The VTEC Support Document

Background evidence for the Public Health Management of infection with Verotoxigenic *Escherichia coli* (VTEC)

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Author	GI Programme Board VTEC working group (HQSD)	
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CONTACT INFORMATION	
	Trish Mannes
Telephone	08452799879
Email	trish.mannes@hpa.org.uk

RELATED DOCUMENTS:

This guidance should be used in conjunction with the companion document; **The VTEC Operational Manual**: *Essential Operational Guidance for the Public Health Management of Infection with* Verotoxigenic *Escherichia coli (VTEC)*.

Other closely related documents are:

HPA Incident and Emergency Response Plan[i]

Further information on the recommended laboratory standard methods is found on the *E. coli* pages of the HPA website: http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/EscherichiaColiO157/Laboratory or from http://www.hpa-standardmethods.org.uk/

SUPERSEDED DOCUMENTS:

Together, this VTEC Support Document and the VTEC Operational Manual supersede and replace previous operational guidance, including:

Guidelines for the control of infection with Vero cytotoxin Producing Escherichia coli (VTEC) – published in 2000 by the PHLS Advory Committee – GI Infections.

HPA criteria for reopening farms affected by E. coli O157, September 2009

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Acknowledgements

This guidance is based on the guidance produced by the Scottish Health Protection Network Strategy Group and was adapted for local use in England by members of the HPA Gastrointestinal Programme Board VTEC working group. Thank you to our Scottish colleagues for providing permission to use and adapt the SHPN guidance.

The working group thanks HPA Regional gastrointestinal leads, project managers in Yorkshire and Humber Region, and other colleagues who contributed to and commented on the content of this guidance.

Abbreviations

CPHM	Consultant in Public Health Medicine
CHP	Consultant in Health Protection
CCDC	Consultant in Communicable Disease Control
CfI	HPA Centre for Infections
Defra	Department for Environment, Food and Rural Affairs
EH	Environmental Health
E.coli	*Escherichia Coli*
EHO	Environmental Health Officer
ELISA	Enzyme-linked immuno-sorbent assay
ESQ	Enhanced Surveillance Questionnaire
FSA	Food Standards Agency
FWEL	Food, Water and Environment Laboratory
GEZI	Gastrointestinal, Emerging and Zoonotic Infections
GI	Gastrointestinal
GP	General Practitioner
HPA	Health Protection Agency
HPP	Health Protection Practitioner
HPU	Health Protection Unit
HQSD	High Quality Service Development
HSE	Health and Safety Executive
HUS	Haemolytic uraemic syndrome
ICT	Incident Control Team
IgM	Immunoglobulin M
IMS	Immuno-magnetic separation
ICN	Infection Control Nurse
IERP	HPA Incident and Emergency Response Plan
IRIS	HPA Incident Reporting & Information System
LARS	Local and Regional Services
LA	Local Authority
LGP	Laboratory of Gastrointestinal Pathogens, Colindale
NSAID	Non-steroidal anti-inflammatory drug
NSF	Non-sorbitol fermenting
OCT	Outbreak Control Team
PCR	Polymerase Chain Reaction
PCT	Primary Care Trust
REU	Regional Epidemiology Unit
RMN	Regional Microbiology Network
RMP	Registered Medical Practitioner
SF	Sorbitol-fermenting
TMA	Thrombotic microangiopathy
TTP	thrombotic thrombocytopaenic purpura
VLA	Veterinary Laboratories Agency
VTEC[1]	Verotoxigenic *Escherichia coli*

[1] The term VTEC refers to all strain of *E. coli* that produce Verocytotoxin (VT) or possess VT genes. VTEC of serogroup O157 are the most common type in the UK and are the only VTEC for which routine standard tests are performed in diagnostic laboratories. A small number of other VTEC are isolated from infections in England and Wales, generally in the Reference Laboratory (LGP) and they should not be ignored. However 'VTEC' as referred to in this document will in practice refer almost exclusively to VTEC O157.

1. Introduction

This guidance provides advice on the diagnosis and public health management of infection with Verotoxigenic *Escherichia coli* (VTEC) in England and Wales, of which serogroup O157 is the commonest.

The guidance was produced by the VTEC working group of the Health Protection Agency (HPA) Gastrointestinal Diseases Programme Board, and supersedes previously published guidance. It is adapted from the Scottish VTEC guidance document produced by the Scottish Health Protection Network Strategy Group[ii] to reflect local working arrangements, and draws on guidance and standard operating procedures previously published by the Agency[iii].

The guidance is aimed at those involved in the public health management of VTEC infections, including colleagues in Health Protection Units (HPUs), Local Authorities and Microbiologists, and provides basic information for frontline clinicians. It is acknowledged that the division of responsibility for public health follow-up and management of VTEC illness by HPUs and Local Authorities vary across England. Local arrangements should be considered when interpreting this guidance.

1.1 Aim and scope

The guidance provides easily accessible advice based on evidence, or expert consensus, on the public health management of cases, groups of cases, and contacts of possible, probable and confirmed VTEC infection. It is intended to support health protection professionals, and is not a replacement for professional judgment.

The guidance aims to:

- Improve the initial detection and management of cases to reduce the potential morbidity and mortality associated with VTEC infection;
- Prevent cases occurring either as a result of continuing exposure to a primary source, or secondary spread from person to person;
- Describes arrangements to be undertaken promptly by the HPA and partner agencies to protect the public from the consequences of infection with VTEC O157 or other VTEC.

The guidance does not provide advice on the clinical management of cases once diagnosis has been confirmed. GPs and front-line hospital staff should obtain such advice from specialist clinicians.

This document does not provide advice on the detailed operational conduct of outbreak investigations, as this information is available at local level in outbreak plans. More information about investigation and management of VTEC in specific settings such as open farms and schools is contained in the operational manual[iv].

More detailed background information and resources may be obtained from the *E. coli* pages on the HPA website.

2. Background

2.1 Clinical features

Incubation period

The incubation period for diarrhoeal illness caused by infection with VTEC is usually three to four days, is seldom less than one day or more than eight, but has been occasionally recorded as long as 14 days. Occasional reports of incubation periods of longer than 8 days may reflect secondary transmission rather than a prolonged incubation period[v].

Clinical presentation and sequelae

VTEC infection can be asymptomatic, or cause a spectrum of illness from mild non-bloody diarrhoea, through bloody diarrhoea and haemorrhagic colitis, to Haemolytic Uraemic Syndrome (HUS), other presentations of Thrombotic Microangiopathy (TMA), and death. Bloody diarrhoea is seen in 50% of cases of VTEC O157 cases in England and Wales[vi]. The illness is usually self limiting and resolves within 7 days[vii]. Children less than 5 years of age are the group most at risk of developing VTEC related HUS. A surveillance study of 3,464 VTEC cases in the US found that the proportion of cases who developed HUS was 15.3% among patients under 5 years, 7.9% among those aged 5–9 years, 3.4% among those aged 10–17 years, 1.2% among those aged 18–59 years, and 3.8% among those aged ≥60 years[viii]. However, this study found that those aged >60 years had the highest rate of death due to VTEC, whether or not they developed HUS. The frail, the immuno-compromised and the pregnant are especially vulnerable to other forms of HUS and may be predisposed to VTEC-related disease although the association is not proven[ix].

Period of excretion

Some of the earliest outbreaks and sporadic cases to be investigated suggested that excretion was short lived (less than five days)[x]. Prolonged excretion of the organism can occur, however, notably in young children[xi]. In one American study of preschool childcare facilities excretion was recorded in a child 62 days after developing symptoms[xii], and half of the cases were still excreting the organism 17 days after onset. A second study recorded shedding for a median of 29 days (range 11-57)[xiii]. It is possible that the period of excretion may differ for VTEC O157 and other VTEC. In an outbreak of O26 at an Irish nursery, clearance of the infecting organism took between three and five weeks[xiv].

2.2 Transmission

Introduction

VTEC O157 and other VTEC strains can colonise the gastrointestinal tract of farm animals, especially cattle and sheep, usually without causing illness. Other domestic and wild animals including birds can carry these organisms and act as vectors. Any food, water, or environmental surface contaminated by the excreta of an animal, human case, or asymptomatic excreter is a potential source of infection. Transmission from person-to-person is by the faecal-oral route. The number of *E. coli* O157 organisms that can cause human infection is low: estimates from analyses of vehicles incriminated in outbreaks suggest that the infectious dose is well under 1000 organisms[xv] and has been reported to be less than 50 bacteria[xvi]. The sources and routes of transmission of VTEC O157 and non- O157 serogroups of VTEC are probably generally similar, although information on sources and reservoirs for some VTEC is sparse[xvii].

Food

The surface of meat can become contaminated during slaughter and processing. Minced or ground products such as hamburgers or sausages where surface contamination of the meat

is spread throughout the whole product pose a particular risk if inadequately cooked. Surveys of retail meats not linked to outbreaks shows that VTEC O157 is rarely found although other VTEC may be present. Nevertheless milk may become faecally contaminated and VTEC may survive to cause illness if milk is unpasteurised or inadequately pasteurised. Raw vegetables and water may also be contaminated, by exposure to animal faeces. Foodborne infection may commonly result from the contamination of ready to eat products such as cooked meats, either at point of sale or in a domestic setting, probably by contact with raw meat. Large outbreaks of VTEC O157 in the UK have resulted from food hygiene failures at butcher premises[xviii] [xix].

