

# Verocytotoxigenic *Escherichia coli* (VTEC) and Haemolytic Uraemic Syndrome (HUS)

(Urgently Notifiable)<sup>1</sup>

**Description:** *Escherichia coli* are gram-negative rods that form part of the microbiota or normal flora of the lower GI tracts of vertebrates. They synthesise Vitamin K in the

Parents of small children should be advised on diagnosis that their child might continue to shed for extended periods and will not be able to return to childcare while still excreting VTEC

bowel and, through their sheer volume, displace other, pathogenic organisms from occupying the human GIT. VTECs were first identified as human pathogens

in 1982 and since then have evolved and spread to become one of the commoner and most serious IIDs in Europe and North America. VTEC produces a potentially serious, highly infectious diarrhoeal and systemic illness. In about 10% of cases it causes haemolytic uraemic syndrome (HUS) the commonest cause of renal failure in children.

**Annual numbers:** Between 200 and 250 cases per year. Ireland has the highest VTEC notification levels in the EU.

**Seasonal Distribution:** There a sustained peak in VTEC incidence from August until October.

**Causative Agent:** *E. coli* O157 is the most frequently implicated VTEC serogroup. Other examples include *E. coli* O26, O111, O103 and O145.

**Reservoir:** VTEC is a normal commensal in the gastrointestinal tract of ruminants, including cattle, sheep, goats and other farmed mammals. Rarely, it can cause disease in young ruminant animals.

## Transmission:

**Primary:** VTECs are transmitted through ingestion of food or water contaminated with infected faeces and by direct contact with an animal carrier. It is likely that waterborne and person-to-person transmission accounts for more than 80% of cases in the US. In Ireland it is likely that less than a quarter of cases are directly attributable to foodborne spread.

**Secondary:** Person to person transmission is a secondary, but extremely significant, mode of transmission.

**Incubation period:** Medium: typically 3-4 days with a range of 1-8 days. Duration of illness is generally seven to 10 days.

**Outbreak Potential:** VTEC has high outbreak potential if transmitted through food and from person to person and very high to extremely high outbreak potential if transmitted through water.

**Period of communicability:** Patients are infectious from onset of symptoms until disappearance of viable bacteria from the stools, but are considerably more infectious whilst symptomatic. VTEC may be shed in the stool for several weeks following resolution of diarrhoea. Children tend to continue to shed for longer than adults. An asymptomatic carriage state is increasingly recognised, in which individuals who show no clinical signs of disease, nonetheless shed and can go on to infect others. This risk appears greatest in children under 5 years of age. In one documented instance a small child shed VTEC for more than 6 months being unable to return to school during this period.

**Epidemiology:** VTEC was initially considered almost solely a foodborne pathogen (this is still the case in a number of countries) but it has a marked propensity for person-to-person spread. Recently in Ireland, it has been identified in a number of waterborne outbreaks and is not infrequently found in untreated private well supplies. The inoculum is tiny, as few as 2 or 3 organisms.

VTEC gastroenteritis is a serious illness – HUS complicates up to 10% of cases

Descriptive epidemiology of cases indicates that food is suspected in 12% of cases, animal contact is reported in 52% of cases and 43% of cases had potential exposure to a private well (as compared with 10% of the general population). It has a marked tendency to produce HUS (more than 90% of HUS cases are thought to be caused by VTEC and about 10% of cases of VTEC will go on to develop HUS, this risk being highest in children under the age of five). Most outbreaks are restricted to individual households but general outbreaks most commonly occur in crèches.

**Exposure-prone groups:** farming families, children in daycare, daycare staff, those consuming untreated, unprotected water (e.g. from wells and ground water), those exposed to contaminated food, food handlers, residents in institutions.

