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THE CHANGING EPIDEMIOLOGY OF VEROCYTOTOXIGENIC *ESCHERICHIA COLI* IN THE UK*

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The clinical significance of verocytotoxigenic *E.coli* (VTEC) was unknown until 1982 when Riley in the USA described outbreaks of haemorrhagic colitis (HC) due to *E.coli* O157, associated with fast-food restaurants,[1] although in 1977 the production by certain strains of *E. coli* of a toxin with a cytotoxic effect on cultured Vero cells had been reported.[2] Subsequently, an association was shown between haemolytic-uraemic syndrome (HUS) and faecal verocytotoxin, and the presence of VTEC in stools.[3] In the wake of this report considerable interest in these organisms developed, particularly in North America. A number of outbreaks were described in association with ground-beef products, often within the setting of fast-food restaurants or domestic barbecues, and frequently with evidence of inadequate cooking.[4] Most of these related to a single serotype, *E.coli* O157:H7. Initially regarded as relatively rare, it soon became apparent that it was otherwise. By the late 1980s the picture prevailed that the majority of infections due to *E.coli* O157:H7, were mainly associated with consumption of ground-beef products and that outbreaks were predominantly in the 'fast food' restaurant or barbecue setting.

It is apparent with hindsight that this is probably somewhat over-simplistic, and it is inadequate to describe the epidemiology as we understand it now. I intend to concentrate on how the situation has developed in the UK, with particular reference to Scotland.

It is first worth asking why the O157:H7 serotype appears so pre-eminent among VTEC organisms. It is now recognised that over 100 serotypes of *E.coli* can produce these verocytotoxins, which are thought to be responsible for the more severe manifestations of infection, particularly the development of HUS.[5] However, not all VTECs produce human disease. This may be because they lack adhesins and other colonisation factors which would allow them to establish infection in the human gut. Nevertheless, an increasing number of non-O157 VTECs have been associated with human illness, similar in nature to that produced by O157, and a number of outbreaks have been documented. It would appear that O111, O26 and O103 are amongst the commonest serotypes implicated. There persists little information on the true rates of infection with non-O157 VTEC. To understand why, we have to consider the microbiology of these organisms.

MICROBIOLOGY OF O157

Unlike the majority of *E.coli* isolates from our faecal flora, most O157 strains do not ferment the sugar D-sorbitol. This led to the development of sorbitol MacConkey agar (SMAC) as a simple, rapid, screening medium, on which the majority of organisms of the faecal flora yield pink colonies, whilst the O157 colonies are colourless.[6] However, as yet, there is no similar simple cheap and rapid screening test for non-O157 VTEC

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which can be used in the routine laboratory. To detect these one either has to look for free verotoxin using a variety of biological or immunological assays, or with DNA probes or PCR for toxin genes. Although some commercial kits are available, these are not in widespread use.

There are a number of techniques which further enhance sensitivity of detection of O157 organisms, such as broth enrichment, enzyme immunoassay for O157 antigen, and the Immunomagnetic Separation technique (IMS), which can enhance sensitivity between 10- and 100-fold.[7] There are four consequences of the current situation:

- The true incidence of non-O157 VTEC infection remains unknown.
- The relative importance of O157 amongst VTEC organisms as a whole may be overestimated.
- The significance of the detection of VT alone remains uncertain.
- Data which are available may be difficult to compare because of the different methods used for detection.

Table 1 compares the incidence of *E.coli* O157 and non-O157 VTEC detected in faecal samples from various studies and shows the great variation, both in the absolute and relative percentage of positive samples. Currently the realistic option remains to look routinely only for O157 VTEC.

TABLE 1
A comparison of *E.coli* O157 and non-O157 VTEC detection rates in faecal samples.