Although meat or dairy products were implicated in large food-borne outbreaks of VTEC O157 in the United Kingdom[xx], food vehicles identified in outbreaks worldwide include salad leaves[xxi], white radish sprouts[xxii] and raw vegetables[xxiii] [xxiv]. Other food vehicles identified include ready-to-eat food items such as wraps[xxv] and more unusually, unpasteurised apple juice[xxvi] and fermented sausage[xvi].

Food (or water) contaminated with VTEC does not necessarily smell or taste unwholesome. Food-poisoning organisms are not food spoilage organisms.

Water

Exposure to surface water contaminated with animal excreta poses a risk of infection with VTEC, as does the consumption of water from private water supplies[xxvii]. Visitors to rural areas may be more susceptible to infection than local residents[xxviii]. Although unusual, failures in the treatment of the public water supply can cause large outbreaks[xxix]. A very large outbreak in Canada was caused by contamination of municipal bore-hole supply by run-off from agricultural premises[xxx].

Livestock and their environment, including open farms

VTEC infection may follow occupational or recreational exposure to animals, especially ruminants, their excreta (including in slurry), or any part of the environment contaminated by them[xxxi]. The importance of livestock and environmental exposures has been demonstrated in case-control studies of sporadic infections[xxxii] [xxxiii]. General outbreaks have occurred in the UK at farm premises of various kinds that are open to the public [xxxiv] [xxxv] [xxxvi] [xxxvii].

Cattle have been shown to be a reservoir of infection in many countries[xxxviii]. VTEC O157 was identified in 15.4% of faecal specimens from cattle for slaughter at one British abattoir and from 2.2% of sheep, but not from the pigs and poultry[xxxix]. In England and Wales VTEC O157 were recovered from 0.47% of beef carcasses at slaughter and from 0.83% of faeces from live cattle submitted for diagnostic purposes in 1994 and 1995[xl]. More recent large abattoir studies in Great Britain identified VTEC O157 on carcasses of sheep, cattle and pigs entering the food chain[xli] [xlii]. A large survey in Scotland found that 23% of farms and 7.9% of animals on these farms were shedding VTEC O157 at the time of survey[xliii]. VTEC O157 have been isolated from live sheep, horses, farmed deer, goats, dogs, geese, pigs, and wild birds (including gulls and rooks)[2] [xliv].

Husbandry practices may influence the prevalence in herds[xlv] [xlvi] [xlvii]. VTEC O157 can survive for over 12 months in cattle faeces and for over 20 weeks in soil samples[xlviii]. Agricultural workers may harbour VTEC asymptomatically[xlix] and have serological evidence of exposure to VTEC[l].

Person-to-person spread

Person-to-person spread of infection with VTEC is common. Secondary spread may cause up to 20 to 30% of cases in outbreaks[li], and 6 to 17% in the general population[lii]. Children aged <6 years are at particularly high risk of transmitting infection to others. Over a 17 year period, there were 24 reports of outbreaks due to person-to-person transmission of

VTEC in nurseries in England and Wales (see table 1). Over the same time period there were 5 reports of outbreaks with person-to-person spread in primary schools, although only two of these primary school outbreaks were reported to involve children over the age of 5 years, and one of these involved two children only. This coincides with data from a review of 90 published outbreaks from around the world[li], which found that statistically significant higher rates of secondary transmission were found in outbreaks with a median age of <6 years, and those with secondary transmission via person to person spread in nurseries. Although this review found that secondary cases were also reported from some primary and secondary school outbreaks, secondary transmission in these outbreaks seems to be limited to family members[li] above. The reason for a particularly high rate of secondary cases in nursery outbreaks is likely to be multifactorial, facilitated by close contact between children with immature immune systems, poor personal hygiene and a higher likelihood of shedding bacteria for extended periods.

Between four and 15% of sporadic infections appear to have occurred as secondary infections in households[liii]. Infection does not have to be direct; it can, as with transmission from animals, spread via the environment including surfaces, paddling pools, and even shared towels. An infectious dose may be present on the hands or the environment without visible contamination.

Table 1 shows the number of VTEC outbreaks in different settings reported to HPA (Gastrointestinal Emerging and Zoonotic Infections Department, GEZI):

TABLE 1. General outbreaks of Vero-cytotoxin producing E coli O157 caused by person-to-person transmission - outbreak setting types in England and Wales (1992-2009) (courtesy Bob Adak, HPA)

SETTING TYPE	NUMBER OF PERSON TO PERSON OUTBREAKS
NURSERY OR PRESCHOOL	24
PRIVATE HOUSE	11
NURSING/CARE HOME	7
COMMUNITY	6
HOSPITAL	5
PRIMARY SCHOOL	5
OTHER	2
TOTAL	**60**

2.3 Epidemiology

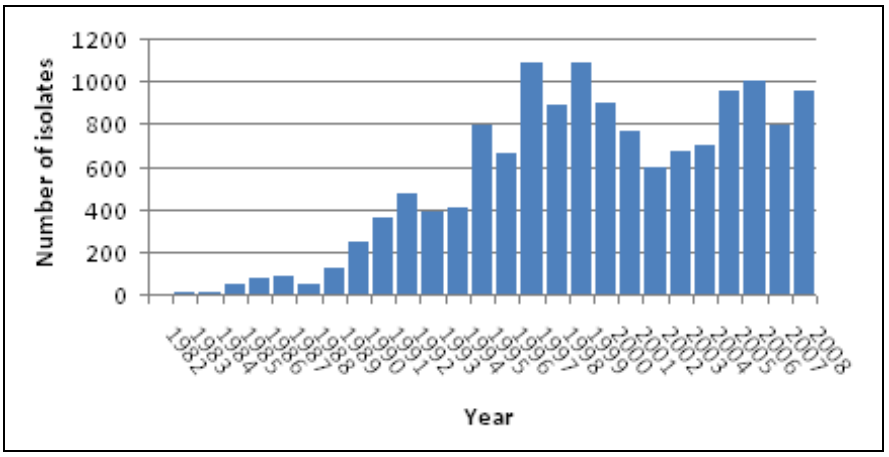
E. coli O157 is the most common serogroup of VTEC causing infections in the UK. It is also the most likely E.coli serogroup to cause bloody diarrhoea in the UK, and HUS/TMA worldwide[liv]. Non-sorbitol fermenting (NSF) VTEC O157 are the only strains that can be routinely screened for in UK diagnostic laboratories by current methods, so the true incidence of non-O157 VTEC is not known. There are more than 300 serotypes of VTEC. Most serotypes are not known to be pathogenic, although a variety of serotypes of E. coli can contain VTEC genes and cause disease; including O26 and O111[lv lvi].

In the late 1980s confirmed human isolates of VTEC O157 in England and Wales increased markedly, peaking in the late 1990s. Since 2005 between 828 and 1034 isolates of VTEC O157 have been confirmed from human sources. A small number of VTEC strains (<10) per year in addition to NSF VTEC O157 are isolated annually from faeces, and some of these are linked to serious illness. In Scotland more than 97% of VTEC isolates are serogroup O157 but isolations of other serogroups have increased in recent years.

The annual incidence of VTEC O157 in England and Wales is shown in Figure 1. There were 1034 isolates of VTEC O157 confirmed in 2009 in England and Wales (provisional numbers HPA).

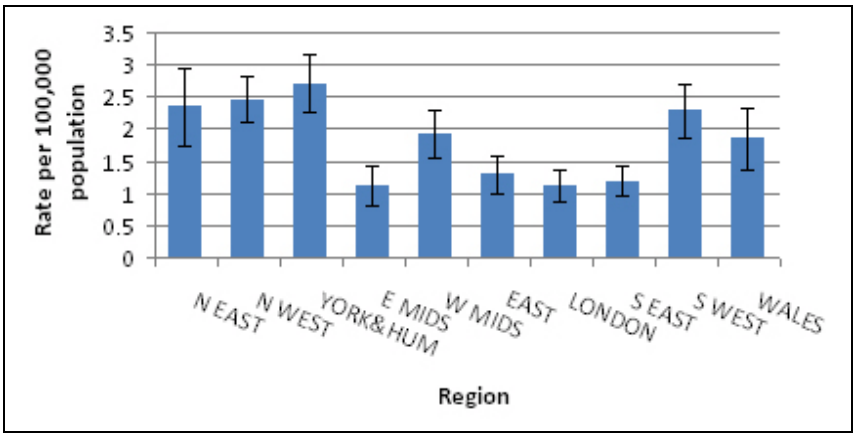
Reported incidence of VTEC O157 varies within England and Wales, with highest rates occurring in the Yorkshire and Humber region (Figure 2).

