Epidemiology of infection due to *Escherichia coli* O157: a 3-year prospective study

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SUMMARY

A 3-year study of *Escherichia coli* infections in Grampian Region was conducted to ascertain the incidence, document clinical sequelae and identify at-risk groups. Approximately 30000 stools from patients with acute diarrhoea were screened for *E. coli* O157, and an epidemiological questionnaire filled in for each patient whose stool was positive. Eighty-three patients were studied. The annual incidence was 6 per 100000. Proportionately more infections occurred in people involved in agriculture. Evidence was seen of case-to-case transmission, and contamination of a water supply. Eight cases developed haemolytic uraemic syndrome (HUS). There were 2 deaths due to HUS and 2 due to haemorrhagic colitis (HC). Symptomatic *E. coli* infection is relatively common in the Grampian Region, more common in the agricultural community, and is the main cause of HUS in this Region.

INTRODUCTION

Escherichia coli O157 has emerged as a significant cause of diarrhoeal illness and haemorrhagic colitis (HC) over the last decade [1–4]. A proportion of people infected with *E. coli* O157 develop haemolytic uraemic syndrome (HUS) [5, 6] and there is evidence to suggest that this and HC are due in part to the action of the ribosome toxins VT1 and VT2 [7]. VT1 or a very similar toxin is found in *Shigella* spp., and both toxins are found in some other strains of *E. coli* [7]. It appears that these other verocytotoxigenic strains can also cause HC and HUS [5, 8, 9].

Estimates of true incidence and comparisons of *E. coli* O157 infection between different populations are hampered in two ways. First, isolation techniques and protocols continue to evolve and vary between studies. Secondly, success in isolating the organism has been shown to be higher when samples are obtained early in the course of an infection [10]. For these reasons, currently available data are probably an underestimate of the true incidence of the infection, although in an earlier study, Grampian had a relatively high incidence of *E. coli* O157 infection and HUS [11].

Since 1987 a standard procedure has been used to test diarrhoeal stools sent to the Regional Laboratory, City Hospital, Aberdeen. In an attempt to understand better the nature of *E. coli* O157 infection in this community, a continuing clinical and epidemiological study based on laboratory isolations of *E. coli* O157 was also begun at this time. This descriptive paper presents the main findings after 3 years and looks at future lines of investigation. It updates a previous report from Grampian and includes data previously published in that report [11]. For the purpose of this study, a case was defined as any person identified during the course of this study whose stool culture was positive for *E. coli* O157.

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MATERIALS AND METHODS

Between September 1987 and December 1988 only diarrhoeal stools with blood, or stools from patients with a history of bloody diarrhoea were examined for *E. coli* O157, but from January 1989, all specimens of diarrhoeal stool sent to the Regional Laboratory were examined for *E. coli* O157. Stools were inoculated onto sorbitol MacConkey agar and incubated overnight at 37 °C, as described previously [11]. Up to five non-sorbitol fermenting colonies were then serotyped with *E. coli* O157 antiserum (Oxoid). Strains identified by serotyping were characterized using API 20E strips (API, Montalieu, Vercieu, France).

Water or food samples were cultured by the same method after filtration or homogenization as appropriate. Identified strains were sent to the Laboratory of Enteric Pathogens, Central Public Health Laboratory, Colindale, London for confirmation of verocytotoxin production. Salmonella, shigella, aeromas, campylobacter, *Clostridium difficile*, giardia, cryptosporidium, adenovirus and rotavirus were also sought routinely. The Regional Laboratory provided the public health bacteriology service for Grampian and received all specimens from general practice during the period of this study. Patients whose stool yielded *E. coli* O157 were contracted by either a Community Infection Nurse, Public Health Medicine Medical Officer or an Environmental Health Officer. Household contacts were identified and stool specimens obtained. An epidemiological questionnaire was completed for each case, covering demographic and clinical features and a food history. Where two or more cases appeared to be related these were investigated further by food and water sampling, and by extended contact tracing. The proportion of the population involved in agriculture was obtained from estimates in the 1991 mid-year report of the Registrar General for Scotland, and included those working in agriculture as employer, employee or self-employed and their families.

RESULTS

Ninety-two cases of *E. coli* O157 infection were identified over the 3-year study period from January 1988 to December 1990, and a further three cases over the period September 1987 to December 1987. For the purposes of this study, these three cases have been combined with the 1988-90 data. Eighty-three completed questionnaires were returned.

