3.3 Verotoxigenic *E. coli*

Summary

Number of VTEC cases, 2013: 702
Crude incidence rate, 2013: 15.3/100,000
Number of VTEC-associated HUS 2013: 31
Number of VTEC cases, 2012: 554

Introduction

The reported verotoxigenic *E. coli* (VTEC) incidence rate in Ireland is generally high relative to other European countries. In 2012 (the latest year for which data are published), the overall VTEC incidence rate in the European Union was 1.15 per 100,000.[1] For many years, Ireland has reported the highest VTEC incidence rate of any Member State in the EU, except in 2011 Germany reported the highest rate due to a large VTEC O104 outbreak linked with fenugreek seeds.[2-3]

The dominant transmission routes reported for VTEC infection in Ireland have been person-to-person spread, especially in childcare facilities and among families with young children, and waterborne transmission associated with exposure to water from untreated or poorly treated private water sources. [4-7] Other important transmission routes identified internationally include food (often minced beef products or fresh produce such as lettuce and spinach), and contact with infected animals or contaminated environments.[3, 8-9]

Materials and Methods

Infection with verotoxigenic *E. coli* became a notifiable disease in 2012; prior to that VTEC were notifiable under the category Enterohaemorrhagic *E. coli* (EHEC) since 2004. Enhanced epidemiological information was supplied as in previous years by HSE personnel, and the VTEC National Reference Laboratory at the Public Health Laboratory HSE Dublin Mid Leinster (VTEC-NRL at PHL HSE DML) provided VTEC confirmation and typing data. Data from all sources are maintained in the Computerised Infectious Disease Reporting (CIDR) system. Outbreaks of VTEC are notifiable since 2004 and data are provided to CIDR by regional public health departments. The data used in this report were extracted from CIDR on 7th July 2014.

Data from the Central Statistics Office (CSO) 2011 census were used to provide denominators for the calculation of national, regional and age-specific incidence rates in 2013.

Results

Incidence

In 2013, there were 702 notifications of VTEC, equating to a crude incidence rate (CIR) of 15.3 per 100,000 (95% CI 14.2-16.4). This compares to an overall rate of 12.1 per 100,000 in 2012, an increase of 27%. 569 notifications in 2013 were reported as confirmed cases (CIR 12.40 95% CI 11.38-13.42), 130 were probable and there were 3 cases reported in the possible case class. The criteria under which notified cases were reported in 2013 under the VTEC case definition is outlined in Table 1. As the classification of VTEC cases changed significantly upon the amendment of the Irish VTEC case definition in 2012, it is not valid to directly compare the number of notifications by case classification with the period before 2012.

Table 1. Number of VTEC notifications by criteria for notification, Ireland 2013

Notification criteria	Confirmed	Probable	Possible	Total
Culture confirmation[a]	471	111		582
Laboratory confirmation by PCR[b]	97	11		108
Serodiagnosis (valid for HUS only)	1			1
Reported solely on the basis of epidemiological link		8		8
Clinical HUS not meeting lab or epi criteria			3	3
Total	569	130	3	**702**

[a]Symptomatic culture confirmed cases are classified as confirmed cases, while asymptomatic culture confirmed cases are classified as probable cases

[b] Symptomatic PCR-confirmed cases are classified as confirmed cases, while asymptomatic PCR-confirmed cases are classified as probable cases

Of the 691 cases with laboratory evidence of infection, 215 cases were reported as being infected with *E. coli* O157 (4.7 per 100,000 (95% CI 4.1-5.3), 212 with *E. coli* O26 (4.6 per 100,000 (95% CI 4.0-5.2), 255 with other VTEC strains, and 9 cases had mixed VTEC infections, being infected with more than one VTEC strain. Of the 8 probable cases reported on the basis of an epidemiological link to a confirmed case, 4 were linked to *E. coli* O157 outbreaks, and 4 were linked to *E. coli* O26 outbreaks. Figure 1 illustrates the distribution of VTEC cases in Ireland by serogroup since 1999. The serogroup distribution this year represents a 6.6% decrease in O157 infections, a 2.4% increase in O26 infections, and a 180% increase in other non-O157 infections compared to 2012.