Figure 1: Number of VTEC isolates from England and Wales (1982-2008)



Source: www.hpa.org.uk

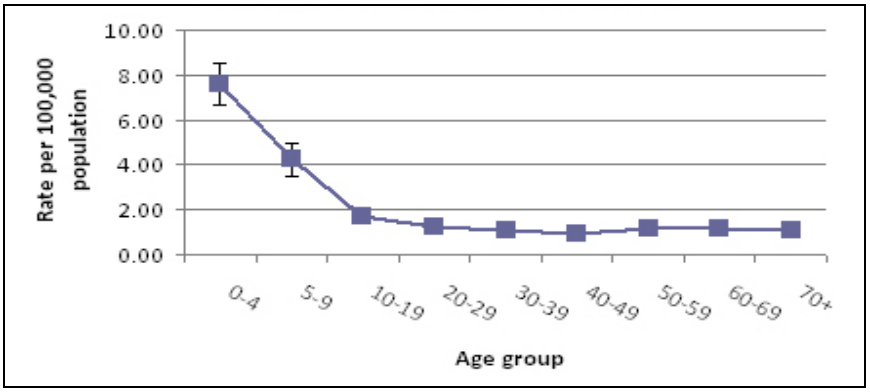
Figure 2: Regional rates of VTEC O157 laboratory isolations from England & Wales 2008



Source: *www.hpa.org.uk*

Almost 50% of cases are in children under 16, and rates of infection are highest in children under 5 years (Figure 3). Some of this excess may reflect screening policies as young children are routinely screened for VTEC following a case in a household, whereas adult contacts may not be screened unless they are in a risk group, although we also know that clinical illness more commonly occurs in children aged 5 years and under. Up to 43% of patients are hospitalised[54 lvii]. HUS occurs in up to 11% of cases and 85% of patients with HUS are under 16 years[54 lvii]. Up to 85% of cases are apparently sporadic or occur in households, with a minority from identified general outbreaks. Eighteen percent of cases in the second quarter of 2009 in England were thought to have been acquired overseas[lviii].

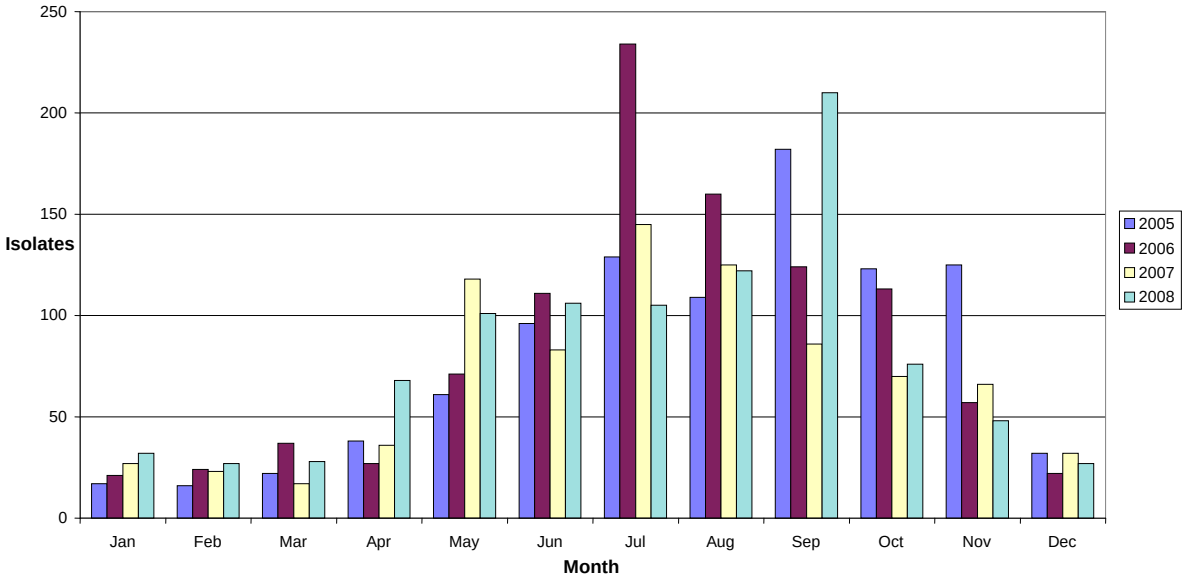
Figure 3: Average rate per 100,000 population of VTEC by age group, England & Wales, 2005-2008



Source: www.hpa.org.uk

Seasonality of VTEC O157 infections in England and Wales has been reported since 1989 and shows a peak in the third quarter with very few infections in the first quarter. Monthly data for 2005 to 2008 (Figure 4) show variation in isolates confirmed per month during the summer and autumn periods that are often associated with general outbreaks.

Figure 4: Monthly confirmations of VTEC O157 from human infections in England & Wales, 2005 - 2008



Source: www.hpa.org.uk

2.4 Organisational arrangements

Numerous professionals, teams and organisations have a role in the public health management of VTEC infection, including GPs, front-line hospital staff, Health Protection Units (HPU), HPA Microbiology Services, Local Authorities' Environmental Health (EH) departments, microbiologists, veterinary surgeons and others. The precise roles of HPUs and EH departments differ across England. This guidance assumes that the HPU deals with the human aspects of public health management, and that EH departments deal with the environmental aspects. However, local authorities may be well placed to undertake face-to-face interviews of cases in the community and can also assess household conditions at

the same time.

3. Case definitions

The following case definitions should be used to guide the public health response to individual cases of VTEC. Public health action is required for probable or confirmed cases. Possible cases require further laboratory testing or epidemiological assessment.

Case definitions are based on clinical, laboratory and epidemiological criteria (Table 2). More detailed information on laboratory testing is in Sections 4.3 and 4.4.

Table 2: VTEC case definitions for public health action

	Clinical features	Epidemiological link to CONFIRMED VTEC case or source	Laboratory findings (see Sections 4.3 and 4.4 of the VTEC Support Document)	Action required
Possible	Acute **non-bloody** diarrhoea	Present	Awaiting lab testing	**Initiate or complete testing at local lab**
	Acute **non-bloody** diarrhoea	Absent	Local lab testing incomplete. Isolate has the following characteristics: - POSITIVE typical colony morphology on appropriate selective medium - POSITIVE O157 (by slide agglutination OR latex kit) - **AWAITING** biochemical identification of *E. coli*	**Complete assessment for epidemiological links**[2]
Probable	Acute **non-bloody** diarrhoea	Present	Local lab testing incomplete. Isolate has the following characteristics: - POSITIVE typical colony morphology on appropriate selective medium - POSITIVE O157 (by slide agglutination OR latex kit) - **AWAITING** biochemical identification of *E. coli*	**Initiate public health actions (A-C in Box 1)** **Initiate or complete confirmatory testing**
	Acute **bloody** diarrhoea	Present	Awaiting lab testing	
	Acute **bloody** diarrhoea	Present or absent	Local lab testing incomplete. Isolate has the following characteristics: - POSITIVE typical colony morphology on appropriate selective medium - POSITIVE O157 (by slide agglutination OR latex kit) - **AWAITING** biochemical identification of *E. coli*	
	Symptomatic or asymptomatic	Present or absent	Local lab isolate identified as "presumptive (locally confirmed) *E. coli* O157" - POSITIVE typical colony morphology on appropriate selective medium - POSITIVE O157 (by slide agglutination OR latex kit) - **POSITIVE** biochemical identification of *E. coli*	
	HUS without known alternative aetiology	Present or absent	Awaiting lab testing	
Confirmed	Symptomatic or asymptomatic	Present or absent	Reference lab (Laboratory of Gastrointestinal Pathogens, HPA, Colindale) confirmed isolate - POSITIVE confirmation of *E.coli* - POSITIVE O157 or other O-serogroup - POSITIVE genes for Vero cytotoxin	**Initiate or continue public health action**
	HUS	Present or absent	Reference lab (Laboratory of Gastrointestinal Pathogens, HPA, Colindale) POSITIVE serological evidence of infection with *E. coli* O157 or other VTEC (presence of antibodies to O-antigen)	

[2] Some public health action may be initiated at this stage if considered appropriate by local teams

4. Public Health Management of VTEC: role of GPs, other front-line clinicians, and laboratories

4.1 Notification

Clinicians: Haemolytic Uraemic Syndrome, infectious bloody diarrhoea, and food poisoning are notifiable by Registered Medical Practitioners (RMP) under the Health Protection (Notification) Regulations 2010[lix].

Laboratories are required to notify their local HPU if *"presumptive (locally confirmed)"* isolates of VTEC O157 and any other suspect VTEC are identified (effective 1st October 2010). These 'locally-confirmed' isolates remain presumptive until they are confirmed or otherwise by the Reference Laboratory, but notification should **not** be delayed while this confirmation is awaited.

Notifications should be treated as urgent, as VTEC is often associated with outbreaks and secondary cases frequently occur. Therefore VTEC O157 or other suspect VTEC should be notified within 24 hours of clinical suspicion or laboratory isolation (or as soon as possible), to enable prompt investigation and public health management. Laboratories should inform the local HPU out of hours of any cases or suspected cases that they become aware of.

4.2 By GPs and front-line hospital staff

GPs and front-line hospital staff should consider VTEC infection in the differential diagnosis of anyone presenting to them with diarrhoea. VTEC infection may be suspected on clinical grounds (e.g. acute bloody diarrhoea, frequent motions, severe pain, and absence of fever) or epidemiological grounds (e.g. contact with farm animals or other biologically plausible exposure).