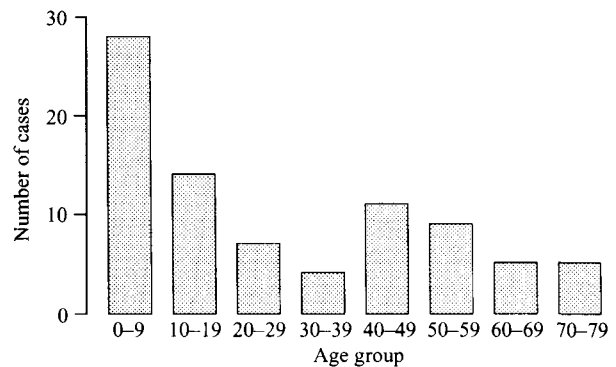Over the period January 1988 to December 1990

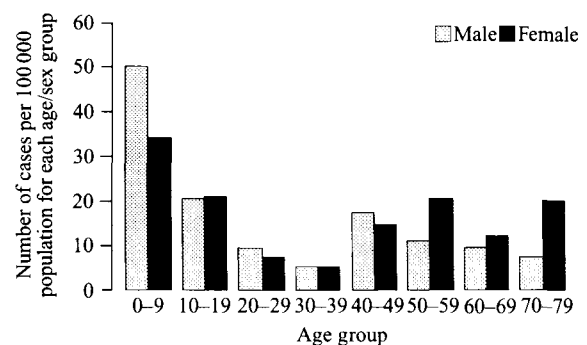**Fig. 1.** Age distribution of *E. coli* O157 infection in Grampian, 1988-90.

Fig. 2. Distribution of *E. coli* O157 infection according to age and sex in Grampian, 1988-90.
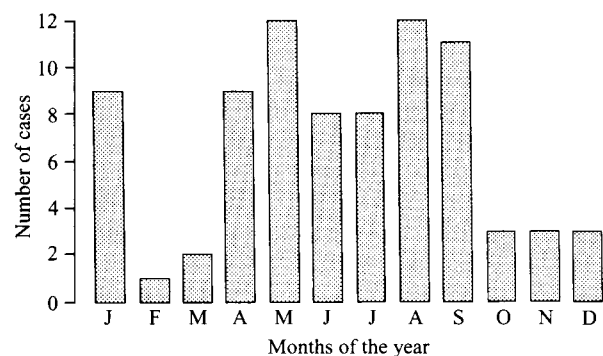

Fig. 3. Monthly incidence of *E. coli* O157 infection in Grampian, 1988-90.
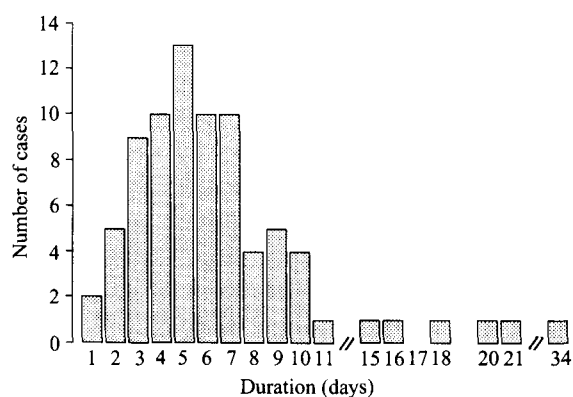
approximately 45000 stool specimens were submitted to the laboratory from new cases of diarrhoea, and of these, approximately 30000 were examined for *E. coli* O157. The mean age of the cases was 27·5 years, with a median of 18 years, and a modal age of 1 year (six cases). There was a much higher frequency in the under-10-year-olds (Fig. 1). Sex ratios were balanced overall, but there was a higher proportion of males in the under-10s (Fig. 2). A seasonal variation was present, with 61 out of 83 cases occurring between April and September (Fig. 3).