**Pathogenesis:** Verotoxin (similar to the Shiga toxin of *Shigella dysenteriae*) released by VTEC strains adheres to and disrupts the intestinal epithelium leading to a haemorrhagic colitis. There are verotoxin receptor cells in the renal epithelium (and to a lesser extent in the CNS), and toxin-mediated inflammation leads to thrombin and fibrin deposits in the microvasculature,

1. HUS alone (i.e. in the absence of bloody diarrhoea or other gastroenteric symptoms) should be assumed to be caused by VTEC and should be notified to the local Medical Officer of Health either as a **probable** case of VTEC if there is an epidemiological link to a known case of VTEC or as a **possible** case of VTEC if there is no such epidemiological link.

most notably in the kidneys, leading to thrombocytopenia, microvasculature thrombosis, thrombus formation, tissue oedema and acute renal failure.

**Clinical Features:** Abdominal pain which may often be severe (>90%), diarrhoea (severe in >60%) and haemorrhagic colitis (bloody diarrhoea in >25%). Fever is not a common finding in children and highly unusual in adults. In children headache (50%) and myalgia (25%) are prominent. At all ages anorexia is invariable. Haemolytic uraemic syndrome (HUS) develops in about 10% of cases, particularly in children and the elderly. In

**Every** case of HUS should prompt a search for VTEC; stool should be submitted for examination for toxin-producing *E. coli*.

the US, the hospitalisation rate for VTEC has been estimated to be 2-3%, while the case fatality rate is 8:10,000 cases. In Ireland, the hospitalisation rate

from national data is in excess of 40%. So close is the association between HUS and VTEC, that each case of HUS must be assumed to be caused by VTEC unless proven otherwise.

#### Management of Cases

Enteric precautions.

Individual cases should be referred to hospital as soon as early symptoms of HUS appear. In addition, paediatric and elderly patients should be admitted if the clinical picture suggests the need (i.e. copious diarrhoea indicating the onset of dehydration or heavy bleeding).

Obtain information on:

- food and water consumption for preceding 7 days
- recent travel
- recent contact with people with GI symptoms
- recent animal contact

In the case of children:

- information on attendance of crèches
- petting farms
- other risk factors.

The case should be notified to the local Department of Public Health. It is important to determine if the case is aware of similar cases suggesting the possibility of an outbreak. Determine if case is in a risk category. HPSC has published extensive national expert guidance on the [management of VTEC infection](#). This document should be consulted for definitive advice on the management of VTEC infection and outbreaks. Information on the [management of VTEC infection in childcare facilities](#) is also available.

**Food Hygiene Implications:** Food hygiene re-education is necessary for food handlers.

#### Management of Contacts

Screen contacts if in risk groups.

Reinforce hygiene advice to contacts in particular hand washing. Children's handwashing in nurseries should be closely supervised.

**Exclusion:** All cases: Until 48hr after first normal stool. If case or contact is in a risk group, exclude until microbiological clearance. It is

important that parents of small children be alerted to the fact that such children can excrete for extended periods of time and will not be allowed to rejoin classes until microbiologically clear.

**All cases** of VTEC should be excluded as soon as confirmed. Cases in Risk Groups **must not** return to work/crèche until microbiological clearance is confirmed

**Microbiological Clearance:** Two consecutive negative stool samples taken at least 48 hours apart. In the case of symptomatic cases, both negative stool samples must have been taken after recovery from diarrhoea.

**Resources:** on VTEC are available at <http://www.hpsc.ie/hpsc/A-Z/Gastroenteric/VTEC>.

**Notifiable:** **urgently**, to the local [Medical Officer of Health](#).

### **Haemolytic Uraemic Syndrome (HUS)** (Notifiable under VTEC)<sup>2</sup>

**Description:** HUS is a clinical syndrome characterised by a haemolytic anaemia, acute renal failure and thrombocytopenia. First described in 1955, it is today most frequently associated with diarrhoeal infection with VTEC. HUS is the commonest cause of acute renal failure in children. The diarrhoeal form most commonly affects children under the age of five and, unlike the non-diarrhoeal form without an infectious element, is generally associated with recovery of renal function.