Severity of illness

Five hundred and seventy-nine of the 702 notified cases were symptomatic (82.5%), 234 (40.4%) of which developed bloody diarrhoea (43.8% when only cases with this variable completed are included). Thirty-one individuals (4.4%) developed HUS, a decrease of 3% on 2012. There was one death in a confirmed VTEC case and one death in a possible VTEC case; four other persons diagnosed in 2014 with VTEC infection died, but their deaths were not due to VTEC. Where reported (n=680), 242 (35.6%) of notified cases were hospitalised (42.0% of symptomatic cases).

Twelve HUS cases were infected with *E. coli* O157, with a further two HUS case infected with both VTEC O157 and VTEC O26. Five had laboratory evidence of VTEC O26 infection, two had VTEC O55 infections, and seven were infected with other VTEC strains (Table 2). The remaining three HUS cases were reported as possible VTEC notifications. HUS cases ranged in age from 10 months to 81 years, with 25 of the 31 cases being less than 10 years. Eighteen were sporadic cases, nine were part of family outbreaks (including two cases in one household), and four were part of general outbreaks (including two in one small community outbreak).

Seasonal distribution

Figure 2 shows the seasonal distribution of notifications

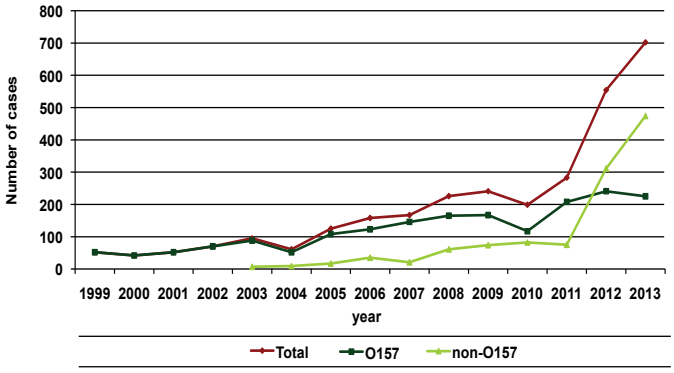

Figure 1. Annual number of confirmed and probable VTEC cases by serogroup, Ireland 1999-2013

Note: For simplicity in this figure, cases with mixed VTEC O157/other serogroup infections are included in the data for O157, as are probable cases linked to known E. coli O157 outbreaks. Non-O157 data includes cases with mixed non-O157 infections and probable cases linked to known O26 outbreaks

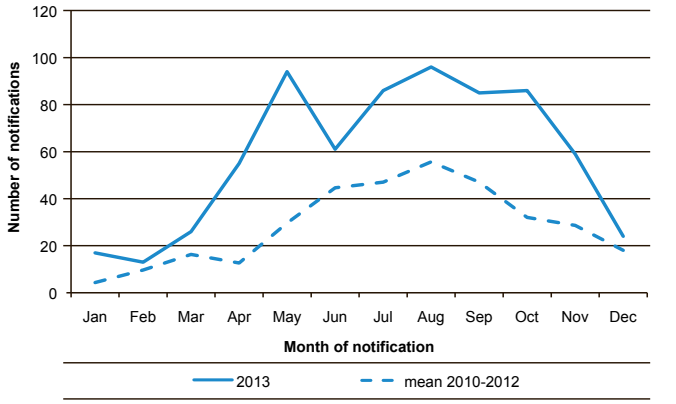

Figure 2. Seasonal distribution of VTEC notifications, Ireland 2013 compared to the mean number of notifications 2010-2012

Table 2. Number of VTEC notifications by infecting serogroup and verotoxin and HUS status, Ireland 2013

