infections ($n=3$).

Temporal and geographical distribution

The incidence of domestic STEC infections declined from 0·64 in 1998 to 0·17 in 2002 per 100 000 population (Fig. 1). The most prominent decline was observed between 1999 (0·62) to 2000 (0·21). Only in 1998 was the incidence of O157 infections higher (0·47) than that of non-O157 (0·17).

Domestic sporadic and index STEC infections were more prevalent during the summer months (June, July and August) than in other seasons (Fig. 2). However, the seasonal variation was similar among the strains of O157 and non-O157 that were causing these infections.

STEC infections occurred in 14 (67%) out of 21 hospital districts, O157 infections occurring in 13 and

Table 3. *Exposures of sporadic cases and cluster- and family-related index patients with microbiologically confirmed STEC infection among 53 patients during 1998–2002*

Exposure	Number of patients exposed/responders (%) All cases ($n=53$)
Food	
Minced meat products*	36/42 (86)
Raw minced meat	3/37 (8)
Unpasteurized milk	9/50 (18)
Unpasteurized cheese	4/48 (8)
Untreated water	1/32 (3)
Environmental factors	
Animal contact†	20/50 (40)
Visiting cattle farm	12/48 (25)
Living on cattle farm	10/48 (21)
Swimming	4/34 (12)

* Hamburgers, meatballs, minced meat patties or dishes made of minced meat (kebab, pizza, barbecue, pasta).
† Includes rodent, rabbit, cat, dog, horse or simultaneous contact with different animal species: dog and horse, dog and sheep.

non-O157 infections in nine hospital districts. Of all 99 cases, 28% occurred in the Helsinki region but the overall incidence was highest (10·3) in northwest Finland (hospital district of central Ostrobothnia). The highest incidence of the O157 infections was observed in southeast Finland (Kymenlaakso, 4·9), where also two (C2 and C3) of the three O157 clusters occurred, whereas the highest incidence of non-O157 infections was observed in central Ostrobothnia (7·7). The most common O157:H7:PT2:stx_2:stx_{2c}:*eae*:1.1 subtype was also most widely distributed occurring in five of the 21 hospital districts.

Potential sources of STEC infections

Of the 99 patients, 68 were interviewed in order to collect data on exposures to previously known risk factors prior to their STEC infection; 53 represented sporadic or index cases (26 O157 cases; 27 non-O157 cases). Among these patients, there seemed to be no difference in the distribution of the risk factors between O157 and non-O157 infection. The majority (47 of the 53 patients) reported exposure to at least one of the recognized STEC risk factors. Contact with cattle or other animals was reported by 42 patients (Table 3), and of these 33 (79%) were <10 years old (data not shown). Of all 53 patients, 86% had consumed minced meat products (three had eaten raw minced meat), and 18% unpasteurized milk. It was strongly suspected that the C1 cluster was due to person-to-person spread, and that the C2 cluster was associated with consuming hamburgers. Further, a foodborne source was implicated as a vehicle for the C3 cluster.

DISCUSSION

In our study on all domestically acquired cases of STEC infections in Finland between 1998 and 2002, we observed a decline concordant with national measures aimed at improving conditions potentially contaminating beef on its way from farm to fork.

Between 1998 and 2002, 99 domestically acquired, microbiologically confirmed STEC infections were identified by national surveillance in Finland. Almost half (49%) of these infections were family-associated infections and small children, in particular, seemed to be susceptible to the infection. This is in accordance with other studies where STEC infections were common among family members [22, 23]. STEC infection has typically been asymptomatic or mild in adults [19, 23], potentially posing a risk for a secondary infection by person-to-person transmission or by easy cross-contamination of food items from asymptomatic older family members to younger ones. This finding may explain the high proportion of STEC infections within families as shown in this study. Another explanation might be that small children are more likely to receive primary care than older children or adults.

Among all strains studied, the most common subtype, O157:H7:PT2:stx_2:stx_{2c}:*eae*:1.1, was found in patients living in five of the 21 hospital districts. Strains of this subtype were previously reported to be common among all human O157 isolates in Finland [12], and were also found in dairy farms [17]. This subtype was implicated in an outbreak in 1997 [11, 24] that preceded cluster C1, caused by an indistinguishable strain, by only a few months. However, the geographical location and the sources (swimming *vs.* person-to-person contact) of these two outbreaks were different. This might indicate persistency of a domestic O157 strain of this particular subtype. Instead, C2 was linked with consuming hamburgers. The subtypes of these strains were clearly distinguishable from the subtype of C1. This might be an indication for either another domestic reservoir of the O157 strains, or for some imported food item contaminated with this strain. According to the literature,

hamburgers have caused several STEC O157 outbreaks especially in the United Kingdom and North America, unlike continental Europe [1, 23]. The C3 cluster caused by the strain of subtype O157:H7:PT14:$stx_{1,2}$:*eae*:1.67 was also foodborne. This outbreak involved *E. coli* O157 strains transmitted by kebab meat from The Netherlands [25].