**Onset:** the mean interval between onset of VTEC diarrhoea and onset of HUS is seven days (range 2-14 days).

**Causative Agents:** most commonly associated with VTEC and occasionally *Shigella dysenteriae* and very occasionally *Campylobacter* or HIV infection. Neuraminidase-producing organisms such as *Streptococcus pneumoniae* and *Clostridium butyricum* very occasionally produce HUS. Non-infectious causes include drugs (contraceptive pill and cyclosporine), malignancy, post partum and idiopathic.

**Annual numbers:** Between 15 and 20 VTEC associated HUS cases per year.

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2. Cases of HUS (irrespective of the age of the patient) are notifiable under VTEC as "Possible cases of VTEC".

**Clinical Features:** As many as 95% follow infection with VTEC. Anaemia and uraemia usually present with weakness, lethargy and sleepiness. Irritability in children may be a presenting feature. There may be purpuric areas on the skin.

- **Renal:** microscopic haematuria is common but gross haematuria can occur. Albuminuria is common, renal failure varies from mild to that requiring dialysis.
- **Cardiovascular:** diarrhoeal associated HUS patients are normotensive. Hypertension can occur in the non-infectious form with ocular involvement including retinopathy and exudates. Heart failure can occur particularly in the post partum form. DIC is very rare.
- **CNS:** microvascular damage can lead to developmental retardation and focal motor deficit. Seizures are not uncommon.
- **GIT:** very occasionally GI perforation due to microvascular ischaemic infarction and, in children, intussusception.
- **Skin:** pallor and purpura.
- **General:** fatigue, irritability, low/absent urinary output, oedema and confusion.

**Investigation:** should be commenced when symptoms of HUS (renal failure

- **RBC:** Anaemia is typical (Hb = 7-9g/L)
- **Platelets:** usually fall to below  $50 \times 10^9/L$
- **Leucocytes:** often rise to  $20-30 \times 10^9/L$
- **Clotting:** PT and APPT tend to be normal. FDPs and clotting time are raised.

**Clinical Management:** In a VTEC case, symptoms and signs of HUS (such as falling urinary output, weakness, lethargy, sleepiness, irritability, pallor, purpura, occasionally seizures) should prompt an urgent nephrological opinion. Supportive therapy is still the mainstay during the acute phase. Antibiotics should be avoided. Fluid replacement is necessity in patients who are volume depleted. Electrolyte imbalance should be corrected. Transfusion may be necessary if the anaemia is very severe. Dialysis is only needed in the more severe cases. The case should be notified to the local Department of Public Health. It is important to determine if the case is aware of similar cases suggesting the possibility of an outbreak. Determine if case is in a risk category.

#### **Public Health Investigation and Management:**

Irrespective of the presence or otherwise of diarrhoea, all HUS cases should be investigated and managed from a public health perspective, as suspected cases of VTEC infection until proven otherwise. All cases of HUS should be reported to the local Department of Public Health.

**Outcome:** Spontaneous recovery is the rule. Children with HUS tend to less ill than adults, particularly the elderly, and adults require more aggressive therapy such as plasmapheresis and dialysis, more often than children. Infection-related HUS has a better prognosis than the non-infectious form.

After an average of four years after experiencing diarrhoea associated HUS, 9% of patients have died (most during the acute phase of illness), an additional 3% develop permanent end stage renal disease and 25% demonstrate renal sequelae. Severity of the acute illness, especially the presence of CNS symptoms, is strongly associated with worse long-term outcome.

In the elderly, the case fatality ratio is considerable higher than in children, possibly in excess of 50%.

**Notifiable:** **urgently**, to the local [Medical Officer of Health](#).

The cardinal features of HUS are

- **Falling urinary output**
- **Weakness**
- **Lethargy/malaise**
- **Sleepiness**
- **Pallor**
- **Purpura**
- **Epistaxis**
- **Oedema**

Appearance of such features in a case of VTEC (particularly if a child or elderly patient) should prompt an **urgent** paediatric/nephrological opinion.