Chapter 1: Clinical Features and Epidemiology of VTEC

I. Introduction

Verotoxigenic *E. coli* cause an acute diarrhoeal illness that can be complicated by haemorrhagic colitis and Haemolytic Uraemic Syndrome (HUS), the latter particularly in children. In fact, VTEC are the commonest cause of paediatric diarrhoea-associated HUS (12), (13), (14).

VTEC were first recognised as a cause of serious human illness in 1982 following two outbreaks of gastrointestinal illness in the United States among 47 customers of a fast-food restaurant chain (15). The report described 'a clinically distinctive gastrointestinal illness associated with *E. coli* O157:H7, apparently transmitted by undercooked meat'. Since then, VTEC have been recognized worldwide and have caused numerous large outbreaks by a variety of transmission routes.

In Sakai City in Japan in 1996, a massive VTEC outbreak linked to white radish sprouts caused over 6000 cases of bloody diarrhoea and over 100 cases of HUS (16). Fortunately, only three deaths resulted from this outbreak. More recently in 2000, the drinking water supply of the town of Walkerton, Canada, became contaminated with *E. coli* O157:H7. As a result, 2300 of the 4800 residents of the town became ill. Twenty seven cases of HUS and at least seven deaths were reported (17). And in November 1996, 512 people became ill with *E. coli* O157 in Scotland, 17 (all of whom were elderly) dying as a result of the outbreak. This outbreak was linked to cold cooked meats from a specific food premises or premises supplied by it (18).

II. Verocytotoxigenic *E. coli*

VTEC are so-called because of their ability to produce one or both of two verotoxins (VT1 and VT2), VT1 being closely related to the shiga-toxin produced by *Shigella dysenteriae*. The most renowned VTEC serotype causing illness in humans is *E. coli* O157:H7, but other VTEC serogroups, for example, *E. coli* O26, O111, O103 and O145 are capable of causing the same spectrum of illness. The World Health Organisation listed these four serogroups as the four most epidemiologically important non-O157 VTEC serogroups (19).

A Taxonomy

The systems used to describe *E. coli* strains that cause diarrhoea have become quite confusing. VTEC strains that cause bloody diarrhoea in humans are known as enterohaemorrhagic *E. coli* or EHEC. Another term, used by the EU Scientific Committee on Veterinary Measures relating to Public Health was Human Pathogenic

VTEC (HP-VTEC). VTEC are also known in some parts of the world as Shiga toxin *E. coli* (STEC), and various nomenclature has been used to refer to the toxin genes including verotoxin (*vtx*), Shiga toxin (*stx*) and Shiga-like toxins (*slt*) genes (20).

Currently, under Irish legislation, EHEC are the notifiable pathogens, however, under the EU case definition non-toxin producing strains may be included. Non-toxin producing strains, however, are of little clinical or epidemiological importance and for clarity, the term VTEC will be used throughout this report to describe *E. coli* O157:H7 and the other verotoxin-producing *E. coli* strains that cause this distinctive illness in humans. Heightened public health, infection control, environmental health and veterinary actions are only required for cases confirmed as verotoxin positive.

In their report on VTEC in Foodstuffs (21), it is notable that the European Union (EU) Scientific Committee on Veterinary Measures relating to Public Health made a recommendation that 'A common terminology, case definition, diagnostic and reporting procedures would help clarify the epidemiological situation within the EU regarding HP-VTEC'.

B Infectious dose

The number of organisms of *E. coli* O157 believed to be sufficient to cause infection is very low, possibly as few as 10 organisms. This compares with approximately 500 organisms in the case of campylobacter and in excess of 100,000 in the case of salmonella (7). This has implications for the ease of transmission of VTEC infection both from person-to-person and by food, water and environmental means.

C Incubation period

The incubation period for VTEC infection ranges from 1 to 8 days but is typically between 2 and 4 days. The relatively long incubation period of VTEC has significant implications for investigation. It makes recall bias (inability to remember accurately what foods were eaten or where the patient was during the possible exposure period) more likely. A longer incubation period will also make it more likely that:

- Any implicated foodstuffs or other vehicles will have been destroyed making definitive identification of VTEC less likely;
- Any contaminated foodstuffs/other vehicles will have been distributed widely making case finding more difficult;
- VTEC cases may have become widely distributed away from the point of initial exposure making identification more difficult and increasing the possibility of secondary spread of disease.

III. Clinical Features

VTEC disease manifests itself in a range of severity, from mild diarrhoea to severe bloody diarrhoea, to complications such as HUS that can result in death.

Table 1.1 shows the clinical features associated with VTEC O157 infection as listed by Todd et al. 2001 (22)

Table 1.1. Clinical features of VTEC O157 infection

Clinical feature	Frequency (%)
Vomiting	**30-60%**
Fever	**<30%**
Abdominal Pain	**70-80%**
Diarrhoea	**95%**
Bloody diarrhoea	**>70%**
HUS/TTP	**2-7% among sporadic, up to 20% in some outbreaks**
Asymptomatic infection	**10-15%**

Adapted from Todd, Dundas & Coia. 2001 (22)

Although infection may be asymptomatic, it typically begins with watery diarrhoea, frequently accompanied by abdominal pain (often severe). Fever is uncommon, although patients may occasionally experience nausea and vomiting. After 1-2 days, diarrhoea may become bloody. In Ireland, 55% of confirmed cases were reported as having bloody diarrhoea. Diarrhoea lasts for about 1 week during which abdominal pain and tenderness can be severe (Fig. 1.1) (23)