Table 1. *Relationship of* E. coli *O157 cases to farming in Grampian*

	Number	Percent	E. coli O157 Cases	Percent
Farming persons	18650	3·8	11	13
Non-farming persons	477550	96·2	72	87
Total persons	496220	100	83	100

Table 2. *Clinical features of all cases of* E. coli *O157 in Grampian 1988–90*

	Number	Percent
Diarrhoea	81	97
Bloody diarrhoea	61	74
Nausea	60	72
Vomiting	46	55
Abdominal pain	35	42
Dehydration	32	39
Fever	33	40
URTI	10	12
Number admitted to hospital	30	36
Total number of cases	83	100

Table 3. *Further features of hospital cases of* E. coli *O157 in Grampian 1988–90 (n = 30)*

	Total	HUS	Non-HUS
Anaemia	10	8	2
Thrombocytopenia	8	8	0
Uraemia	12	8	4
Raised creatinine	8	8	0
Hyponatraemia	4	4	0
Leucocytosis	22	7	15
Leucopaenia	4	3	1
Prior antibiotic therapy	15	5	10
Dialysis	4	4	0
Death	4	3	1
Surgery other than dialysis	5	1	4

Fig. 4. *E. coli* O157 infection in Grampian 1988–90: duration of diarrhoea in days.

Eleven out of 83 cases were people directly involved in agriculture: either farmers, farm-workers, livestock handlers, or their children (Table 1). Twenty out of the 83 cases were found by contact tracing: 8 of these were asymptomatic and 12 had symptoms of gastroenteritis, including 2 with bloody diarrhoea. Of the 63 primary cases 59 had bloody diarrhoea (Table 2). The mean duration of illness was 6·5 days and the mode 5 days, with a range of 1–34 days (Fig. 4).

Using the dates of notification it was concluded that there were five instances where two members of a family were infected simultaneously, suggesting a common source. In one of these groups two other close contacts (fiancée, grandfather) were notified a fortnight later suggesting person-to-person spread. Thus the first members of the family to become symptomatic might have been exposed to an environmental source of *E. coli* O157, which was subsequently transmitted to other family members by person to person spread. In a group of four primary cases simultaneously occurring in the town of Tarves a contaminated water supply was identified [12].

E. coli O157 was not isolated from any of the samples of foodstuffs or water examined (data not presented).

Thirty cases were admitted to hospital. Of these, eight developed HUS as defined by Karmali, with microangiopathic haemolytic anaemia, thrombocytopenia and uraemia (Table 3). Four were dialysed following the development of HUS. Three of the HUS cases died, one of whom had been dialysed. One non-HUS case died of complications of HC. Details of cases who died or underwent surgical procedures other than dialysis are given below.

Case 1: A 46-year-old man presented with a 1-day history of vomiting, abdominal pain and severe bloody diarrhoea. An initial clinical diagnosis of campylobacter gastroenteritis was made. His condition deteriorated over the next 24 h with the development of abdominal distension and rebound tenderness. Sigmoidoscopy showed oedema, haemorrhage and ulceration. A barium enema showed pancolitis with ulceration. Emergency subtotal colectomy was performed. Histological features were similar to pseudomembranous colitis. He made a full recovery.

Table 4. *Stool isolates*

Year	1988	1989	1990
E. coli O157	18*	20	57
Yersinia	ND†	ND†	43
Salmonella spp	336	448	476
Campylobacter spp	548	614	700
Rotavirus	408	554	314
Adenovirus	ND†	288	224
Shigella spp	18	14	14
Cryptosporidium sp	100	190	117
Giardia	27	22	43
Aeromonas	42	18	129

* Includes cases from September–December 1987.
† ND, no data.

Case 2: A 48-year-old man, with a past medical history of rheumatoid arthritis, presented with a 2-day history of diarrhoea, rectal bleeding, vomiting and abdominal pain. Because of right iliac fossa tenderness a laparotomy was performed, but only oedematous bowel was found. Ten days after admission he developed HUS, and proceeded to have convulsions, pseudomonas pneumonia, a brainstem infarction, and multi-organ failure which resulted in death. No cause other than *E. coli* O157 was found for this sequence of events.

Case 3: A 73-year-old woman presented with a 7-day history of diarrhoea, vomiting and abdominal pain, which she attributed to eating a sausage at a Burn's Supper. She developed HUS and subsequently convulsions, shock and death, 10 days after admission.

Case 4: A 62-year-old woman presented with a 3-day history of bloody diarrhoea and vomiting. In hospital she developed renal failure with a massive leucocytosis, and despite dialysis, died following cardiac arrest 1 week after admission.

Case 5: A 5-year-old boy presented with abdominal pain and bloody diarrhoea. Intussusception was suspected, but X-ray was not diagnostic. At laparotomy, his appendix was removed which showed histological features similar to pseudomembranous colitis. A colonic biopsy, taken at the same time, was reported as showing acute haemorrhagic colitis of infectious origin. He made a complete recovery.