Acute bloody diarrhoea is a medical emergency especially in a child under 16 years of age. Early identification and management of HUS can greatly improve the prognosis. VTEC infection should be suspected and faeces always sent for culture as quickly as possible in all cases of acute bloody diarrhoea without another explanation. Diarrhoeal stools should be screened for the presence of *E. coli* O157 by the diagnostic microbiology laboratory (NSM BSOP 30[lx]); identification of the isolates is performed as in BSOP ID22 (http://www.hpa-standardmethods.org.uk/documents/bsopid/pdf/bsopid22.pdf).

Faecal specimens should always be cultured from cases with acute diarrhoea (whether bloody or not) who:

- Are especially vulnerable[3];
- Have severe or protracted illness;
- May be part of an outbreak or household/extended family spread;
- Have recently returned from abroad;

[3] In this context this is the young (aged under 16 years), the elderly (over 60 years), the frail, the immunocompromised and the pregnant. There is no strict definition of frail or immuno-compromised, and clinical judgement must be applied.

- Have had a biologically plausible exposure.

In confirmed, probable, or possible VTEC infection:

- Antibiotics should not be administered[liv].There is no evidence to suggest that antibiotics improve the clinical course of infection[lxi]. Children[lxii] and adults[lxiii] may suffer a higher rate of HUS when given antibiotics;

- Anti-motility agents and opioid narcotics should also be avoided[liv] as these have also been associated with a risk of HUS or neurological complications of the disorder[lxiv] [lxv];

- Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided because of their adverse effect on renal blood flow[lxvi].

- In confirmed VTEC infection:
    - GPs and front-line hospital staff should discuss case management, including the use and frequency of baseline blood tests (e.g. full blood count, blood film for fragmented blood cells, urea and electrolytes, lactate dehydrogenase and C-reactive protein) with a specialist clinician.

4.3 By the diagnostic microbiology laboratory

Diagnostic laboratories should investigate all diarrhoea for the presence of *E. coli* O157 preferably using the procedures recommended in the National Standard Methods (http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/EscherichiaColiO157/Laboratory/).

Specific procedures used by local diagnostic laboratories may vary, and therefore the exact tests carried out may not be identical across all diagnostic laboratories. However, most diagnostic laboratories will carry out a morphological identification, a slide agglutination (or latex kit) test, and a biochemical test to identify the organism. When all of these three types of procedures have been conducted and are positive, their result may be referred to in laboratory terms as a **presumptive (locally confirmed) isolate** i.e. an isolate that satisfies all the following conditions:

- Positive typical colony morphology on appropriate selective medium
- Positive O157 (by slide agglutination OR latex kit)
- Positive biochemical identification of *E. coli*

Clarification of terminology - distinction between laboratory isolates and human cases: It should be noted that the term *"presumptive (locally confirmed)"* refers to laboratory *isolates* (as defined above) and NOT human cases. Please refer to Table 2 for details of case definitions based on laboratory as well as clinical and epidemiological information.

Reporting results of diagnostic tests

Prompt transmission of both positive and negative results is essential for the maintenance or cessation of public health measures.

Identification of a presumptive (locally-confirmed) isolate of VTEC O157 or other VTEC should be notified immediately **to the patient's responsible clinician and the local HPU** according to the Health Protection Regulations 2010 (effective 1st October 2010).

Referral to the Reference Laboratory

Diagnostic laboratories should immediately refer to the Laboratory of Gastrointestinal Pathogens (LGP) LGP:

- Presumptive (locally-confirmed) isolates of NSF *E. coli* O157 for confirmation of identity, verotoxin gene detection and phage typing;
- Other strains of *E. coli* (possibly SF O157 or non-O157) for confirmation of identity and verotoxin gene detection if there is high clinical suspicion of VTEC infection.
- Faecal samples from cases of suspected HUS/TMA, or bloody diarrhoea in whom conventional laboratory testing has failed to yield presumptive VTEC O157 or any other pathogen.
- Faecal samples from symptomatic contacts of cases of VTEC infection or any VTEC outbreak- associated case in whom conventional laboratory testing has failed to yield a pathogen. These referrals should be discussed with the LGP prior to submission to ensure that there is the capacity for testing;

- Faecal samples from all symptomatic contacts of cases of infection with reference-laboratory confirmed SF VTEC O157 or non- O157 VTEC;

- Serum samples (if available) from likely cases HUS in which culture of a stool sample has failed to recover presumptive VTEC O157 or other potential VTEC, or for which faeces are not available. Testing is carried out for serological evidence of VTEC infection.

Receiving and forwarding results of tests done at the Reference Laboratory
The LGP sends results to the diagnostic laboratory in paper form, but in urgent situations the LGP should also telephone results. HPUs have access to VTEC reports from the LGP via the Gastro Data Warehouse (GDW).

The diagnostic laboratory should forward all results from the LGP to their local HPU by telephone. HPUs should be informed irrespective of whether the results are positive or negative for VTEC infection.

Safety Note:
All strains of VTEC are classified in Hazard Category 3 by the Advisory Committee on Dangerous Pathogens in Accordance with EU regulations[lxvii]. Transport of presumptive (locally-confirmed) isolates and faecal samples to the LGP should be carried out according to the LGP User Manual (http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1247816548297).

4.4 Role of the Reference Laboratory

For England and Wales, this is the Laboratory of Gastrointestinal Pathogens (LGP), HPA Colindale.

Isolates of VTEC O157 identified at local diagnostic laboratories in England and Wales are required to be sent to the LGP for confirmation.

Processing at the LGP covers:

- Confirmation of the identity, serotype and presence and type of Vero cytotoxin genes in all human presumptive (locally-confirmed) isolates; isolates also tested from food, animal and environmental sources in relation to human infections.

- Phage typing of all isolates of *E. coli* O157 to provide front-line epidemiological discrimination essential for identification of potentially linked isolates.

- Subtyping of VTEC O157 isolates by DNA-based methods including multi-locus variable number tandem repeat typing (VNTR) and pulsed field gel electrophoresis (PFGE). These methods are used in outbreak and incident investigation to support epidemiological data, exclude outlying infections and identify sources. Screening of sporadic isolates by phage type and VNTR may also indicate potential clusters of cases.

SOPs for the isolation and identification of VTEC O157 in faeces by diagnostic laboratories may result in presumptive (locally-confirmed) isolates that are not subsequently confirmed in the LGP. Between 2007 and 2009, about 280 referred cultures were found not to be *E. coli* O157 or VTEC, compared with the 2812 VTEC O157 confirmed by LGP in that period, i.e. about 90% of referred cultures were confirmed by the reference lab. There were also about 90 isolates of NSF *E. coli* O157 that were VT gene-negative (i.e. they were non-VTEC) but possessed other virulence factors characteristic of VTEC O157. Over 50% of these strains belonged to a single phage type and have been found in the animal reservoir. Such strains

lack Vero cytotoxin genes and are not associated with HUS but can cause diarrhoea. They may be as transmissible as VTEC O157 and have caused family outbreaks.

It is also possible that some VTEC strains may lose their VT genes during passage though the patient or on subculture.

Implications of negative VT genes for public health action:

In the event that a presumptive isolate of *E. coli* O157 is negative for VT genes, public health action such as screening and exclusions should not be automatically discontinued. The HPU clinician should review the risk assessment, taking account of the total clinical and epidemiological circumstances. Advice should be sought from the reference laboratory on the pathogenicity of the strain, which will also take account of phage typing and surveillance questionnaires and follow up of similar strains. In some cases it may be deemed suitable to discontinue public health action provided that the usual 48 hour symptom free exclusion criteria is applied to a symptomatic person. However, HPUs may decide to continue public health action on the basis of their risk assessment, particularly if the situation is linked to a case of HUS.

5. Public Health Management of VTEC: role of the HPA

The frontline health protection role in VTEC management rests with local Health Protection Units (HPUs), with support as appropriate from regional and national levels of the HPA.

The aim of public health management of probable or confirmed VTEC cases is to undertake prompt action to prevent further cases associated with a primary source and interrupt secondary transmission.

Public health actions include:

- Pursuing microbiological confirmation:
  - As soon as the HPU is informed of a possible or probable case of VTEC infection it should facilitate the laboratory confirmation of the diagnosis by liaison with the reporting clinician, local diagnostic laboratory and the LGP. Testing of cases of HUS should be facilitated in collaboration with the treating clinician.

- Undertaking rapid risk assessment to:
  - Identify any associated cases and links to known or suspected outbreaks,
  - Identify possible sources of exposure,
  - Determine if there are vulnerable contacts and
  - Assess the risk of secondary transmission.

- Implementing appropriate measures for control and prevention measures, depending on the suspected source of infection and the risk of person-to-person spread.

- Identifying and responding to potential clusters or outbreaks.
  - If the HPU is informed of, or identifies a potential outbreak, it should consider establishing an incident control team as appropriate. Further details are contained in Section 5.2 and in the Operational Manual.

5.1 Management of cases and contacts

5.1.1 Investigation

The principal objectives of the public health investigation are to:

- Suggest a possible source or vehicle of infection;
- Identify any associated cases resulting from secondary spread or a common exposure;
- Identify any vulnerable contacts;
- Advise source-specific control measures, and
- Advise control of secondary spread.

A detailed case history for the seven days prior to illness[4] should be obtained using the current National Enhanced Surveillance Questionnaire for VTEC and forwarded to Gastrointestinal, Emerging & Zoonotic Infections (GEZI, HPA Colindale) as soon as possible. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1246952918295. The questionnaire includes information on demographic details, clinical condition and laboratory investigations, potential sources or vehicles of infection (e.g. travel, food, water, animals, environmental), household or other close contacts, and whether they are in high-risk groups. The responsibility for completing the Questionnaire should be clearly agreed at the local level between the HPU and the local Environmental Health Department.