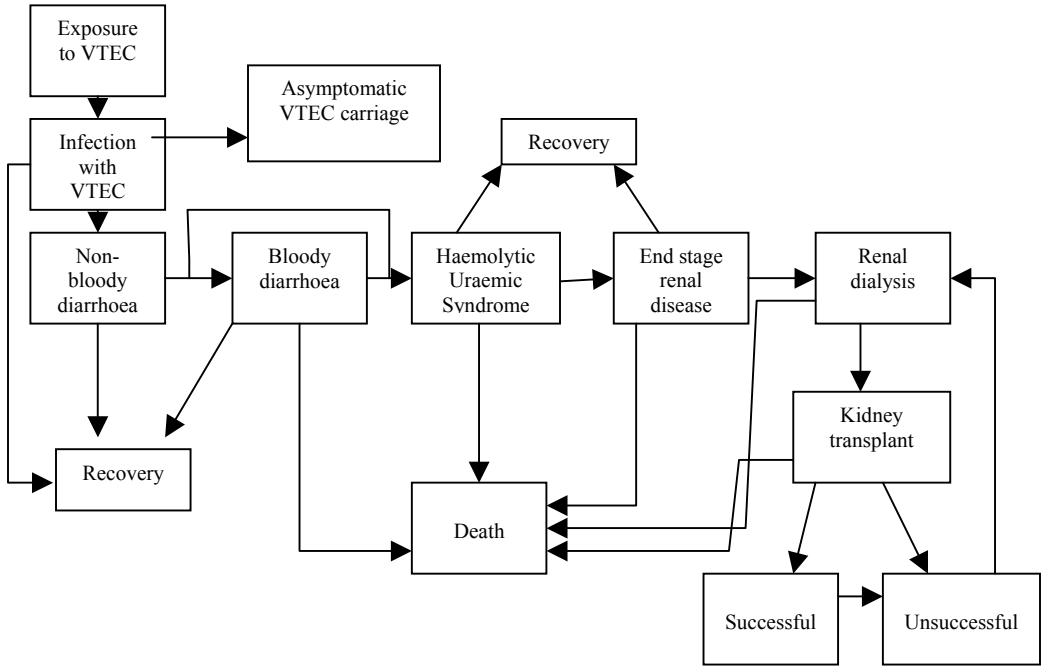

Figure 1.1 Disease progression in VTEC patients
Adapted from Havelaar et al. 2004 (24)

The most common gastrointestinal complication is rectal prolapse, which occurs in approximately 10% of patients. Other gastrointestinal complications include ischaemic colitis, appendicitis, oesophageal stricture and large bowel perforation (22).

The most common systemic complication is haemolytic uraemic syndrome (HUS), a triad of microangiopathic haemolysis, thrombocytopaenia and acute renal impairment, characterised by an elevated serum urea and creatinine, and presenting as progressive oliguria.

Laboratory criteria for diagnosis of haemolytic uraemic syndrome

The following are both present at some time during the illness:

- **Anaemia (acute onset) with microangiopathic changes (i.e. schistocytes, burr cells, or helmet cells) on peripheral blood smear and**
- **Renal injury (acute onset) evidenced by either haematuria, proteinuria, or elevated creatinine level (i.e.,$\geq$ 1.0mg/dL in a child <13 years or $\geq$ 1.5mg/dL in a person aged 13 years or over or $\geq$ 50% increase over baseline)**

Note: a low platelet count can usually, but not always be detected early in the illness, but it may then become normal or even high. If a platelet count obtained within seven days after the onset of the acute gastrointestinal illness is not<150,000mm^3, other diagnoses should be considered.

A less common complication is thrombocytopoenic purpura (TTP) characterised by a low platelet count and a propensity to bleed which increases the risk of microangiopathic haemorrhagic neurological complications. Both TTP and HUS are sometimes considered to be overlapping syndromes (22). Neurological symptoms occur in 25% of HUS cases and include drowsiness, cerebrovascular accidents, seizure and coma. Pleural and pericardial effusions occur commonly among elderly patients with HUS/ thrombotic thrombocytopoenic purpura (TTP) (22).

HUS tends to appear 2-14 days after the onset of diarrhoea (23), with children and the elderly being at greatest risk. Between five and eight percent of VTEC cases progress to HUS, although higher rates have been reported during outbreaks. In Ireland between 1999 and 2002, nine percent of cases progressed to HUS (25), one of whom died; among children under 15 years of age, 12.5% developed HUS (25).

Key message: In contrast to Campylobacter and Salmonella, the proportion of patients experiencing severe symptoms is high.