Serogroup[a]	HUS	non-HUS	Total
O157 VT1[b]	0	1	**1**
O157 VT2 or epi-linked to O157 VT2 outbreak	11	178	**189**
O157 VT1+VT2 or epi-linked to O157 VT1+VT2 outbreak	3	32	**35**
O26 VT1 or epi-linked to O26 VT1 outbreak	1	102	**103**
O26 VT2 or epi-linked to O26 VT2 outbreak	0	10	**10**
O26 VT1+VT2 or epi-linked to O26 VT1+VT2 outbreak	3	102	**105**
O26 serodiagnosed	1	0	**1**
Other VT1	1	114	**115**
Other VT2	7	80	**87**
Other VT1+ VT2	1	52	**53**
No organism	3	-	**3**
Total	**31**	**671**	**702**

[a]For simplicity mixed infections were recorded as O157 if at least one strain was O157, as O26 if at least one strain was O26 but not O157, and as Other if only non-O157 non-O26 strains were detected.
[b]One case was reported as positive for *vt1* and O157 by PCR; it is possible that these genes were not detected from the same strain

in 2013 relative to the mean monthly number of cases in the years 2010-2012. Despite the very large increase in the number of notifications, the typical summer seasonal peak was maintained, but was slightly higher than previously in the early part of the summer the peak months were May and August, followed by July, September and October.

Like 2012, there was variation in the seasonal distribution by serogroup, with VTEC O157 showing the typical peak in numbers in late summer; in contrast, VTEC O26 notifications peaked in May and July during 2013 (Figure 3). Other non-O157 serogroups were also more common in early summer in 2013.

Regional distribution

While the overall VTEC incidence rate nationally increased significantly compared to 2012, examining by VTEC serogroup showed that the increase was due to a large significant increase in the reported rate of non-O157 infections, while the reported rate for VTEC O157 actually decreased although not significantly.

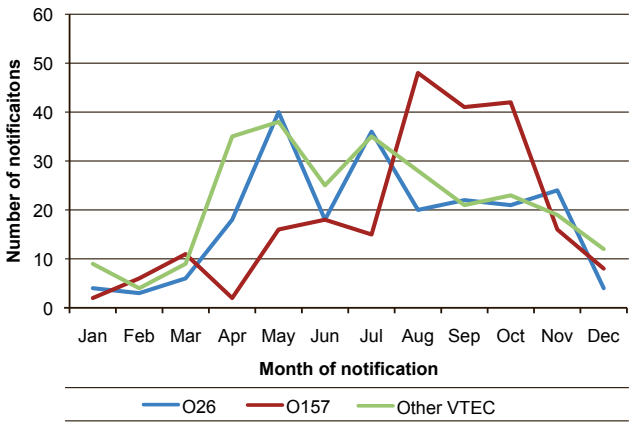

Figure 3: Seasonal distribution of VTEC notifications by serogroup, Ireland 2013

Reviewing at the regional incidence rates for VTEC O157, the reported incidence rates by area were not significantly different compared to 2012. The HSE E reported a rate significantly lower than all other areas in 2013, while the rate for the HSE NE was significantly lower than for four of the other HSE areas.

The crude rate for non-O157 infections was higher than for VTEC O157 in six HSE areas (Table 3; Figure 4). There were significant increases in the reported incidence of non-O157 for three HSE areas: the HSE E, HSE MW and HSE SE; this is likely to have been influenced at least in part by changes in local diagnostic practices.

The highest VTEC incidence rate overall were reported in the HSE MW followed by the HSE SE, where the rates were two to two and half times the national crude rate (Table 3). Atypically, the HSE NE reported the lowest overall crude incidence rate (Table 3), followed closely by the HSE E and HSE NW. The reported incidence rates in these three areas were significantly lower than the rates reported in the other five areas.

The relative ranking of HSE areas by overall VTEC incidence was fairly similar to the the ranking of areas by HUS incidence rate suggesting that the differences observed are likely to be a reasonable reflection of the true differences in risk between HSE areas.