The proportion (47%) of non-O157 infections in our study was high, as also previously reported [13]. The high prevalence of STEC non-O157 findings in Finland may be due to screening for not only sorbitol-negative O157 strains, but also Stx toxin in the stool cultures in several hospital laboratories which enables the detection of all STEC bacteria. Estimates from the United States and Australia have suggested that the total number of the non-O157 infections is 20–50% of that of O157:H7 infections [26, 27]. Similarly to Finland, a large proportion of STEC infections in The Netherlands and Denmark have been caused by strains of non-O157 serotypes [26]. Also, in Sweden, sporadic STEC non-O157 infections were diagnosed as frequently as those of O157 during 1997–1998 [28], and in Germany about two-thirds of all reported STEC strains fell into non-O157 serogroups [7, 29]. In Spain, of the 70 STEC infections detected, 63% were caused by strains of non-O157 serogroups [5].

The incidence of all STEC infections was high in northwest Finland, potentially explained by the high density of cattle farms in this area. A statistically significant association between cattle density and human infections of STEC O157 has been reported from Sweden [9] and Canada [30]. However, little has been published on the geographical relationship of cattle densities or the prevalence of non-O157 strains in cattle and STEC infection in man [31]. However, the prevalence of STEC non-O157-positive cattle on farms in Germany has varied from $\sim$30% to over 80% [32]. Similarly in Finland, the prevalence of STEC non-O157 strains in cattle has been very high at slaughter; $\sim$30%, and in calves $>$90% [33]. Of the non-O157 serotypes detected from Finnish cattle, eight have also occurred among Finnish human isolates [33]. In addition, an O145 isolate from cattle was phenotypically, genotypically and epidemiologically linked recently to a human O145 STEC infection [18], indicating that cattle represent a risk factor for STEC non-O157 infections. Our finding of the increased incidence of O157 infections in southeast Finland, however, is difficult to explain. One speculative reason for this increase might be the busy cross-border traffic of people and food items.

In our study, the STEC infections caused by either O157 or non-O157 strains seemed to be more common in summer (June–August) than in other seasons. Other studies have reported STEC O157 infections to be more prevalent in summer or early autumn [2, 34, 35], although outbreaks have been documented during other seasons as well [1, 3, 36]. Among cattle, but not in hides, the shedding of STEC O157 and non-O157 bacteria in faeces also peaks in summer [37] but shedding of STEC O157 may continue during colder months [38]. However, contradictory results have been reported on the effect of a forage- or grain-based diet on shedding of STEC in cattle [39].

During the study period, the annual incidence of STEC infections declined between 1999 and 2000. In the same period, nationwide hygienic counselling for the prevention of STEC in cattle farms, abattoirs and during transportation of cattle was enhanced in Finland [40]. As cattle are considered a major reservoir of STEC [14, 39], the decline in the incidence of STEC infections in Finland after 1999 is at least partly due to these orders resulting in overall improvement in the hygiene in the whole 'from farm to fork' chain. Interestingly, in Germany between 1997 and 2000, the prevalence of STEC O157 and O103 cases was highest (33 and 16% respectively) in 1999 but declined by half during 2000 [41]. This decline might also be due to enhanced hygienic control at the farm level, which was laid down by national legislation and directives of the European Union [42]. Compared to the situation in Finland, the incidence of STEC O157 infections per 100 000 has been higher in most countries, for example in Wales [43], the United States [44], Sweden [26] and Norway [10].

According to the in-depth interviews of the subjects, most had consumed minced meat. Unfortunately, meat samples were not available for studies to determine the presence of STEC bacteria. The range of exposure factors inquired about was limited, and did not include the use of raw vegetables or salads. The distribution of specific exposures from the patient interviews was not unexpected. In the absence of a comparison group, no conclusions could be drawn on the origin of the infection or vehicle of transmission.

The majority of the strains studied possessed the *stx* genes belonging to the stx_2 group. The strains harbouring these virulence characteristics formed separate clusters whereas the strains possessing stx_1 alone did not. This suggests the higher potential for transmission in society, outside families, of the strains possessing the particular genes, such as stx_2 alone or

with other *stx*. In addition, as STEC bacteria are considered to have a very low infectious dose – even less than 100 cells [14], active hygienic counselling of consumers and food producers or handlers, as well as continuous laboratory-based surveillance of STEC findings should be emphasized in the prevention of these infections.

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