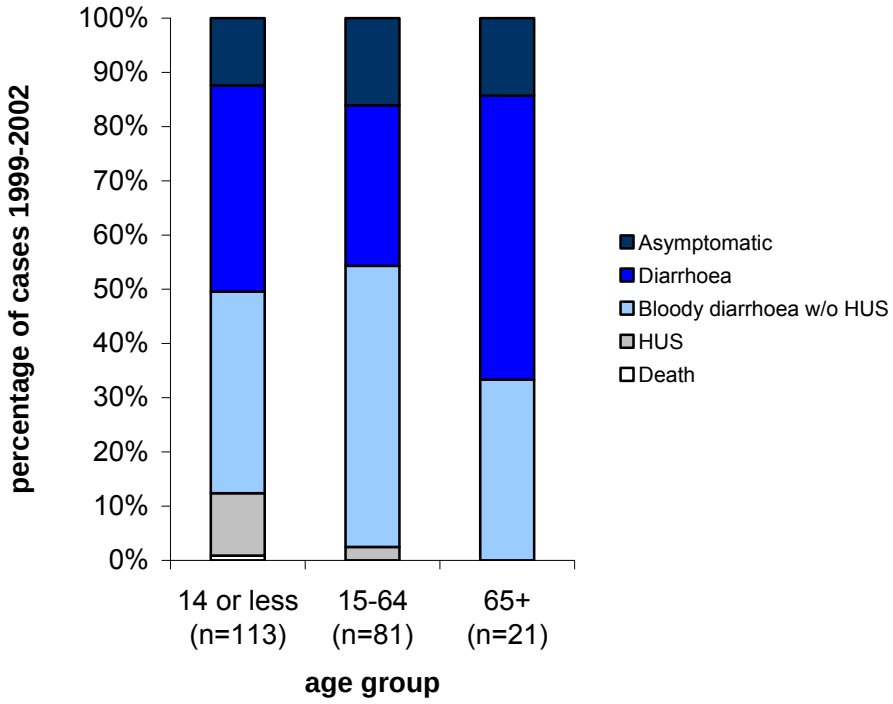

Figure 1.2. Severity of illness of VTEC O157 cases 1999-2002 by age

The British Paediatric Surveillance Unit (BPSU) study of VTEC-associated HUS in children in the UK in (1997-2001) (26) demonstrated that the majority of children recovered uneventfully, although a significant minority (11.6%) had an abnormal outcome and 2.6% died. Other Paediatric HUS studies show a range of mortality rates of 2.6%-7.4% (26). However, limited data on mortality in the elderly with VTEC disease complicated by HUS/TTP during two VTEC outbreaks indicated a mortality rate among the elderly of 88% (22). It must be borne in mind that these figures refer to mortality in outbreak situations, However, they do suggest a significant difference in age-specific mortality rates for HUS.

Key message: HUS can appear 2-14 days after the onset of diarrhoea (23), with children and the elderly being at greatest risk.

Garg et al. (27) estimated that a further 3% of HUS patients developed end-stage renal disease (ESRD) within 4 years of having diarrhoea-associated HUS. ESRD has important human health implications; once established ESRD must be managed either by renal dialysis or transplantation.

IV. Pathogenicity

The verotoxins are considered to be the most important virulence factors of these organisms. They are made up of a single A-subunit and 5 B-subunits, the latter of which bind to globotriasylceramide (Gb_3), which is found in the membranes of eukaryotic cells. Once absorbed, the A-subunit blocks intracellular protein synthesis. Strains may produce either VT1, VT2 or both toxins. Strains that produce VT2 are associated with an increased risk of HUS (28).

Other factors that are believed to play a role in pathogenicity including intimin (and other factors encoded by the Locus of Enterocyte Effacement (LEE) pathogenicity island) and haemolysin, the genes for which are carried on a pathogenicity plasmid.

The proteins encoded by the LEE pathogenicity island are responsible for the organism forming an intimate attachment with the host intestine through the production of an attaching effacing lesion in the gut mucosa. The disruption caused by the attachment of the organism in this way may be responsible for the initial non-bloody diarrhoea.

The verotoxins produce further local and systemic disease. The local effect on the intestine causes the development of bloody diarrhoea while HUS results when the toxins enter the bloodstream and bind to endothelial cells via the Gb_3 receptors. These receptors are especially abundant in the kidney and the brain.

Not all VTEC have been identified as causing human disease, Figure 1.3 shows the relationship between VTEC and other human pathogenic *E. coli*.

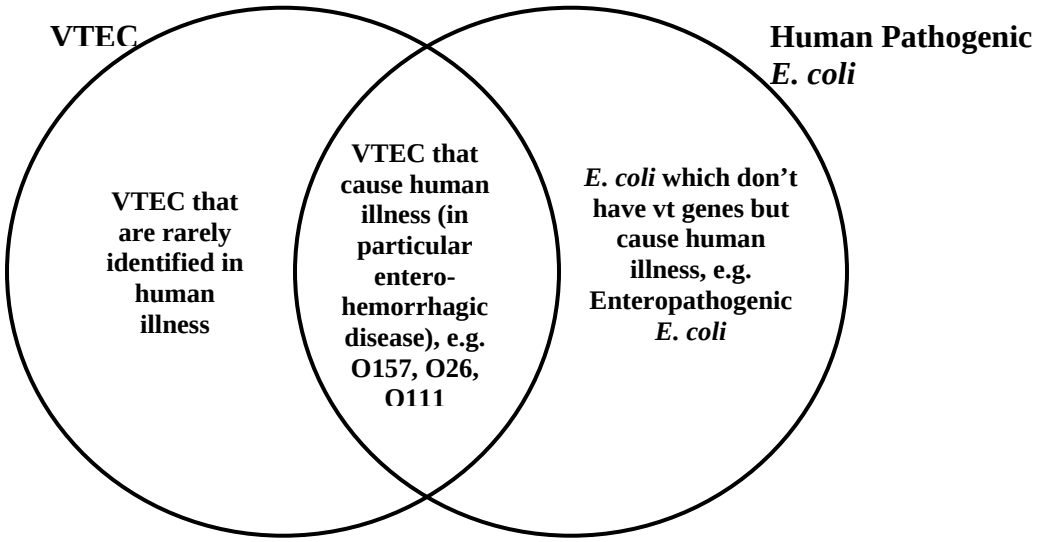

Figure 1.3 *E. coli* and human illness

A Serogroups of VTEC implicated in human illness

E. coli O157 was the first VTEC serogroup to be identified as clinically significant and it remains the most commonly isolated in Ireland (29), the UK (6) and the US (30). The most common non-O157 VTEC serogroups reported internationally are O26, O111, O103, and O145 (19).

V. Prevalence and Distribution

Illness due to VTEC has been identified on all continents (31). Although variation between different surveillance systems makes direct comparison difficult (some countries like Ireland have routinely recorded only VTEC O157 cases while others record all VTEC cases), evidence exists to suggest that there is geographical variation in incidence and in the distribution of causative strains. While not routinely reported, cases of non-O157 have also been reported in Ireland since 1999, in particular *E. coli* O26. Comprehensive data on non-O157 infections are available since 2004 when all became notifiable.

Variation, regionally within Ireland (and internationally), in laboratory screening practice, diagnostic procedures and case finding procedures, influence the distributions of VTEC cases reported in the following sections. With a more uniform approach to VTEC diagnosis, the age and regional distribution of this disease may change.