Investigation should enable HPUs to determine if there are other associated cases or possible links.

The National Surveillance System for VTEC in England provides a web portal which is a valuable resource to determine common exposures among different cases, potentially facilitating the detection of outbreak sources. The database is monitored by a national team which holds primary responsibility for it, but HPUs can also access it to aid their local investigations.

Further information on public health responsibilities and management at national, regional and local levels is available in the Operational Manual.

Although all VTEC cases should be regarded as potentially infectious, measures to avert secondary spread are guided by the likelihood of the case or contact posing a special risk of spreading infection. Therefore, information should be sought on individual, environmental, or other factors increasing the risk of transmission. The groups that pose an increased risk of spreading infection are listed in **Box 1**.

[4] Although the incubation period may be longer than seven days, this is very uncommon. It is usually three to four days. So, including potential exposures in the seven day period before symptoms should capture most potential exposures. In rare cases at the discretion of the investigating team, it may be considered useful to extend the history beyond the 7-day period up to 14 days, such as if a cluster is suspected but no common sources are identified in the 7 days preceding symptoms. This could be through retrospective re-interview if appropriate. For cases of HUS, exposures prior to the onset of preceding diarrhoea should be sought.

Box 1: Groups (cases and contacts) posing an increased risk of spreading VTEC infection

Group A: Any person of doubtful personal hygiene or with unsatisfactory toilet, hand-washing or hand drying facilities at home, work or school. Particular consideration should be given as to whether individual infant- school-aged children (aged 6 or 7 years) are able to satisfactorily observe good personal hygiene.

Group B: Children aged 5 years old or under who attend school, pre-school, nursery or other similar groups.

Group C: People whose work involves preparing or serving unwrapped food to be served raw or not subjected to further cooking.

Group D: Clinical, social care or nursery staff who work with young children, the elderly, or any other particularly vulnerable persons, and whose activities increase the risk of transferring infection via the faeco-oral route. Such activities include helping with feeding, or handling objects that could be transferred to the mouth.

5.1.2 Communication

HPUs should communicate with other parts of the HPA and partner organisations as necessary for each situation. In most cases HPUs will need to:

- Ensure that any relevant cases and possible exposures are reported promptly to national and regional surveillance systems
- Report cases to local authority environmental health departments
- Notify other HPUs of possible exposures that may have occurred in another HPU area.

5.1.3 Control

The control of specific sources suspected as being associated with VTEC infection as a result of investigations of an outbreak is addressed in section 5.2. Detailed investigation of suspected sources will clearly be required for potential clusters and outbreaks. Any investigation of potential sources for individual sporadic cases, including restaurants or farm exposures, must be coupled with a detailed risk assessment which considers issues such as numbers of potential exposures to the potential source, and the inspection history of premises. Detailed investigation, including joint visits of all potential exposures in the 7 days preceding illness for sporadic cases, cannot be justified.

Person-to-person spread from cases and contacts is always a risk, whatever the primary source. Secondary spread of VTEC is common and requires specific control measures.

Control measures to prevent person-to-person spread from cases consist of three broad areas:

- Personal hygiene especially thorough hand-washing;
- Infection control and environmental cleaning;

- Exclusion until microbiological clearance of cases and contacts who pose a special risk of spreading infection (Groups A-D as detailed in Box 1 in Section 5.1.1).

The first and second of these measures apply to many other pathogens. They should be in place even in the absence of a case of VTEC infection and should be applied whether or not cases and contacts are excluded. Detailed advice on personal hygiene and infection control can be found elsewhere[lxviii].

Personal hygiene

All cases of diarrhoea should be regarded as infectious unless evidence suggests otherwise. Diarrhoea is more likely than formed faeces to contaminate hands and the environment and are consequently at greater risk of spreading faecal pathogens. Asymptomatic or recovering cases are less likely to transmit infection if personal hygiene is good. Scrupulous personal hygiene should be reinforced when a case has occurred. Hands should be washed with soap and warm running water and dried thoroughly after use of the lavatory, changing nappies or clearing up faecal contamination. Use of hand-sanitising gels should not be regarded as a replacement for hand washing. Useful advice is available on the HPA web site (http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/EscherichiaColiO157/)

Infection Control

Infection control is important in the domestic setting as well as in childcare and healthcare settings, including hospitals and care homes. If a case has occurred in the domestic setting it is vital to ensure that members of the household are made aware of and implement appropriate infection control measures. Those suffering or recovering from VTEC infection should avoid preparing food for others where possible. Ideally, standards of infection control in childcare and healthcare settings including hospitals and care homes will be satisfactory even in the absence of a case. Should a case occur, however, practice should be assessed; a visit to the site may be required and additional measures introduced to improve infection control practice if required. Infection control in the domestic setting is based on the same principles as elsewhere but is much more difficult to achieve[lxix]. Even modest efforts to interrupt community spread may however reduce case numbers by up to 11%[lxx].

Exclusion and microbiological clearance

Determine whether the case or contact is at particular risk of spreading infection by the faeco-oral route, and determine the risk group classification of each case and contact. Decisions about risk; exclusion and timing of microbiological clearance can be highly dependent on specific local circumstances (Box 1, Section 5.1.1).

Exclusion of cases (Box 2):

All VTEC cases (probable and confirmed) should be regarded as potentially infectious and should normally be excluded from work, institutional settings, nursery, school or other similar groups, ***until at least 48 hours after the person is free from diarrhoea***.

Confirmed cases in risk groups A-D (Section 5.1.1) should, in addition, be excluded ***until they have microbiological clearance.*** Exclusion can present problems for carers and families, particularly if prolonged, so they may require advice and support. Primary school children whose ability to practice good hygiene is doubtful should be managed as Group A.

Cases aged 5 years and under have been shown to be a particular risk to their siblings; separation of these cases from their siblings has been recommended to prevent the risk of secondary transmission in the household, but the effectiveness of this is unproven[lxix]. Separation can often not be practically achieved and HPUs should work closely with families to provide clear advice on infection control in these homes[lxix]. Care should also be taken not

to introduce infection into other households with vulnerable people when separating siblings.

Swimming: Cases of VTEC *in Groups A and B* should be advised not to use public swimming pools or domestic paddling pools until their exclusion has been lifted. For all other cases not until at least 48 hours after their diarrhoea has stopped.

Exclusion of contacts (Box 2):
Contacts in risk groups A-D (with or without symptoms) should also be excluded until they have microbiological clearance.

It should be noted that although the risk of VTEC transmission is reduced by exclusion until microbiological clearance is confirmed, the risk is not completely eliminated. Prevention of transmission cannot be guaranteed for a number of reasons, including the possibility of intermittent excretion.

Symptomatic contacts who are not in risk groups: Should be screened and excluded until their results are available. If the stool samples are positive for VTEC, then they should be managed as a new case.

Asymptomatic contacts who are not in risk groups: An individual risk assessment should be carried out to determine whether screening such asymptomatic contacts would be appropriate (e.g. a child aged 5 years or under who does not attend an nursery but plays with other children).

Microbiological clearance in cases:

Microbiological clearance consists of two negative faecal samples taken at least 24 hours apart.

For cases, clearance samples should not be taken until 24 hours after symptoms have ceased. If a clearance sample is positive, the HPU may consider delaying further sampling for up to a week.

Microbiological clearance for cases with NSF E. coli is carried out by the diagnostic laboratory according to National Standard Methods, and any presumptive isolates detected should be sent to the LGP for confirmation in the usual way. Clearance testing of cases infected with SF VTEC O157 or non-O157 strains should be performed in the LGP by the same PCR and culture methods used to isolate VTEC from the original specimen.

Microbiological clearance in contacts:

Timing of sampling for microbiological clearance in contacts: When determining the timing of sampling for microbiological clearance the HPU should assess the understanding of the case and their contacts and their likelihood of compliance with the advice on personal hygiene and infection control in the home. In theory, while the case is still excreting VTEC, contacts may continue to be exposed, for example, in a household setting. Screening of such contacts should ideally be delayed until the case is symptom free and microbiologically clear. However, if good hygiene and infection control measures are implemented, these may be sufficient to control the ongoing risk of exposure to the contacts.

Contacts in groups C and D should be able to comply with personal hygiene and infection control advice. Clearance samples from asymptomatic contacts in these groups could be taken before the case is symptom free or microbiologically clear, providing a careful risk assessment concludes that infection control and personal hygiene is practised appropriately. The risk of re-exposure is likely to be less if the case is not in risk group A or B.

Contacts in groups A and B: Minimising the risk of secondary spread in a household with cases and contacts in Group A or Group B is challenging. The risk of continuing exposure of contacts is likely to be greatest when both the case and contacts are in Groups A or B. Stringent hygiene and infection control should be in place for all cases, parents should be advised to supervise young children's toileting and hand hygiene.

Strictly, if contacts in Group A and B have continuing contact with a case, they should not be screened until the case is both asymptomatic and has been cleared microbiologically. However, at the discretion of the HPU, a decision may be taken to start screening contacts in before this, following a careful assessment of the risk of transmission in the household.