Year	Country	Illness/patients	Methods	Sample Nos	O157 +ve	NON-O157 +ve
1984-6	Canada	Diarrhoea/All	SMAC/Cytotoxin	5415	2.4%	0.5%
1990	Canada	Diarrhoea/All	SMAC/Cytotoxin PCR & Probe	3577	0.6%	0.6%
1989-90	Canada	Diarrhoea/All	SMAC/Cytotoxin	9449	0.6%	<0.1%
1990-93	Belgium	Diarrhoea/All	PCR	10241	0.1%	0.6%
1985-88	England	HUS/Children	SMAC/Probe	196	19.4%	7.6%
1991-93	England	Diarrhoea/All	VT ELISA	439	2.9%	0.9%
1990	Switzerland	Diarrhoea/All	VT Probe	405	0%	1.9%
1995	Germany	HUS/Children	SMAC/Cytotoxin PCR & Probe	30	60%	17%

Adapted from Law.[5]

INCIDENCE IN THE UK

In England and Wales, throughout the latter part of the 1980s and during the 1990s, there has been a continuing increase in the number of laboratory-confirmed cases of VTEC O157, with a reported rate of infection of 1.29 per 100,000 population in 1996. Between 1992 and 1996, 37 outbreaks of VTEC O157 infection involved 381 people of whom 31% required hospitalisation, 15% developed HUS, and 4% died.[6] These figures for serious sequelae are remarkably similar to those which were found in a study of sporadic cases of O157 infection in Scotland,[8] although the number admitted to hospital was rather higher (59%).

In Scotland the first isolates of O157 were reported in 1984.[9] Since then there has been a dramatic increase in cases such that we now have rates of infection amongst the highest in the world (Figure 1). The total number of laboratory-confirmed cases for 1997 was 422 (8.23 per 100,000 population) which was lower than the 506 cases in 1996.[6] However, 1996 was unusual because of the occurrence of a large outbreak in central Scotland, which accounted for over half of the culture-confirmed cases in that year. Figure 2 shows how these rates of infection compared to those in the rest of the UK over a similar period.

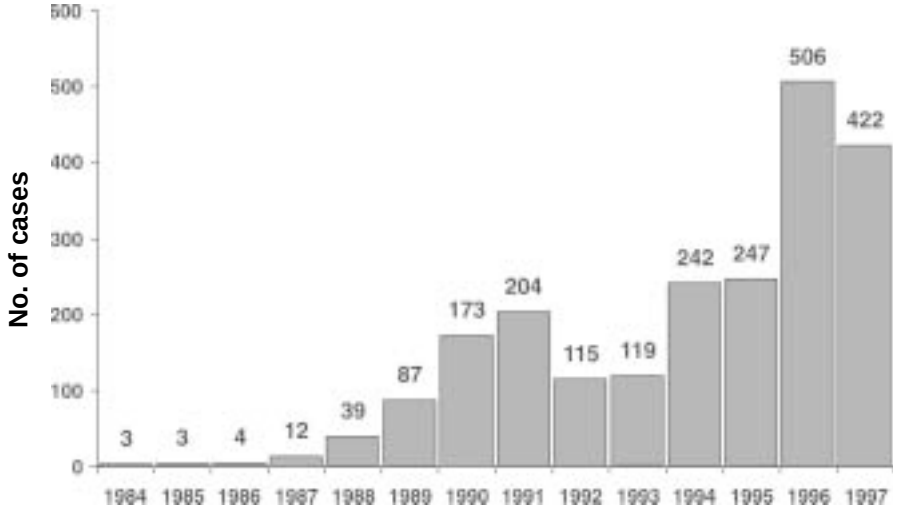

FIGURE 1
E.Coli O157 in Scotland 1984-1997. (Data supplied by SCIEH.)

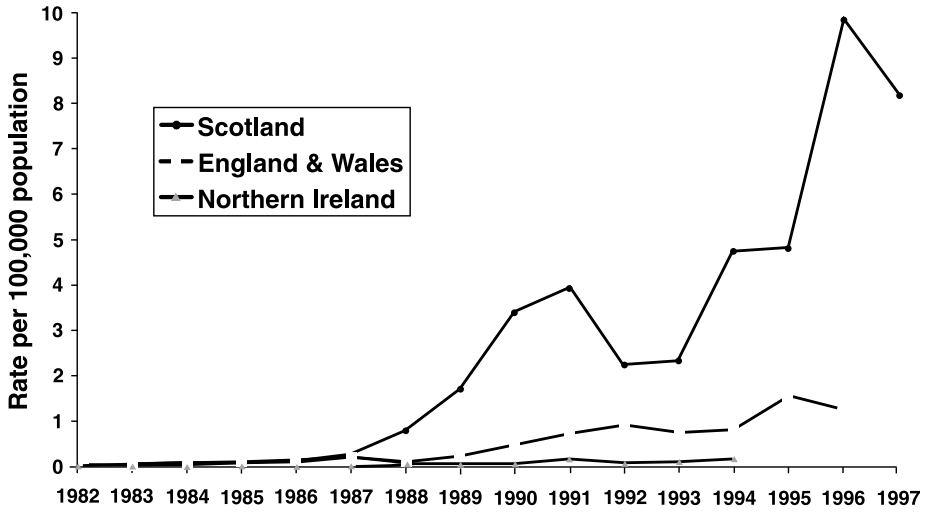

FIGURE 2
A comparison of the rates of *E.coli* O157 infection in the United Kingdom.
(Data supplied by LEP PHLS/SCIEH/DHSS[NI].)