A VTEC O157

The UK and Ireland have some of the highest reported rates of VTEC O157 infection in Europe. Table 1.2 shows the Irish incidence rates for VTEC O157 infection compared with countries within the UK. Rates in Ireland are in general comparable to those published for England and Wales and Northern Ireland. Higher rates have historically been reported for Scotland (32).

Eighty-six confirmed cases of human VTEC O157 infection (2.1 per 100,000 population) were reported in Ireland in 2003, the highest rate recorded here since 1998. This declined again in 2004 to 52 (1.3 per 100,000) confirmed VTEC O157 cases (provisional data), although the rate in Ireland remains higher than that reported for many EU countries. There is considerable variation year on year in the data from the Republic of Ireland. This is due in part to the evolving methods of surveillance, heightened awareness of the pathogen and to more intensive investigation of sporadic cases and outbreaks. In addition, we may be also seeing a real increase in the incidence of this pathogen.

Key message: The incidence of VTEC O157 infection in Ireland increased between 2000 and 2003.

Table 1.2. Crude incidence rate of VTEC O157 by year, in England & Wales, Scotland, Northern Ireland and Ireland, 1996-2004*.

Year	Ireland	Northern Ireland	England&Wales	Scotland
1996	0.2	0.8	1.3	10.0
1997	0.8	1.8	2.1	8.4
1998	2.1	1.7	1.7	4.3
1999	1.4	3.2	2.1	5.8
2000	0.9	3.2	1.7	3.9
2001	1.3	3.1	1.5	4.6
2002	1.7	1.6	1.1	4.5
2003	2.1	3.1	1.3	2.9
2004*	1.3	1.1	1.3	4.1

Data sources for Ireland HPSC, SWAHB PHL and for 1996-1998, FSAI report (11). Data for NI, Scotland and England and Wales were kindly provided by the Communicable Disease Surveillance Centre, Northern Ireland, the Scottish Centre for Infection and Environmental Health and the Health Protection Agency, respectively.
*Please note that all 2004 data are provisional.

Although the data may not be directly comparable, considerably lower incidence rates have been reported for Finland (0.3 per 100,000 in 2001), Norway (0.3 per 100,000 in 2001), Sweden (0.7 per 100,000 in 2001) and Australia (0.3 per 100,000 in 2002) (33). New Zealand reported a VTEC incidence rate of 2.8 per 100,000 in 2003 (34), the US a rate of 1.17 per 100,000 in 2003 (35) and Denmark a rate of 1.7 per 100,000 in 2001, although almost three quarters of those in Denmark were due to non-O157 VTEC (33).

B Non-O157 VTEC

While not reported as frequently as VTEC O157, non-O157 are an important cause of VTEC disease in Ireland. In 2004, nine cases of non-O157 were reported, represented by five different serogroups. Moreover, two of four HUS VTEC-associated cases reported in 2004 were caused by non-O157 VTEC. There was a greater diversity in serogroups reported than previously; prior to 2004, the vast majority of non-O157 VTEC cases reported in Ireland were serogroup O26. Two outbreaks *E. coli* O26 have been reported in Ireland -one family and one general (36), (37).

Key message: While not reported as frequently as VTEC O157, non-O157 are an important cause of VTEC disease in Ireland and an emerging concern internationally

Non-O157 are an emerging concern throughout Europe. In some countries, for example Denmark, non-O157 are reported with greater frequency than VTEC O157. The majority of EU countries, including the UK, report more VTEC O157 than non-O157 cases. The possibility however, should be borne in mind, that varying diagnostic approaches in the different countries might account for some of the variation in the number/proportion of non-O157 VTEC reported.

The data for Ireland indicate that non-O157 play an important role in VTEC disease here. Moreover, given that stool samples are more likely to be investigated for non-O157 in the event of a case of HUS, and that 50% of HUS cases in 2004 were caused by non-O157 in

2004, it is probable that non-O157 are under-diagnosed in Ireland. A more uniform approach to non-O157 diagnosis should generate more information on the role of non-O157 VTEC infection here.

C *E. coli* O157 phage types

While the most common *E. coli* O157 phage type reported in Ireland between 1999 and 2003 was phage type (PT) 32, there has been an increase in the variety of phage types reported in Ireland in recent years (Figure 1.4).

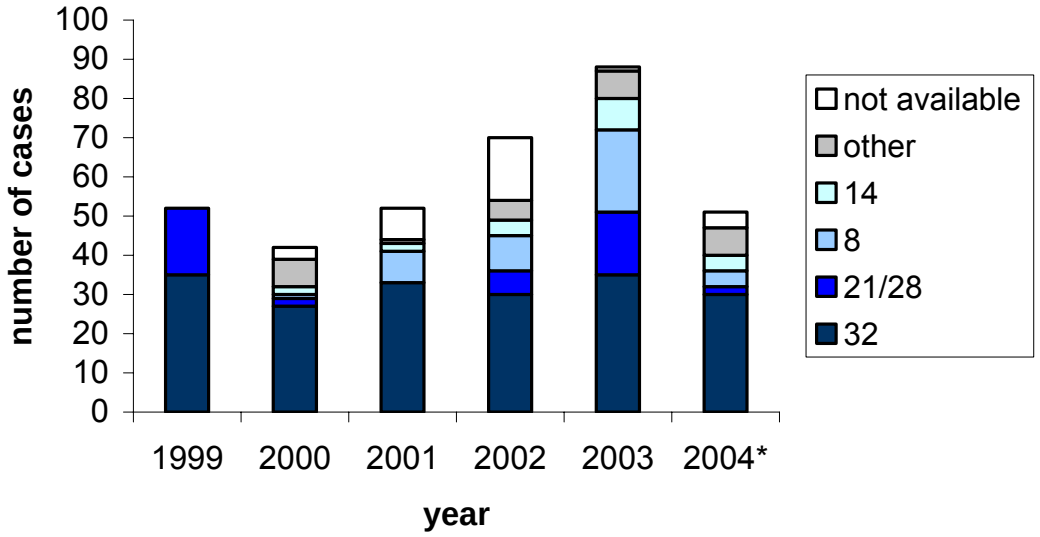

Figure 1.4. VTEC O157 phage types in Ireland 1999-2004* by year
Data source: HPSC Enhanced surveillance and Health Service Executive-South West Area Public Health Laboratory (HSE-SWA PHL) data. *2004 data provisional

D Regional Distribution

Regional variation is noted in the numbers of cases of VTEC O157 reported in Ireland. The crude incidence rates of confirmed VTEC O157 by HSE Area in Ireland, 1999-2004 are shown in Figure 1.5 (it should be borne in mind that these rates are based on small numbers of cases and that the associated confidence intervals are large). Variation noted may also reflect variation in regional policies for laboratory practice, diagnostic methods and case finding procedures.