Box 2: Summary of recommendations for exclusion and microbiological clearance:

CASES
Risk Group A – D*:

- Exclude until two negative results of faecal specimens taken at intervals of not less than 24 hours are obtained. The first clearance samples should not be taken until 24 hours after symptoms have ceased.
- Emphasise the need for good personal hygiene

Not in risk group:

- Exclusion until 48 hrs after first normal stool.
- Emphasise the need for good personal hygiene

CONTACTS
In Risk Group A-D* - with or without symptoms
Exclude until microbiologically clear (two clear stool samples at least 24 hours apart.) If stool sample is positive for VTEC **treat as a new VTEC case**, taking all the appropriate actions for cases in risk groups.

Not in Risk Group – suspicious symptoms

- Microbiological testing recommended (one stool sample) and exclude until results available. If positive for VTEC treat as case in a non-risk group.

Not in Risk Group – asymptomatic

- No routine testing/exclusion. However, an individual risk assessment should be carried out to determine whether screening such asymptomatic contacts would be appropriate (e.g. a child aged 5 years or under who does not attend an institutional setting but plays with other children).

Risk groups described in Box 1

5.2 Management of potential and actual outbreaks

5.2.1 Investigation

When the investigation of a case identifies other confirmed or suspected cases, investigators must consider both person-to-person spread and/or the possibility of a common source/vehicle. The identification of the common source or vehicle is important to prevent continuing primary cases.

Identification of a common source or vehicle depends upon the ***generation of hypotheses*** informed by:

- In-depth interviews with cases to try to identify common exposures;
- Environmental inspections of locations suspected of being foci of infection to identify characteristics compatible with the hypothesis;
- Microbiological testing of foods and environmental samples or of animal sources suspected as being responsible for infection. Tests may identify an organism in the food, environmental or animal sample that is phenotypically and genotypically indistinguishable (within accepted interpretation parameters) with that infecting the case or cases. The methods use for comparison of isolates from human and non-human sources are performed in the LGP and are outlined in section 3.4.

Advice on the detailed investigation of outbreaks is beyond the scope of this guidance, and will depend upon the hypothesised source or vehicle.

Once a hypothesis as to likely source has been generated, then analytic studies may be undertaken to confirm or refute such an association. However, analytical studies are rarely timely enough to promote appropriate public health actions.

5.2.2 Control

Control of outbreaks consists of:

- Applying specific measures depending on the suspected vehicle and source of infection (Section 5.3)
- Prevention of person-to-person spread from cases and contacts (Section 5.1.3).

5.3 Management of suspected sources and vehicles

5.3.1 Investigation and control

The investigation and control of the source of infection will depend on what source is suspected. It is not necessary to obtain proof of the source before control measures are applied. Some control measures such as hygienic food preparation, precautions to prevent the spread of infection from animals, and public education are desirable in the absence of a case or outbreak, or any link to a case or outbreak, and the occurrence of a case is an excellent opportunity to reinforce their importance. The HPU should consider the establishment of an outbreak control team that may include representatives from organisations with responsibilities for different aspects of the investigation (see section 2.4).

Food

Investigation consists of generating a hypothesis as to the vehicle, source and cause of infection and testing the hypothesis epidemiologically, microbiologically and environmentally. A formal epidemiological investigation is appropriate if there are sufficient cases to give any study sufficient statistical power to test the hypothesis. Control measures may precede or follow the confirmation of the hypothesis depending on the assessment of risk. Foodborne spread of VTEC illness generally results from in food hygiene during production, handling, pasteurisation or cooking leading to failure to kill contaminating organisms or contamination

of ready-to-eat food with raw foods. The range of foods implicated or proven to be the source of VTEC outbreaks is now very large.

For an infection as potentially serious as VTEC, the threshold for action should be low. Appropriate action may include food withdrawals or closure of premises. The HPA, where appropriate, will work with local authorities and other partners to take this forward. Advice on the identification and rectification of food production or catering errors is beyond the scope of this guidance but can be found elsewhere[lxxi].

Water

Chlorinated mains water supply should not be a source of VTEC infection unless there is damage or treatment failure. However contamination of taps and stand-pipes by animal faeces in rural settings has been linked to infections. Where a case occurs in a household served by a private supply and the private water supply is suspected as the cause of the illness, HPUs and local authorities should work together to assess the risk to other users of the private water supply. In some cases it may be necessary to advise other water users to boil water prior to consumption. The supply should be sampled for faecal indicators and VTEC. Sampling should take account of the presence or otherwise of appropriate water treatment facilities at all residential and commercial properties on the supply. The prompt provision of an alternative water supply should be considered, especially where social or other circumstances make boiling water particularly difficult or dangerous.

Surface water such as streams and lakes may be a source of VTEC due to pollution from grazing animals' faeces, and seepage or run-off of agricultural slurries and sewage. If surface water is suspected as a source of infection environmental sampling may be appropriate. The EC Bathing Water Directive sets microbiological standards for designated bathing water sites. In designated bathing water sites levels of faecal coliforms should not exceed 2000/100ml. In all other waters not designated for bathing, any control measures would have to be devised locally in line with the perceived risk from the individual source concerned. Children may be at particular risk from recreational contact with varied informal water sources in rural areas. Infections can be linked to streams that pass across beaches and whose waters derive from an agricultural area[lxxii]. Swimming pools are rarely a source of VTEC infection because of chlorination, but where this fails outbreaks are possible[lxxiii].

Livestock and their environment

When farm livestock are the suspected source of infection, on either an open or a private farm, HPUs, Local Authorities (LA) and/or the HSE should work together and consider the following measures[lxxiv]:

- Alert the farm owner, emphasise the risks posed by VTEC and advise that residents, staff and visitors, including contractors who visit farms to work, should be made aware that the premises is a suspected source of infection.
- The cessation of direct contact with animals in an open farm setting (especially ruminants) early in any potential outbreak; and avoiding contact with animal manure.
- Review and advice on infection control measures e.g. hand-washing after animal/environmental contact; before eating or preparing food; removal of work clothes and footwear before entering home/food preparation areas.
- Direct managers of animal amenity premises (open farms, petting zoos, animal sancturaries) to HSE and other detailed official guidance on avoiding infection.

Note that Inadequate hand-washing facilities, poor separation of eating and animal areas and inadequate signage indicate that further investigation or advice is required.

The Veterinary Laboratories Agency (VLA) can provide advice on veterinary aspects of

VTEC infection in animals and should be consulted as soon as a potential outbreak linked to a farm is identified. VLA may provide advisory support through attendance at OCT meetings and on farm visits, including animal sampling where agreed. The purpose of animal sampling is to confirm the farm as the likely source of infection by molecular matching of animal isolates to those obtained from human cases. Consider sampling animal faeces, animal environments, manure and water, particularly if there is a potential for livestock contamination of private water supplies. VTEC can exist for many weeks in soil and faeces.

If contaminated dairy produce is implicated, sample primary filters or washings, farm pasteurisers if in use and raw milk from bulk milk tanks on dairy farms. Infection has been associated with consumption of raw milk, failure of on-farm pasteurisers and contamination post-pasteurisation.

Particular considerations with regard to prevention and control apply when the suspected source of infection is an open farm.

- Signage to indicate risk of infection and need for parents and carers to supervise children at all times. Special care must be taken with very young children who may suck pacifiers/thumbs or put objects in their mouths.

- Sufficient hand-washing facilities of an acceptable standard (with hot running water, soap, hand drying facilities, and cleaning and disinfection programmes) should be provided for the maximum number of visitors expected. They should be adequately signposted, especially on the approaches to eating areas. Alcohol hand gels/rubs are not sufficient.

- Eating facilities should be clearly defined and situated away from areas where contact with animals, including dogs, is likely. Eating should be prevented/discouraged in other areas.

- Animals from the farm should not have access to public areas such as car parks to prevent faecal contamination.

- Farm staff must be appropriately trained in the management of the premises in accordance with HSE requirements.

Further Reading

References that provide general further reading on VTEC, infection control and health protection are shown below. Sources of information and guidance available on the Internet include:

HPA *E. coli*
pages: http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/EscherichiaColiO157/

HPA Leaflet : Avoiding infection on farm visits:
http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1270122184581

Understanding and managing the risks from *E. coli* O157 in an open farm context:
http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1267551712693

Health and Safety Executive
http://www.hse.gov.uk/campaigns/farmsafe/ecoli.htm

Zoonoses Report UK 2007 (Defra)
http://www.defra.gov.uk/animalh/diseases/zoonoses/zoonoses_reports/ zoonoses2007.pdf

Guidelines for the investigation of zoonotic disease (England and Wales) April 2009: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1240530336599

Appendix 1 - Group Membership

Trish Mannes, Consultant in Health Protection, Thames Valley HPU

David Ishola, Specialist Registrar, CfI

Lucy Thomas, Consultant in Communicable Disease Control, North West London HPU

David Tompkins, Regional Microbiologist, Yorkshire and Humber RMN

Geraldine Smith, Clinical Scientist, CfI

Bob Adak, Head of Epidemiological services, CfI

Martin Schweiger, Consultant in Communicable Disease Control, West Yorkshire HPU, Y&H

Ruth Ruggles, Consultant in Public Health Medicine, CfI

Ciaran Sundstrem, Regional and Divisional Health Protection Manager, Yorkshire and Humber. (Secretariat)

References

[i] Health Protection Agency. Incident and Emergency Response Plan. 2008

[ii] Health Protection Network. Guidance for the Public Health Management of Infection with Verotoxigenic *Escherichia coli* (VTEC). September 2008. Available at: http://www.hps.scot.nhs.uk/giz/e.coli0157.aspx

[iii] PHLS Guidelines for the Control of Infection with Verocytotoxin Producing *Escherichia coli* (VTEC) http://www.hpa.org.uk/cdph/issues/CDPHvol3/No1/vtec.pdf Commun Dis Public Health 2000; 3: 14-23.