Age-sex distribution

As in previous years, the highest reported age-specific incidence rate was in the 0-4 years age group (~ 80 per 100,000). Incidence rates were higher among females in all age groups over 25 years, and were slightly higher in males than females in the 0-4 year age group (Figure 5).

Laboratory typing

In 2013, the serogroup and verotoxin profiles of VTEC isolates/samples referred to the PHL HSE Dublin Mid Leinster, Cherry Orchard Hospital are displayed in Table 4. The most common serogroup reported was VTEC O157 (n=215), closely followed by VTEC O26 (n=213). Among the other serogroups listed by the World Health

Table 3. Number and crude incidence rate VTEC by serogroup and HSE area, and number and crude incidence rate VTEC-associated HUS by HSE area, Ireland 2013

HSE-area [a]	Number [CIR (95% CI)] VTEC O157 [b]	Number [CIR (95% CI)] non-O157 VTEC [c]	Number [CIR (95% CI)] all VTEC [d]	Number [CIR (95% CI)] VTEC-associated HUS
E	34 [2.1 (1.4-2.8)]	53 [3.3 (2.4-4.2)]	**89 [5.5 (4.4-6.6)]**	5 [0.3 (0.0-0.6]
M	20 [7.1 (4.0-10.2)]	50 [17.7 (12.8-22.6)]	**70 [24.8 (19.0-30.6)]**	2 [0.7 (-0.3-1.7)]
MW	29 [7.7 (4.9-10.4)]	122 [32.2 (26.5-37.9)]	**151 [39.8 (33.5-46.2)]**	4 [1.1 (0.0-2.1)]
NE	13 [3.0 (1.4-4.6)]	2 [0.5 (-0.2-1.1)]	**15 [3.4 (1.7-5.1)]**	2 [0.5 (-0.2-1.1)]
NW	12 [4.7 (2.0-7.3)]	4 [1.6 (0.0-3.1)]	**16 [6.2 (3.2-9.2)]**	0 [0.0 (0.0-0.0)]
SE	36 [7.2 (4.9-9.6)]	111 [22.3 (18.2-26.5)]	**148 [29.7 (25.0-34.5)]**	10 [2.0 0.8-3.3)]
S	45 [6.8 (4.8-8.8)]	66 [9.9 (7.54-12.3)]	**111 [16.7 (13.6-19.8)]**	4 [0.6 (0.0-1.2)]
W	36 [8.1 (5.4-10.7)]	66 [14.8 (11.2-18.4)]	**102 [22.9 (18.5-27.4)]**	4 [0.9 (0.0-1.8)]
IE	225 [4.9 (4.2-5.5)]	474 [10.4(9.4-11.3)]	**702 [15.3 (14.2-16.4**	31 {0.7 (0.4-0.9)]

[a]Rates per 100,000 calculated using CSO census 2011 for denominator data
[b] For simplicity, cases with mixed VTEC O157/other serogroup infections are included in the data for O157, as are probable cases linked to known E. coli O157 outbreaks.
[c] Non-O157 data includes cases with mixed non-O157 infections and probable cases linked to known O26 outbreaks.
[d] Possible cases (i.e. those with no associated organism are also included in this column), and therefore the total in this column will not always be the sum of the previous two columns.

Organisation as having the highest association with HUS internationally, there were eighteen VTEC O103 cases, seven VTEC O111, and seventeen VTEC O145. There was a large increase in the variety of other non-O157 serogroups reported, and in the number of cases infected with ungroupable strains (this included those cases diagnosed by PCR only).