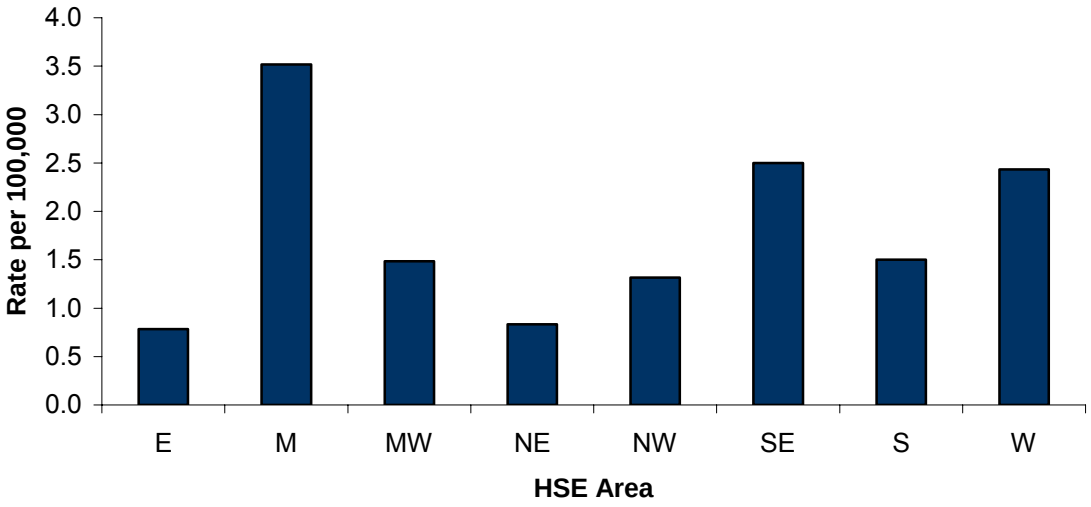

Figure 1.5. Average crude incidence rate (CIR) of confirmed resident cases of VTEC O157 by HSE Area of residence, Ireland, 1999-2004*Data source: HPSC Enhanced surveillance and SWAHB PHL
*2004 data is provisional

E Age Distribution

Figure 1.6 shows the age-specific incidence rate for VTEC cases in 2004. As in previous years, the reported incidence is highest in children under the age of 5 years. These data are likely to be a reflection of the group most affected, laboratory diagnostic policy and case finding procedures.

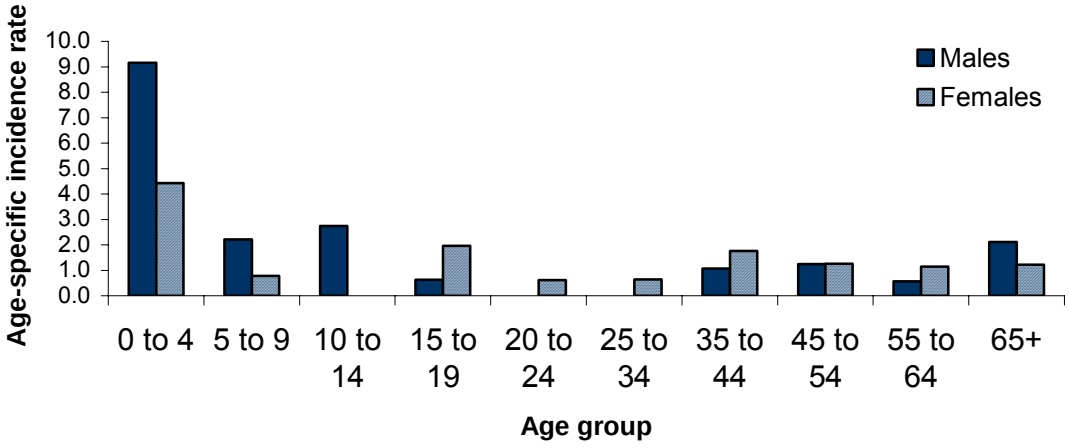

Figure 1.6. Age-specific incidence rate of confirmed VTEC cases in Ireland, 2004
Data source: HPSC Enhanced surveillance and SWAHB PHL
*2004 data is provisional

Key message: The incidence and severity of VTEC infection is highest in children under the age of 5 years.

F Seasonal Distribution

In common with other countries (12), (35), the disease exhibits a seasonal distribution in Ireland with the highest number of cases in the third quarter of the year. In total between 2001 and 2004, 50% of VTEC cases occurred in the 3 months July through September.