[iv] Health Protection Agency. The VTEC Operational Manual: Essential operational guidance for HPA staff dealing with incidents of VTEC infection. 2010.

[v] Griffin PM. *Escherichia coli* O157:H7 and other enterohaemorrhagic *Escherichia coli* In: Blaser MJ, Smith PD, Ravidin JI, Greenberg HB and Guerrant RL. Eds. Infections of the Gastrointestinal Tract. New York, Raven Press, 1995, 739-61.

[vi] Thomas A, Chart H, Cheasty T, Smith HR, Frost JA, Rowe B. Vero cytotoxin-producing *Escherichia coli*, particularly serogroup O157, associated with human infections in the United Kingdom: 1989-1991. Epidemiol Infect 1993; 110: 591-600

[vii] Sharp JCM, Reilly WJ, Coia JE, Curnow J, Synge BA. *Escherichia coli* O157 infection in Scotland: an epidemiological overview. PHLS Microbiology Digest 1995; 12: 134-40

[viii] Gould LH, Demma L, Jones TF, Hurd S, Vugia DJ, Smith K, Shiferaw B, Segler S, Palmer A, Zansky S, Griffin PM. Hemolytic uremic syndrome and death in persons with *Escherichia coli* O157:H7 infection, foodborne diseases active surveillance network sites, 2000-2006. Clin Infect Dis. 2009;49(10):1480-5.

[ix] Brenner & Rector. Microvascular and macro vascular Diseases of the Kidney. Chapter 32.The Kidney 2004; Saunders Elsevier.

[x] Riley LW, Remis RS, Helgerson SD, et al. Hemorrhagic colitis associated with a rare *Escherichia coli* serotype. N Engl J Med 1983; 308: 681-5

[xi] Swerdlow DL, Griffin PM. Duration of faecal shedding of *Escherichia coli* O157:H7 among children in day-care centres. Lancet. 1997 Mar 15;349(9054):745-6.

[xii] Belongia EA, Osterholm MT, Soler JF, Ammend DA, Braun JE, MacDonald KL. Transmission of *Escherichia coli* O157:H7 infection in Minnesota child day-care facilities. JAMA 1993; 269: 883-8.

[xiii] Shah S, Hoffman R, Shillam P, Wilson B. Prolonged fecal shedding of *Escherichia coli* O157:H7 during an outbreak at a day care center. Clin Infect Dis 1996; 23: 835-6.

[xiv] McMaster, C., Roch, E., Willshaw, G. A., Doherty, A., Kinnear, W. & Cheasty, T. (2001). Verocytotoxin-producing *Escherichia coli* serogroup O26 : H11 outbreak in an Irish crèche. *Eur J Clin Microbiol Infect Dis.* **20**, 430–432

[xv] Tuttle J, Gomez T, Doyle MP, Wells JG, Zhan T, Tauxe RV, Griffin PM. Lessons from a large outbreak of *Escherichia coli* O157:H7 infections: insights into the infectious dose and method of widespread contamination of hamburger patties. *Epidemiol Infect* 1999; 1 22: 185-92.

[xvi] Tilden J Jr, Young W, McNamara AM, Custer C, Boesel B, Lambert-Fair MA et al. A new route of transmission for *Escherichia coli*: infection from dry fermented salami. *Am J Public Health* 1996; 86: 1142-5.

[xvii] EFSA. Scientific Opinion of the Panel on Biological Hazards on a request from EFSA on monitoring of verotoxigenic *Escherichia coli* (VTEC) and identification of human pathogenic VTEC types. The EFSA Journal (2007) 579, 1-61.

[xviii] The Pennington Group. *Report on the Circumstances Leading to the 1996 Outbreak of Infection with E. coli O157 in Central Scotland, the Implications for Food Safety and the Lessons to be Learned.* Edinburgh: Edinburgh Stationery Office 1997

[xix] Pennington, H., *Report of the Public Inquiry into the September 2005 Outbreak of E.coli O157 in South Wales*, HMSO, 2009 available at: http://www.ecoliinquirywales.org.uk (accessed July 2010)

[xx] Upton PA, Coia JE. Outbreak of *Escherichia coli* O157 infection associated with pasteurised milk supply. Lancet 1994; 344: 1015.

[xxi] Webster D, Cowden J, Locking M. An outbreak of *Escherichia coli* O157 in Aberdeen, Scotland, September 2007. *EuroSurveillance* 2007; 12 : E070927.1

[xxii] Michino H, Araki K, Minami S, Takaya S, Sakai N, Miyazaki M, Ono A, Yanagawa H. Massive outbreak of *Escherichia coli* O157:H7 infection in schoolchildren in Sakai City, Japan, associated with consumption of white radish sprouts. *Am J Epidemiol* 1999; 1 50: 797-803.

[xxiii] Uhlich GA, Sinclair JR, Warren NG, Chmielecki WA, Fratamico P. Characterization of Shiga toxin-producing *Escherichia coli* isolates associated with two multi-state foodborne outbreaks that occurred in 2006. *Appl Environ Microbiol* 2008; 74:1268-72.

[xxiv] Wendel AM, Johnson DH, Grant J, Archer JR, Monson T, Koschmann C, Davis JP. Multistate outbreak of *Escherichia coli* O157:H7 infection associated with consumption of packaged spinach, August-September 2006: the Wisconsin investigation. Clin Infect Dis. 2009 Apr 15;48(8):1079-86.

[xxv] Syed Q, Outbreak Control Committee. National outbreak of Vero cytotoxin-producing *Escherichia coli* O157 infection associated with lemon and coriander chicken wraps in England & Wales. Outbreak report, Health Protection Agency 2007. http://www.hpa.org.uk/infections/topics_az/ecoli/O1 57/outbreak_01_07.pdf

[xxvi] Besser RE, Lett SM, Weber JT, Doyle MP, Barrett TJ, Wells JG, Griffin PM. An outbreak of diarrhea and hemolytic uremic syndrome from *Escherichia coli* O157:H7 in fresh-pressed apple cider. *JAMA* 1993; 269: 2217-2220,

[xxvii] Licence K, Oates KR, Synge BA, Reid TMS. An outbreak of *E.coli* O157 infection with evidence of spread from animals to man through contamination of a private water supply. *Epidemiol Infect* 2001; 126: 135-138.

[xxviii] Smith A, Reacher M, Smerdon W, Adak GK, Nichols G, Chalmers RM. Outbreaks of waterborne infectious intestinal disease in England and Wales, 1992-2003. *Epidemiol Infect* 2006; 134: 1141-9.

[xxix] Garg AX, Moist L, Matsell D, et al. Risk of hypertension and reduced kidney function after acute gastroenteritis from bacteria-contaminated drinking water. *CMAJ* 2005; 173: http://www.cmaj.ca/cgi/content/full/173/3/261

[xxx] Hrudey SE, Payment P, Huck PM, Gillham RW, Hrudey EJ. A fatal waterborne disease epidemic in Walkerton, Ontario: comparison with other waterborne outbreaks in the developed world. Water Sci Technol. 2003;47(3):7-14.

[xxxi] Goode B, O'Reilly C. Report: Outbreak of *E.coli* associated with petting zoo at North Carolina State Fair, Nov. 2004. N.C. Division of Public Health, General Communicable Disease Control. http://www.epi.state.nc.us/epi/gcdc/ecoli/EColiReportFinal062905.pdf

[xxxii] Locking ME, O'Brien SJ, Reilly WJ *et al*. Risk factors for sporadic cases of *Escherichia coli*

O157 infection: the importance of contact with animal excreta. *Epidemiol Infect* 2001; 127: 215-220.

[xxxiii] O'Brien SJ, Adak GK, and Gilham C. Contact with farming environment as a major risk factor for Shiga toxin (Vero cytotoxin)-producing *Escherichia coli* O157 infection in humans. Emerg Infect Dis 2001; 7:1049-51.

[xxxiv] Wise, J. Outbreak of *E Coli* O157 is linked to Surrey open farm. BMJ 2009; 339:3795,

[xxxv] Pritchard GC, Willshaw GA, Bailey JR, Carson T, Cheasty T. Verocytotoxin-producing *Escherichia coli* O157 on a farm open to the public: outbreak investigation and longitudinal bacteriological study *Vet Rec*. 2000;147:259-64.

[xxxvi] Pritchard GC, Smith R, Ellis-Iversen J, Cheasty T and Willshaw GA. Verocytotoxigenic *Escherichia coli* O157 in animals on public amenity premises in England and Wales, 1997 to 2007 *Vet Rec* 2009; 164: 545 - 549.