Some of the apparent increase reflects improvement in laboratory screening practices, particularly in England and Wales. However, this cannot account for all the observed increase.

The greatest incidence occurs during the summer and early autumn, with over 60% of cases reported between May and September. Similar seasonality has been described in England and Wales and North America. Traditionally most isolates have come from health boards in the east of the country, particularly Grampian, and south-east Scotland, although while recently an increasing number of cases has been observed throughout Scotland, this east coast preponderance continues, and remains to be explained. The extremes of age are predominantly affected, particularly pre-school children.[6]

TRANSMISSION OF INFECTION

Much of the information on O157 epidemiology comes from outbreaks in the UK, and abroad, as in Scotland differences exist from the traditional picture.

Outbreaks occur in two main categories, with frequent overlap. The main features may be summarised thus:

Foodborne and/or waterborne transmission:

- The range of foodstuffs associated with infections is increasing.
- It is not only ground-beef products which are implicated, but also other meat products, and raw milk and milk products such as yoghurt, or cheese. Other foods have been associated with outbreaks, including cured and fermented meats, and raw vegetables, but in most cases these have either had an animal-derived component (usually bovine) or there has been evidence of contamination with animal by-products e.g. by sewage contamination of pasture lands.
- Outbreaks have been associated with consumption of contaminated water, and with the recreational use of water.
- In a number of outbreaks there has been evidence of inadequate cooking or pasteurisation, or the failure of some other process which should have rendered a protective effect.

Person-to-person transmission:

- This has occurred in a variety of circumstances including institutional settings, residential care facilities for the elderly, nursery school and day-care facilities for pre-school children, as well as within the home.
- Secondary spread is very common. In one US study of outbreaks occurring in day-care centres, a secondary attack rate of 22% was documented.

The epidemiological features fit the emerging knowledge of the microbiological behaviour of the organism. It has been shown that levels of contamination as low as 10 organisms per 25g of food may be sufficient to cause disease. In addition, in a number of foods only relative acidity inhibits the growth of pathogens, e.g. fermented meat products such as salami type sausages. However, this type of product has been associated with a number of outbreaks, and experimental studies show some strains of VTEC O157 are relatively acid tolerant.

Of importance are recent studies suggesting that some strains of VTEC O157 may survive for many weeks in soil, and that survival may occur for up to 35 days when the contaminated material is dried onto stainless steel surfaces.

Although recent outbreaks in Scotland have attracted considerable media attention, they are by no means a new phenomenon (Table 2). In spite of the number of documented outbreaks, the majority of cases are not obviously outbreak-related. What other factors then contribute to the high sporadic levels of infection? In 1992 a national descriptive epidemiological study was performed in Scotland to try to address some of these questions and to generate hypotheses for a case-control study. This involved the administration of a standardised structured questionnaire to all sporadic cases over an 18-month period. The unexpected findings were the relatively high frequency of those who, in the 2-4 weeks prior to the onset of illness, had been involved in gardening activities or garden play (36%), or lived on or had visited farms (20%), had direct or indirect contact with animal manure (17%), or a private water supply (12%) or private water supplies which had recent problems with high coliform counts (12%).

This suggests that contamination with animal faeces is important, and indeed the bovine source of infection was demonstrated as a direct risk factor in rural areas, and the role of possible person-to-person transmission was reaffirmed. In Grampian in 1995, a late peak of infections coincided with unusually high late autumn rainfall levels which caused considerable flooding. It is speculated that associated contamination of the many small private water supplies in this area may have been an important contributory factor, and VTEC O157 were isolated on at least one occasion from such a supply.