Key message: The highest incidence rate of VTEC infection is in late summer

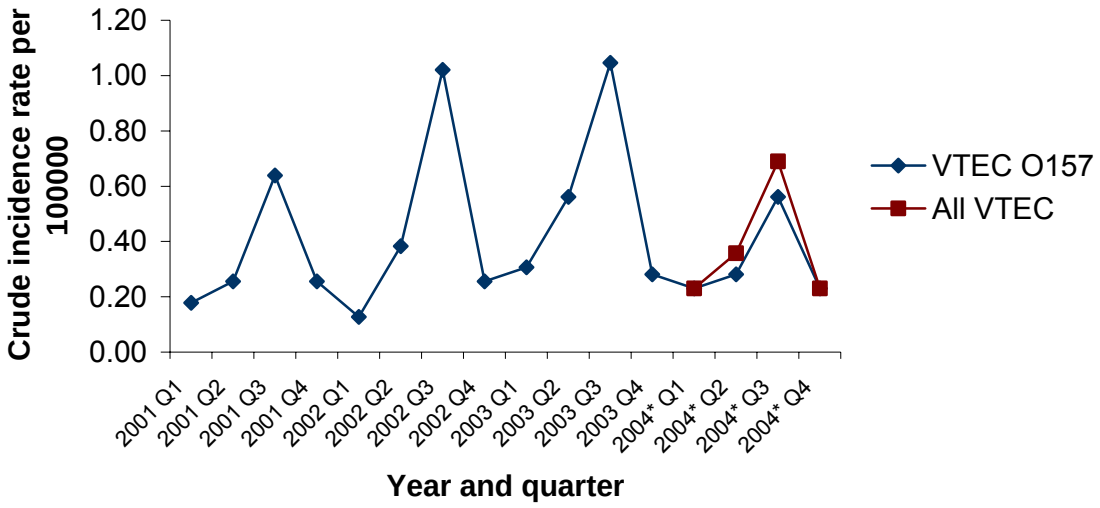

Figure 1.7 Crude incidence rate (per 100,000 population) of VTEC by quarter, Ireland 2001-2004*

Data source: HPSC Enhanced surveillance and SWAHB PHL; date used is date of onset.
*Note data for 2004 is provisional and that comprehensive data for non-O157 VTEC only available from January 2004

VI. Transmission Routes for VTEC Infection

A recent editorial in the New England Journal of Medicine described the investigation of the epidemiology of *E. coli* O157 as 'trying to complete an intricate jigsaw puzzle without the picture on the lid of the box and without knowing whether or not all the pieces are there' (38). Our knowledge of the transmission of the organism has greatly expanded since it was first recognised twenty years ago.

VTEC has established itself as being an effective transmissible agent, utilising a range of modes of transmission. Although it was first recognized as a foodborne pathogen (the "burger bug"), it is now known to be transmitted from its natural animal reservoir to humans through food, water, the environment and by direct contact with the animals. Person to person spread has also been documented.

A The animal reservoir

Cattle are recognised as the principal reservoir for VTEC, although VTEC have been isolated from a variety of animal carriers including sheep, horses, farmed deer, goats, dogs, geese, pigs and wild birds. Moreover, cattle, sheep and goats (and rabbits) have all been linked to cases of infection. VTEC does not however, typically produce bovine disease; cattle carry it as a commensal and only rarely will it produce disease in young, weakened calves.

Key message: Ruminants, in particular cattle, are major reservoirs of VTEC

VTEC O157 are found in both dairy and beef cattle and have a wide distribution in Europe and North America. Shedding by cattle is intermittent with herd members remaining negative for months with only a proportion sporadically becoming positive for a few weeks at a time (39). VTEC can be found intermittently on the majority of farms (40), with prevalence rates of up to 20% being reported among individual animals within herds (41). Carriage rates are higher in calves than in adult cattle, and while detected year round, carriage rates are subject to seasonal effects with higher rates reported in spring and summer (39). Horizontal transmission between animals may be facilitated by contaminated water and feed, with water troughs potentially playing a role in the ecology of VTEC on the farm (42), (43), (44).

Less information is available on other animal species. VTEC O157 rates of 2-7% in sheep have been reported in a number of studies (45), (46), (47), (48).

Key message: VTEC can be transmitted by a variety of routes including:

- **Food, e.g. undercooked beef, unpasteurised contaminated milk and dairy products, or vegetables contaminated with the faeces of animal carriers**
- **Water contaminated with the faeces of animal carriers**
- **Person-to-person transmission**
- **Direct or indirect animal contact**

B Foodborne Transmission

The first reported cases of VTEC infection worldwide were linked to the consumption of undercooked minced beef (15) and since then, minced beef has been implicated in numerous outbreaks (49), (50), (51). Carcass meat can become contaminated with VTEC during the slaughtering process. Infections are rarely associated with meat cuts (52), however, mincing of the meat will distribute any VTEC throughout the volume of the meat, where it may survive if cooking is uneven or inadequate (49).

Following outbreaks of foodborne illness associated with consumption of beef burgers from a restaurant chain in England in 1991, all such major chains imposed stricter cooking and handling procedures. Since the implementation of these changes there have been no further outbreaks in the UK associated with the consumption of burgers from the major chains (53).

Key message: Undercooked minced beef, raw milk and products made from raw milk, and fresh produce consumed raw have all been implicated as vehicles of infection in foodborne VTEC outbreaks

Unpasteurised milk and cream, and cheese made from unpasteurised milk (54) (49) are examples of other foods of animal origin implicated in VTEC outbreaks. Pasteurisation is effective but a small number of incidents of post-pasteurisation contamination have been reported (9); (55). A recent outbreak in Denmark in which 25 people became ill was attributed to ineffectively pasteurised milk (56).

Internationally, there are a growing number of reported outbreaks associated with foods of vegetable origin. The largest reported VTEC outbreak was caused by uncooked white radish sprouts (16). Salad vegetables (Centres for Disease Control and Prevention (51)and unpasteurised apple cider in the US (57) have also been implicated as vehicles during outbreaks. Contamination of fresh produce may be due to contact with faeces from domestic or wild animals at some stage during cultivation or handling, or it may occur in the kitchen due to cross-contamination from raw meat (49).