[xxxvii] Griffin, G. Review of the major outbreak of *E. coli* O157 in Surrey, 2009. HPA 2010. available at: http://www.griffininvestigation.org.uk (accessed July 2010)

[xxxviii] Wells JG, Shipman LD, Greene KD, Sowers EG, Green JH, Cameron DN, et al. Isolation of *Escherichia coli* serotype O157:H7 and other Shiga-like-toxin-producing *Escherichia coli* from dairy cattle. *J Clin Microbiol* 1991; **29**: 985-9.

[xxxix] Chapman PA, Siddons CA, Cerdan Malo AT, Harkin MA. A 1-year study of *Escherichia coli* O157 in cattle, sheep, pigs and poultry. *Epidemiol Infect* 1997; **119**: 245-50

[xl] Richards MS, Corkish JD, Sayers AR, McLaren IM, Evans SJ, Wray C. Studies of the presence of verocytotoxic *Escherichia coli* O157 in bovine faeces submitted for diagnostic purposes in England and Wales and on beef carcasses in abattoirs in the United Kingdom. *Epidemiol Infect* 1998; **120**: 187-92.

[xli] Paiba GA, Wilesmith JW, Evans SJ, Pascoe SJ, Smith RP, Kidd SA et al. Prevalence of faecal excretion of verocytotoxigenic *Escherichia coli* O157 in cattle in England and Wales. *Vet Rec*. 2003 153:347-53

[xlii] Milnes AS, Stewart I, Clifton-Hadley FA, Davies RH, Newell DG, Sayers AR, Intestinal carriage of verocytotoxigenic *Escherichia coli* O157, Salmonella, thermophilic Campylobacter and Yersinia enterocolitica, in cattle, sheep and pigs at slaughter in Great Britain during 2003 Epidemiol Infect. 2008 136:739-51

[xliii] Gunn GJ, McKendrick IJ, Tennant HE, Thomson-Carter F, Foster G, Synge BA. An investigation of factors associated with the prevalence of verotoxigenic *Escherichia coli* O157 shedding in Scottish beef cattle. The Veterinary Journal 174 (2007) 554-564

[xliv] Ejidokun OO, Walsh A, Barnett J et al. Human Vero cytotoxigenic *Escherichia coli* (VTEC) O157 infection linked to birds. Epidemiol Infect 2006; 134:421-3

[xlv] Dargatz DA, Wells SJ, Thomas LA, Hancock DD, Garber LP. Factors associated with the presence of *Escherichia coli* O157 in faeces of feedlot cattle. *Journal of Food Protection* 1997; **60**: 466-70.

[xlvi] Ellis-Iversen J; Smith RP; Van Winden S; Paiba GA: Watson E; Snow LC; Cook AJC **(**2008) Farm practices to control E. coli O157 in young cattle - a randomised controlled trial. Veterinary Research 39:03.

[xlvii] Ellis-Iversen J, Smith RP, Snow LC, Watson E, Millar MF, Pritchard GC, Sayers AR, Cook AJC, Evans SJ, Paiba GA (2007) Identification of management risk factors for VTEC O157 in young-stock in England and Wales. Preventive Veterinary Medicine 82, 29-41.

[xlviii] Maule A. Environmental aspects of *Escherichia coli* O157.*International Food Hygiene*

1999; **9**: 21-3.

[xlix] Silvestro , Caputo M, Blancato S, Decastelli L, Fioravanti A, Tozzoli R, et al Asymptomatic carriage of verocytotoxin-producing *Escherichia coli* O157 in farm workers in Northern Italy. *Epidemiology and Infection,* 2004 **132**: 915-919

[l] Evans, J., Chalmers, R. M., Chart, H., Salmon, R. L., Kench, S. M., Coleman, T. J. et al, Evidence of persisting serum antibodies to *Escherichia coli* O157 lipopolysaccharide and Verocytotoxin in members of rural communities in England. *Eur J Epidemiol* 2000 **16**:885–889

[li] Snedeker KG. Shaw DJ. Locking ME. Prescott RJ. Primary and secondary cases in *Escherichia coli* O157 outbreaks: a statistical analysis. BMC Infectious Diseases. 9:144, 2009.

[lii] Health Protection Agency. Guidelines for the control of infection with Verocytotoxin producing *Escherichia coli* (VTEC). *Commun Dis Public Health* 2000; 3: 14-23. http://www.hpa.org.uk/cdph/issues/CDPHvol3/No1 /vtec.pdf

[liii] Parry SM. Salmon RL. Sporadic STEC O157 infection: secondary household transmission in Wales. Emerging Infectious Diseases. 4(4):657-61, 1998 Oct-Dec.

[liv] Tarr PI, Gordon CA, Chandler WL. Shiga-toxin-producing *Escherichia coli* and haemolytic uraemic syndrome. *Lancet* 2005; 365: 1073-86.

[lv] Jenkins C. Evans J. Chart H. Willshaw GA. Frankel G. Escherichia coli serogroup o26 – a new look at an old adversary. Journal of Applied Microbiology. 104(1):14-25, 2008 Jan.

[lvi] Paton, A W. Ratcliff, R M. Doyle, R M. Seymour-Murray, J. Davos, D. Lanser, J A. Paton, J C. Molecular microbiological investigation of an outbreak of haemolytic-uremic syndrome caused by dry fermented sausage contaminated with Shiga-like toxin-producing Escherichia coli. Journal of Clinical Microbiology. 34(7):1622-7, 1996 Jul.

[lvii] Howie H, Mukerjee A, Cowden J, Leith J, Reid T. Investigation of an outbreak of *Escherichia coli* O157 infection caused by environmental exposure at a scout camp. *Epidemiol Infect* 2003; 131:1063-1069.

[lviii] Quarterly report of VTEC cases in England: Q2 2009 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1250719648669

[lix] Department of Health. Health Protection Legislation (England) Guidance 2010. Available at: http://www.dh.gov.uk/publications

[lx] Investigation of faecal specimens for bacterial pathogens. http://www.hpa-standardmethods.org.uk/documents/bsop/pdf/bsop30.pdf . 13-10-2008. Standards Unit, Department for Evaluations, Standards & Training, Centre for Infections.

[lxi] Dundas S, Todd WTA, Neill MA, Tarr PI. Using antibiotics in suspected haemolytic-uraemic syndrome: Antibiotics should not be used in *Escherichia coli* O157 infection. *BMJ* 2005; 330: 1209.

[lxii] Wong CS, Jelacic S, Habeeb RL, Watkins SL, Tarr PI. The Risk of the Hemolytic-Uremic Syndrome After Antibiotic Treatment of *Escherichia coli* O157:H7 Infections. *N Engl J Med*. 2000 Jun 29; 342: 1930-6.

[lxiii] Dundas S, Todd WTA, Stewart AI, Murdoch PS, Chaudhuri AKR, Hutchinson SJ, The Central Scotland *Escherichia coli* O157:H7 Outbreak: Risk Factors for the Hemolytic Uremic Syndrome and Death among Hospitalized Patients. *Clin Infect Dis* 2001; 33: 923-31.

[lxiv] Pollock KGJ, Beattie TJ, Reynolds B, Stewart A, Cowden JM. Clinical Management of Children with Suspected or Confirmed *E.coli* O157 Infection. *SMJ* 2007; 52: 5-7.

[lxv] Bell BP, Goldoft M, Griffin PM, Davis MA, Gordon DC, Tarr PI, et al. A multistate outbreak of *Escherichia coli* O157:H7-associated bloody diarrhea and hemolytic uremic syndrome from hamburgers: the Washington experience. *JAMA* 1994; 272: 1349-53.

[lxvi] Murray MD, Brater DC. Renal toxicity of the nonsteroidal anti-inflammatory drugs. *Annu Rev Pharmacol Toxicol* 1993; 33: 435-465

[lxvii] Advisory Committee on Dangerous Pathogens. Biological agents: Managing the risks in laboratories and healthcare premises. HSE 2005

[lxviii] http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/EscherichiaColi/

[lxix] Werber D, Mason BW, Evans MR, Salmon RL. Preventing Household Transmission of Shiga Toxin- Producing *Escherichia coli* O157 Infection: Promptly Separating Siblings Might Be the Key. *Clin Infect Dis* 2008; 46:1189-96.

[lxx] Seto EYW, Soller JA, Colford JM. Strategies to reduce person-to-person transmission during widespread *Escherichia coli* O157:H7 outbreak. *Emerg Inf Dis* 2007; 13: 860-866. http://www. cdc.gov/eid/content/13/6/860.htm

[lxxi] Food Standards Agency. Safer Food, Better Business. Available at: http://www.food.gov.uk/foodindustry/regulation/hygleg/hyglegresources/sfbb/.

[lxxii] Ihekweazu C, Barlow M, Roberts S, Christensen H, Guttridge B, Lewis D, et al. Outbreak of E. coli O157 infection in the south west of the UK: risks from streams crossing seaside beaches. Euro Surveill 2006;11(4):128-30.

[lxxiii] Verma A, Bolton FJ, Fiefield D, Lamb P, Woloschin E, Smith N, et al. An outbreak of E. coli O157 associated with a swimming pool: an unusual vehicle of transmission. Epidemiol Infect 2007 Aug;135(6):989-92.

[lxxiv] http://www.hse.gov.uk/pubns/ais23.pdf