As usual among VTEC O157 in Ireland, isolates containing the genes for verotoxin 2 (*vt2*) were more common (84%) than strains containing both *vt1* and *vt2*. VTEC O26 strains containing only *vt1* made up 47% of all VTEC O26 reported, with 48% of VTEC O26 containing the genes for both *vt1* and *vt2*, and those containing *vt2* making up the remaining 5% of VTEC O26. *vt2*-containing strains made up the majority of O145 strains (82%), *vt1*-containing strains made up the majority of O103 strains (89%), while VTEC O111 strains comprised both *vt1*-containing (57%) and *vt1+vt2*-containing (43%) strains.

Risk factors

Under enhanced surveillance for VTEC, risk factor information is routinely collected on VTEC notifications (Table 5).

Exposure to farm animals or their faeces and exposure to private well water were relatively common among cases; 36.7% and 35.0% reported these exposures respectively, although both were less commonly reported than in 2012. According to CSO data, in the general population, around 10.1% of households are served by private wells, indicating that, on a national basis, exposure to private wells appears to be more common among VTEC cases than among the general population.

Unlike salmonellosis, foreign travel plays only a minor role in VTEC infection in Ireland, with the overwhelming majority of infections acquired indigenously.

Where the information was available, around a quarter of VTEC cases in 2013 were reported to attend a Childcare Facility (CCF). When these analyses were restricted to notified VTEC under five years of age, over half reported attendance at a childcare facility. This is higher than the proportion of children in the general population who use non-parental childcare (42%) as reported by the Central Statistics Office.[10]

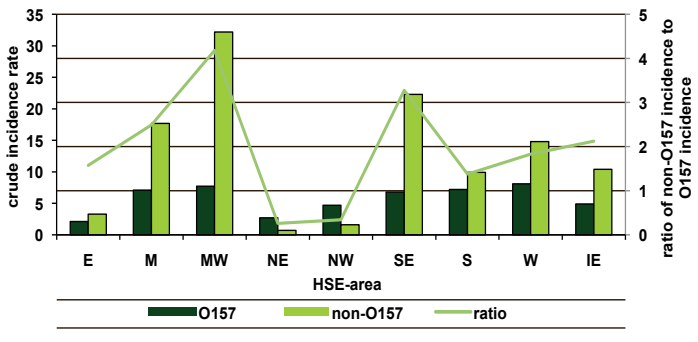

Figure 4: Crude incidence rate VTEC O157 and non-O157, Ireland 2013

Outbreak and environmental investigations

The outbreak surveillance system plays a key role in our understanding of VTEC transmission in Ireland. Ninety-six VTEC outbreaks were notified in 2013, which included 315 of the 702 VTEC notifications. 29 outbreaks were due to VTEC O157, 43 to VTEC O26, eight were mixed VTEC strain outbreaks, and 16 were caused by other VTEC strains.

The majority of outbreaks (83%) were family outbreaks, with sixteen general outbreaks notified. The 80 family outbreaks resulted in 133 persons becoming ill, an

Table 4. Serotype and verotoxin (vt) profiles associated with laboratory confirmed VTEC cases, as determined at the VTEC-NRL at PHL HSE DML in 2013

Sero-group	vt1	vt1+vt2	vt2	N/A	Total
O157	1[a]	34	180		**215**
O26	100	102	10	1[b]	**213**
O103	16	2			**18**
O145	2	1	14		**17**
O111	4	3			**7**
O55	1		5		**6**
O91	1	4	1		**6**
O146	4	1			**5**
O84	4				**4**
O5	3				**3**
O113			3		**3**
O182	3				**3**
O153			3		**3**
O105c			2		**2**
O104	1	1			**2**
O117	1		1		**2**
O130			2		**2**
O165		1	1		**2**
O178		1			**1**
O159			1		**1**
O78	1				**1**
O180			1		**1**
O98	1				**1**
O181	1				**1**
O76		1			**1**
O118			1		**1**
O8			1		**1**
O2			1		**1**
O73	1				**1**
O108	1				**1**
O101		1			**1**
O140		1			**1**
O74			1		**1**
O166		1			**1**
Un-group-able	70	34	49		**153**
Mixed in-fections	~	~	~		**9**
Total	**218**	**190**	**282**	**1**	**691**

[a]One case was reported as positive for *vt1* and O157 by PCR; it is possible that these genes were not detected from the same strain
[b]No vt type for one VTEC O26 case, as diagnosed by serodiagnosis

average of 1.7 (range 1-5) persons ill per outbreak, while the sixteen general outbreaks resulted in 88 persons becoming ill, an average of 5.5 (range 1 to 31) persons ill per outbreak.