Case 6: A 57-year-old woman presented with ascites and bloody fluid per rectum. Sigmoidoscopy showed only oedematous mucosa and rectal biopsy showed mild non-specific proctitis. At laparotomy she was found to have disseminated ovarian carcinoma. *E. coli* O157 was cultured incidentally from stool. She died of carcinomatosis 3 weeks after admission.

Cases 1 and 4 have been reported previously [13]. Pathogens other than *E. coli* O157 which were sought routinely over the study period are reported in Table 4.

DISCUSSION

In this study we found a higher incidence of *E. coli* O157 infection in Grampian than in the rest of Scotland. The isolation rate over the study period rose from 4·2 cases per 100000 in 1988 to 9·1 per 100000 in 1990. Figures for Scotland, while much lower, showed a similar increase, rising from 0·8 per 100000 in 1988 to 3·2 in 1990 [14], based on Registrar General for Scotland estimated mid-year population figures in 1991. This higher incidence in Grampian may be partly artefactual, because even as late as 1990, most Scottish laboratories were only culturing stool for *E. coli* O157 in selected cases (J Coia, C Sharp, personal communication).

Nevertheless, the higher incidence in Grampian is probably real. Our results show that in this study, where *E. coli* O157 was sought routinely – irrespective of the presence of blood in the stool – over 75% of cases did in fact have bloody diarrhoea. This implies that had we cultured for *E. coli* O157 only in selected cases we would have missed only 25% of the cases actually identified. Contact tracing would further improve the isolation rate of a laboratory selectively culturing bloody diarrhoeal stool for *E. coli* O157. A lower referral of bloody diarrhoeal stool from general practice for culture and a greater reluctance of patients to present to their general practitioners could have a bearing in some areas, but no data are available. Non-O157 verocytotoxigenic *E. coli*, although not routinely sought in Grampian, do appear to be present (H Mackenzie, personal communication), but the overwhelming majority of *E. coli* O157 isolates in this study were verocytotoxin positive (F Thomson-Carter, personal communication). If the incidence in Grampian is truly higher, it may be related to the high proportion engaged in agriculture. Studies in Canada, Sheffield and elsewhere have shown VTEC in cattle [14, 16–18]. In this study, 11 out of the 83 cases (13%) had involvement in agriculture, a finding consistent with an animal reservoir. By comparison, the percentage of the general population of the region involved in agriculture is 3·8%. A seasonal variation has been observed in the few other long-term studies of sporadic VTEC infections [4]. This variation is less marked than in Canada which has a greater seasonal

temperature difference [4]. Seasonal incidence was matched with monthly average temperature and rainfall statistics. Using these crude parameters, the expected correlation between temperature and incidence was seen, but the data did not show a connection with rainfall (data not presented) although we still believe contaminated water supplies, as in the Tarves outbreak of 1990, are likely to be responsible for some infections.

Geographical analysis shows that town dwellers are certainly at risk as well as inhabitants of rural areas, perhaps through visits to farms by children. Food outbreaks have been documented in Sheffield [15] although we did not confirm any. Isolation from food is technically difficult although improved methods have been described [18].

Clinical features are comparable with other studies. Fever was present in 30 out of 83 cases which is more frequent than in some studies [1, 2]. Upper respiratory tract infection occurred in only 10 cases suggesting that the latter is not a particularly common precursor of *E. coli* O157 gastroenteritis (Table 2). However three of the HUS cases were thought to have had respiratory infections so the possibility of an association with worse outcome remains [1, 5]. Contact tracing studies suggest a low rate of asymptomatic carriage in this community in accordance with previous reports [4]. The possibility of cross infection as a mode of spread is supported by our data.

In conclusion, verocytotoxin-producing *E. coli* O157 is a gastrointestinal pathogen causing serious sporadic endemic disease in Grampian region. Up to 10% of identified cases go on to develop HUS with significant mortality, and there is also a significant morbidity and mortality associated with HC, which is present in 75% of identified cases. Agricultural and water sources of infection are suggested by this study. Case-to-case transmission appeared to be the mode of spread within families, where members developed infection up to 2 weeks after the index case. Further research is needed to define the rate of asymptomatic carriage and person-to-person spread. Identification of *E. coli* O157 or verocytotoxin in food, water and animal reservoirs should be pursued.

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