Food surveys undertaken in Ireland to investigate the rate of VTEC contamination include a one-year survey of retail minced beef and beef burgers in Ireland conducted for the FSAI in 2000/2001; 2.8% of 1533 samples surveyed contained *E. coli* O157 (58). A further survey undertaken in 2003/2004 to investigate retail minced beef for the presence of other *E. coli* O26 and O111 found two of 800 samples tested positive for *E. coli* O26, however, neither were positive for verotoxin and thus posed no public health risk (59).

C Waterborne Transmission

Humans use water for a variety of purposes such as drinking, food preparation, washing, the irrigation of crops and recreation. Contamination of water sources can occur from faecal wastes from the main animal reservoirs, cattle, sheep and man. In particular, treatment failures in water supplies serving large populations have the potential to cause widespread outbreaks of illness (17). *E. coli* O157 can survive for long periods of time in water, especially at cold temperatures, and studies suggest that it may enter a viable but nonculturable (VBNC) state (60).

The most highly publicised waterborne outbreak of *E. coli* O157 occurred in Walkerton, Canada in 2000 (17). Other large waterborne outbreaks include one in New York State (61) and another in Wyoming (62). These outbreaks affected 2300, 128 and 157 persons respectively.

Key message: Improperly treated water and treatment failures in supplies serving large populations have the potential to cause large outbreaks

Water as a transmission route in Ireland is likely to be important. In general, the quality of water in public water supplies and ‘public’ group water schemes in Ireland is high with 98.7% and 96.1% complying with EU standards for faecal coliforms in 2003. By

contrast, only 74.9% of 'private' group schemes complied with these standards (63). VTEC has never been linked with public water supplies in Ireland.

In addition, there are also a large number of Irish households served by private wells (64), particularly in rural areas. Private wells were responsible for two VTEC O157 outbreaks in Ireland in 2004 and represent an emerging concern.

Key message: Private wells were responsible for two VTEC O157 outbreaks in Ireland in 2004 and represent an emerging concern.

Additional outbreaks internationally have resulted from recreational contact with water. Swimming in contaminated lake water was linked to outbreaks both in the US and in Europe (31). Potential sources of contamination included infected swimmers and faeces from nearby animals being washed into the lakes. Outdoor swimming/paddling pools were linked to a number of outbreaks in the US (31) (51) (65). In these instances, contamination was probably due to infected, symptomatic children.

D Person to person spread

Person to person spread is a major factor in outbreaks associated with residential centres and day care facilities for vulnerable communities (young children, elderly and disabled). It was believed to be the main transmission route during two of the three VTEC outbreaks in childcare facilities in Ireland (Table 1.4), and has also been documented as important in family outbreaks in the domestic setting.

Key message: Person to person spread is a major factor in outbreaks associated with residential centres, day care facilities for vulnerable communities and in households

Person-to-person spread may arise from:

A symptomatic case
An asymptomatic convalescent case or
An asymptomatic carrier

Excretion of the organism following infection can be prolonged, lasting up to a number of months after initial exposure, especially in young children. A recent study of children of a day-care centre outbreak demonstrated a median duration of shedding (interval from onset of diarrhoea to the first of two negative stool culture) of 29 days (range 11-57). (66). It is not clear whether the duration of shedding is related to the severity of VTEC associated illness and conflicting evidence exists. Shedding of VTEC can be intermittent and this complicates efforts to determine the duration of faecal carriage. One Irish case was reported to have protracted VTEC carriage following infection and continued to shed intermittently for 138 days (C. Foley-Nolan personal communication.

Key message: Prolonged excretion of the organism can occur (up to several months), especially in young children.

Contacts of known VTEC cases can be identified as asymptomatic carriers as part of contact tracing during case investigation. Asymptomatic carriers can also be identified in the course of prevalence surveys of samples from "well" populations. There is evidence to suggest that about 6% of members of farming families and 9% of slaughterhouse employees are VTEC carriers (67). Although the VTEC strain has not caused illness in the carrier, the possibility remains that this isolate could cause illness in a susceptible individual.

Key message: Certain groups, when carriers of VTEC organisms, are considered to pose an increased risk of spreading infection (3), and require a risk assessment to determine what school/work restrictions need to be imposed. These are:

- **Food handlers**
- **Health care, preschool nursery, or other staff who have direct contact, or contact through serving food, with highly susceptible patients or people in whom an intestinal infection would have particularly serious consequences.**
- **Children under 5 years of age attending nurseries, play groups, or other similar groups.**
- **Older children and adults who are unable to implement good standards of personal hygiene -for example those with learning disabilities or special needs; and people in circumstances where hygienic arrangements may be unreliable- for example, temporary camps housing displaced persons. Under exceptional circumstances children in infant schools may be considered to fall into this group.**

E Direct or indirect animal contact

Direct spread from animals to farmers and other animal keepers, to farmers' children and to farm visitors had been documented (68). In particular, visits by children to petting zoos/open farms (69), (70), (71), and recreational use of farmland, e.g. camping (72) and other events hosted on farmland (73), have the greatest potential for outbreaks by this mode of transmission. For example, a recent outbreak associated with a fair in the US resulted in 108 cases of infection (74).

Fresh animal manure would appear to pose the greatest risk, although *E. coli* O157 has been shown to survive for several months in manure (75) and in soil (72) (76). A number of recent case control studies have also demonstrated a direct association between human illness and both the concentration of beef cattle and the spreading of manure on land (10) (77) (78) (79).

Key message: Contact with farm animals either directly, or indirectly through contact with their faeces, is a strong risk factor for VTEC O157 infection.

VII. Outbreaks in Ireland

A *E. coli* O157 outbreaks

We have, so far, been fortunate in Ireland in that outbreaks of VTEC have tended to be quite limited in size. Because of the potential seriousness of the illness however, outbreaks involve a very significant amount of public health, environmental and microbiological investigation and management. By way of an illustration, an investigation of an outbreak in 2004 that identified four confirmed VTEC cases uncovered another 38 probable cases; all ill, all requiring clinical, public health and microbiological management on an individual basis. In total, more than 900 people were required to be contacted as part of the management of this outbreak.