Seventy-seven outbreaks occurred in private homes, seven involved childcare facilities, six were community outbreaks (note: two of these also involved childcare facilities), two involved extended families, one was travel-related, one was in a community hospital/long stay unit, and the locations for two outbreaks was not specified.

The suspected modes of transmission are listed in Table 6.

Person-to-person spread is consistently the most common mode of VTEC transmission reported in Ireland, particularly between young children, and was suspected to have played a role in 46 (48%) VTEC outbreaks in 2012 in which 105 persons were reported ill (Table 6 and Figure 5). Thirty seven of these outbreaks were reported as being solely due to person-to-person transmission, including five of the outbreaks which occurred in CCFs.

The second most common transmission route was Animal/Environmental contact, which was reported to have contributed to 10 outbreaks (10.4%) with 15 persons ill. All were family outbreaks in private houses. This is the largest annual number of VTEC outbreaks due to this transmission route since outbreaks became notifiable in 2004 (Figure 6). There are few details available, however, exposure to calves was mentioned in one outbreak, exposure to sheep in another, and exposure to farm manure in a third.

The third most common transmission route reported was waterborne transmission, which was reported to have contributed to 8 outbreaks (8.3%) with 16 persons ill. This is fewer than half the number of waterborne VTEC outbreaks reported in 2012. Two were general outbreaks and six were family outbreaks; these 8 outbreaks were linked to 7 domestic private wells, and one group water scheme. For one outbreak, VTEC other than that identified in the outbreak cases was detected in the implicated supply. Evidence was circumstantial for the water supplies suspected in the remaining outbreaks. For the six family outbreaks, the location was reported as private house. One general outbreak in a childcare facility was reported as waterborne plus person to person spread; initial transmission to the index case in the CCF was by waterborne transmission at home, with onward person-to-person transmission within the CCF. The second general outbreak was a small community outbreak associated with a group water scheme.

Five outbreaks (51 persons ill in total) were reported as being suspected to be foodborne, three general and two family outbreaks. In one small community outbreak in HSE MW with two persons ill, microbiological and descriptive epidemiological evidence implicated an

Table 5. Number of cases of VTEC (and percentage where known) for selected risk factors, Ireland 2013

Risk factor	Number 'Yes' and % where reported	Number 'No' and % where reported	Number where risk factor was unknown or not reported
Food suspected	42 (8.4%)	457 (91.6%)	203
Exposure to farm animals or their faeces	231 (36.7%)	398 (63.3%)	73
Exposure to private well water[a]	223 (35.0%)	413 (65.0%)	66
Travel-associated[b]	16 (2.4%)	651 (97.6%)	35
Attendance at a CCF[c]	155 (26.5%)	430 (73.5%)	117
Attendance at a CCF[c] (among <5 yrs)	146 (55.7%)	116 (44.3%)	41

[a]Composite variable recoded from two different water supply exposure enhanced variables in CIDR
[b]Inferred from CIDR core variable *Country of Infection*
[c] *CCF=Childcare Facility*