Thus the accumulating evidence is that regardless of the ultimate vehicle of infection, animals, particularly but not exclusively bovine animals, are the reservoir for VTEC O157 infection.[6] Many serotypes of *E.coli* may be isolated from animals, and some of these may produce enteric symptoms in young animals, and indeed, some of these are verotoxigenic. However, it appears that although *E.coli* O157 may be found in the gut of a range of animals, including cattle, sheep, goats and deer, it produces little or no disease in them. Cattle surveys in North America and the UK have consistently shown that around 4% of herds are positive for VTEC O157 at any given time, although there is great variability within herds. Carriage in individual animals within a herd appears to be transient and episodic. Human infections have been associated with direct and indirect animal contact on a number of occasions, and particular care should be taken with regard to occupational and recreational exposure to animals or their by-products.

CONCLUSIONS

Control of the VTEC O157 pathogen presents notable problems. It is present in a small, but significant, percentage of animals, particularly cattle. The ability of the organism to survive in soil for long periods of time, and the recent description of carriage in migratory bird populations, are further examples of ways in which *E.coli* O157 persists and circulates in the environment. The low infectious dose ensures that cross-contamination and cross-infection occur readily and can involve a diverse range of vehicles, including those such as water sources, in which dilutional effects might otherwise provide a protective effect. The spectrum of clinical illness is wide, and may include relatively severe sequelae, for which specific therapy is not available.

Our current knowledge and experience of the microbiology and epidemiology of these infections indicates that effective strategies to deal with the problem will have to be aimed at a range of control points. This will include close attention to every stage in production, processing and preparation of foodstuffs from the ‘farm to the fork’, provision of safe water supplies, and measures to contain secondary spread, whether

TABLE 2
Outbreaks of *E.coli* O157 in Scotland. (Data supplied by SCIEH.)

Year	Type of outbreak	Location	Nos. affected(HUS)	Phage/VT type	Mode of spread
1990	Community	Grampian	4	PT2/VT2	waterborne
	Nursing home	Glasgow	8 (2)	PT49/VT2	foodborne?
	Restaurant	Lothian	16 (4)	PT49/VT2	foodborne
	Hospital	Lanarkshire	11 (2)	PT2/VT2	nosocomial
	Nursing home	Edinburgh	5	PT49/VT2	foodborne?
1991	Community	Lothian	5 (2)	PT2/VT2	delicatessen?
	Residential home	Borders	18	PT1/VT1,2	'butcher meat'
	Community	Grampian	10	PT2/VT2	ethnic restaurant
	Restaurant	Glasgow	2	PT31/VT2	'burgers'
1992	Birthday party	Borders	5 (1)	PT49/VT2	paddling pool
	Hospital	Glasgow	5	PT1/VT1,2	nosocomial
1993	Birthday party	Lanarkshire	5 (3)	PT2/VT2	person to person
1994	Community	Central Scotland	24 (1)	PT4/VT1,2	various meats
	Community	Lothian	100 (9)	PT2/VT2	milk
	Community	Highland	8 (3)	PT2/VT2	'milk'
	Community	Lothian	16	PT2/VT2	burger meat
	Community	Borders	4 (1)	PT2/VT2	zoonotic
	Community	Grampian	22 (1)	PT2S/1.0.T2	cheese
1995	Community	Fife	6	PT2/VT2	water & foodborne
1996	Community	Highland	3	PT2/VT2	person to person?
	Sports club	Forth Valley	2	PT2	not known
	Residential home	Glasgow	2		not known
	Butcher/baker shop	Lothian			not known
	?2 x outbreaks	Lothian			not known
	Butcher shop	Central Scotland	400+	PT2/VT2	foodborne

this be within household, nosocomial, day-care or institutional settings. There is a particular need to increase our knowledge of factors which influence acquisition, carriage, and eradication of the organism in animals. We need to gain a better understanding of what makes an individual more susceptible to develop more severe clinical manifestations, and how these may be prevented. The significance of prolonged low-level excretion in asymptomatic individuals, increasingly documented since the availability of more sensitive detection methods, requires clarification. Many of these points were addressed in the report by the working group on verocytotoxin-producing *E.coli* of the Advisory Committee on the Microbiological Safety of Food (ACMSF),[10] and more recently by the Pennington group.[11] It is hoped that actions arising from these initiatives will help achieve these objectives, and provide a continued stimulus to the multidisciplinary approach, involving veterinarians, microbiologists, clinicians, public health doctors, food scientists, government and industry, which is essential to respond to the challenge of VTEC O157.

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