Of the 353 *E. coli* O157 cases reported to HPSC between 1999 and 2003, 192 were apparently sporadic cases and 161 appeared to be related to other cases. Figure 1.8 shows the proportion of cases in each year which were apparently single and which were outbreak (family and general) related.

Key message: Family outbreaks are common with very few general outbreaks.

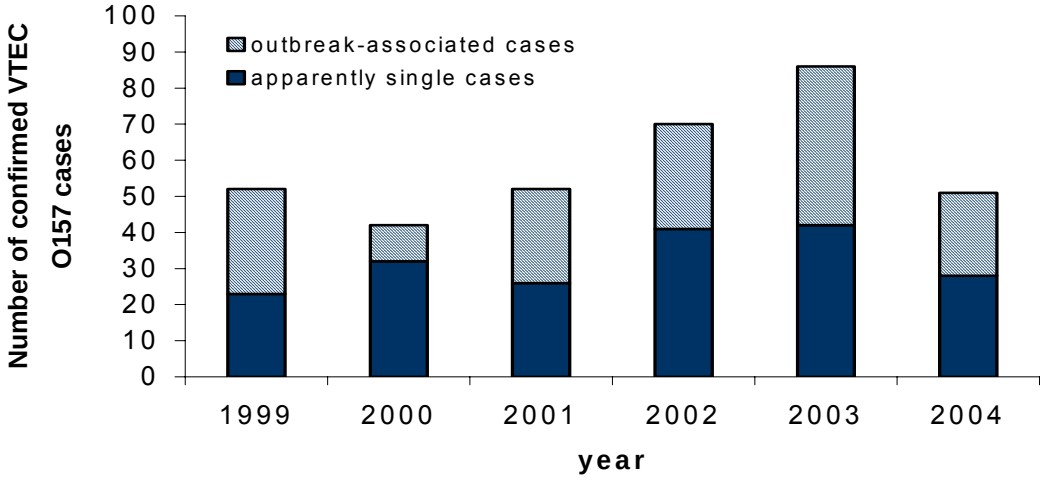

Figure 1.8. Apparently sporadic and outbreak-associated *E. coli* O157 cases 1999-2004*

In total between 1999 and 2004, 63 associations (two or more cases) were identified among VTEC O157 cases. Many of these small outbreaks would have gone unnoticed but for the active investigation of apparently sporadic cases. Family outbreaks predominate with very few general outbreaks. Outbreaks have fortunately tended to be small in size with the vast majority (95%) having fewer than 5 confirmed cases.

B General Outbreaks

A brief examination of general outbreaks of VTEC infection in Ireland highlights some important modes of transmission (Table 1.3).

The appearance of VTEC cases in childcare facilities is a cause of particular concern as young children are among the most vulnerable to VTEC infection. Poor or ineffective hand hygiene in this age-group can lead to a high rate of person-to-person transmission. In total, three VTEC outbreaks in childcare facilities (including an O26 outbreak described below) have been documented in Ireland between 1998 and 2004. In December 1998, 13 confirmed cases of VTEC O157 were reported associated with a childcare facility in the Eastern Regional Health Authority (ERHA) (80) and in the autumn of 2001, four confirmed cases of VTEC O157 were linked to an outbreak in a childcare facility in the Southern Health Board (SHB), one of whom developed HUS; in total 15 cases of gastrointestinal illness were reported associated with the latter outbreak. In both of these *E. coli* O157 outbreaks, transmission among the cases was believed to have been largely by person-to-person spread.

Two further general outbreaks of VTEC O157 occurred during the summer of 2003 (81) that were linked to hotel restaurants in the Eastern Region. Five confirmed, twelve probable and a number of possible cases were reported in one outbreak; seven cases were hospitalised. Investigations found no association between any specific food or drink and the development of illness. In the second outbreak, 3 confirmed cases including one who developed HUS, were reported; there were two hospital admissions. Again, neither the source nor the mode of transmission during this outbreak were established. An important facet in the investigation of these 2 outbreaks was the number of tourists involved, which necessitated considerable international collaboration.

Table 1.3. General VTEC outbreaks in Ireland 1998-2004

Year	Month	HB	Location	No. conf.	No. hosp.	Suspect mode of transmission	Organism
2004	Jun	NEHB	Sports Club	4	3	Waterborne	*E coli* O157
2003	Aug	ERHA	Restaurant	5	7	Unknown	*E coli* O157
2003	Aug	ERHA	Hotel/Restaurant	3	2	Unknown	*E coli* O157
2001	Sep	SHB	Crèche	4	3	P-P	*E coli* O157
1999	Oct	NWHB	Crèche	4	NK	Unknown	*E coli* O26
1998	Nov	ERHA	Crèche	13	NK	P-P	*E coli* O157

C Non-O157 VTEC Outbreaks in Ireland

In 2000, an outbreak of *E. coli* O26 involving six members of an extended family was reported; one child developed HUS. Prior to this, McMaster et al. (36) reported a general outbreak in 1999, involving VTEC O26; several children in a childcare facility became ill, four of whom were confirmed positive for VTEC O26. This situation differs from the UK where no outbreaks of non-O157 VTEC have been reported (82)

VIII. What we know

- **In contrast to bacterial gastroenteric pathogens such as Campylobacter and Salmonella, the proportion of VTEC patients experiencing severe symptoms is high**
- **The number of organisms required to cause infection is very low in comparison to other causes of food poisoning**
- **A variety of transmission routes are possible, with person-to-person spread and water from private wells emerging as important transmission routes in Ireland**
- **The incidence of human VTEC O157 in Ireland has increased from 2000 to 2003**
- **The incidence and severity of illness is highest in children under 5 years of age**
- **The highest incidence rate is in late summer**
- **Many small family outbreaks have been reported but general outbreaks are rare**