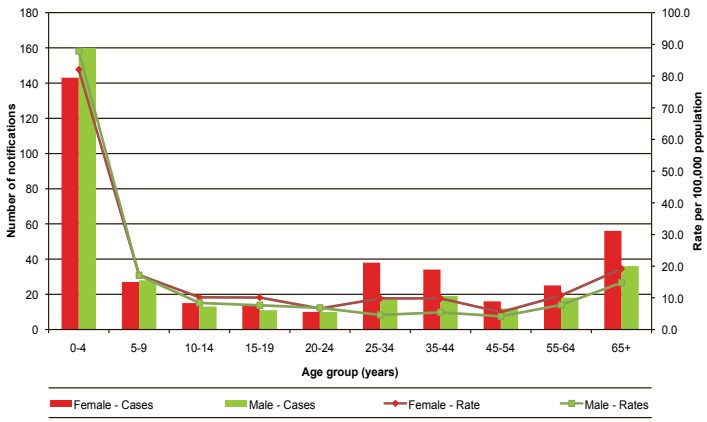

Figure 5. Age-sex distribution VTEC notifications, Ireland 2013

unpasteurised cheese. This is the first time in Ireland where there has been strong evidence implicating a raw milk cheese in a foodborne VTEC outbreak.

Two further general community foodborne outbreaks were notified with 45 persons ill (51 laboratory confirmed cases) between them. Both were national outbreaks, and evidence of the microbiological link between cases was based on detailed laboratory typing undertaken at the VTEC Reference Laboratory at Cherry Orchard Hospital. Cases were diffusely distributed; and although no evidence was obtained suggesting any particular food as the source, foodborne transmission was suspected given the geographical spread of the primary cases and the absence of other exposures common to all which might explain the outbreak. For one of these outbreaks, approximately half of cases in the outbreak appear to result from secondary spread in a childcare facility. A further small family outbreak was suspected to be due to the consumption of raw milk at home, while the remaining foodborne family outbreak was associated with exposure in Africa.

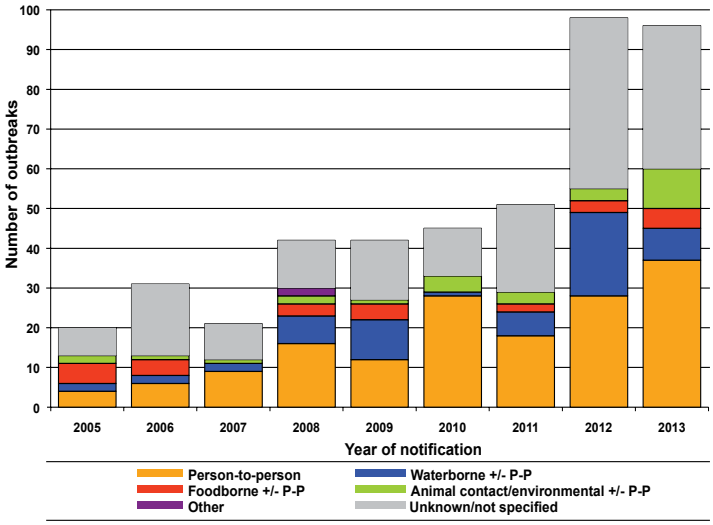

Figure 6. Number of VTEC outbreaks by suspected transmission route and year, Ireland 2004-2013

Note: In this figure, reported transmission routes were grouped for simplicity. Any outbreak where food contributed was reported as foodborne, any outbreak where water contributed was reported as waterborne, any other outbreak where animal contact contributed was reported as Animal contact. Person-to-person outbreaks include only those outbreaks reported as being due only to person-to-person transmission.

For 38% (n=36) of VTEC outbreaks in 2013, the transmission route was reported as unknown or not specified (Table 6 and Figure 6).

In sporadic case investigations, a further seven private supplies investigated as possible sources were positive for VTEC either by culture or PCR. In two instances, the strains detected were similar to those identified in the associated human cases.

Summary

There was a statistically significant increase in the number of VTEC notifications in 2013 relative to 2012. The great majority of this increase was accounted for by non-O157 non-O26 VTEC cases, which increased by 180% relative to 2012, coinciding with continuing changes in diagnostics in primary hospital laboratories during this time. In contrast, the incidence of VTEC O157 actually decreased in 2013 although not significantly.

Guidance for Laboratory Diagnosis of Human Verotoxigenic *E. coli* Infection developed by The Laboratory Sub-Group of the VTEC Sub-Committee of the HPSC Scientific Advisory Committee was issued in September 2014. It is anticipated that this will further contribute to a coordinated approach to VTEC diagnosis in Ireland.[11]

Within the European Union, the latest available data shows that the overall incidence rate for confirmed VTEC cases in Europe in 2012 was 1.15 (range 0.0-8.99).[1] Ireland, Luxembourg, Sweden and Denmark reported the highest confirmed incidence rates at that time. It seems likely when the data are available across Europe for 2013, that Ireland will have one of the highest reported incidence rates in Europe again.

Foodborne transmission was the first recognised transmission route for VTEC infection historically, with minced beef, unpasteurised dairy products, and fresh produce consumed raw all having been implicated

Table 6. VTEC outbreaks by suspected mode of transmission, Ireland 2013

Transmission Route	Number of outbreaks	Number ill	Number of associated CIDR Events
Person-to-person	37	76	102
Foodborne	3	34	35
Person-to-person and Foodborne	1	14	19
Waterborne	7	12	19
Person-to-person and Animal Contact	7	11	17
Person-to-person and Waterborne	1	4	9
Animal contact	2	2	4
Environmental / Fomite	1	2	3
Foodborne and Animal Contact	1	3	2
Unknown	31	57	90
Not Specified	5	6	15
Total	**96**	**221**	**315**

in outbreaks across the world. Foodborne outbreaks typically comprise a small percentage of the total number of VTEC outbreaks in Ireland; in 2013, they made up 5% of outbreaks, however, they caused a disproportionately high proportion of VTEC outbreak cases (23%). This was largely due to the occurrence of two nationally distributed community outbreaks which were suspected to be foodborne but for which the source of infection was not established. Both outbreaks were caused by strains of VTEC O157 VT2 strains (the most common VTEC variant reported historically in Ireland), and molecular typing of VTEC isolates at the VTEC Reference Laboratory was key in determining which cases occurring around the country were included/excluded from each of the two outbreaks.

For the first time in Ireland, there was strong evidence implicating a food product in a VTEC outbreak; an unpasteurised cheese was implicated in a small outbreak with two persons ill in the HSE MW. A thorough investigation was undertaken, alerts were issued and the implicated product was withdrawn from sale. Also in 2013, a small family outbreak was suspected to be due to consumption of unpasteurised milk at home.

Unusually, animal/environmental contact was reported as the second most common route of transmission for VTEC outbreaks in 2013. This has long been recognised as a risk factor for VTEC infection[,8-9] and cases due to this transmission route are not unexpected in Ireland given the large cattle population, the high proportion of rural dwellers, and the large number of farming families. Fortunately, none of these animal contact outbreaks were associated with public venues such as open farms, and so the numbers of people affected were small. Advice is available on the HPSC website on how to minimise the risk of gastrointestinal infections following exposure to farm animals and environments, and for the safe recreational use of farmland.[12]

In 2013, contaminated drinking water contributed to fewer outbreaks that in 2012. As in previous years, all drinking water associated outbreaks reported were linked with private water supplies. Exposure to water from contaminated untreated or poorly treated private water supplies has historically been recognized as a strong risk factor for VTEC infection in Ireland.[6,7] This has been particularly pronounced following periods of heavy rainfall. The lower number of outbreaks in 2013 is likely to have been influenced by lower rainfall levels and less contamination of private water sources. The HSE and EPA have both developed resources for owners of private wells, providing advice on private well maintenance.[13-14]

Transmission by person-to-person spread, however, remained the most common transmission route reported in VTEC outbreaks (48% of outbreaks), as usual being most frequently associated with private house and childcare facility outbreaks. Handwashing and exclusion of cases in risk groups from high risk settings remains a key prevention measures for VTEC.[15]

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