Bloody Diarrhoea and Clinically Suspected or Confirmed Shiga toxin-producing *Escherichia coli* (STEC) Infections

Clinical Guidance on the Assessment and Management of Children and Adults in Primary and Secondary Care

Evidence Based Guidance

Scottish Health Protection Network
2019

Contents

Abbreviations

STEC	Shiga toxin-producing *Escherichia coli*
HUS	Haemolytic Uraemic Syndrome
E. coli O157	*Escherichia coli* O157
PCR	Polymerase chain reaction
RRT	Renal replacement therapy
NSAID	Non-steroidal anti-inflammatory drugs
RBC	Red Blood Cell
WBC	White Blood Cell
CRP	C Reactive Protein
PIL	Patient Information Leaflet

Audience

This guidance has been produced to support the assessment and management of clinically suspected or confirmed Shiga toxin-producing *Escherichia coli* (STEC) infection, both *E. coli* O157 and non-O157 STEC. It is aimed at:

- Primary Care Teams
- Emergency Departments
- Paediatric Medicine Departments
- Physicians in Infectious Diseases, Nephrology and Gastroenterology
- Microbiologists
- Public Health Practitioners

This guidance should support individual expert clinical judgement and local response.

Aims

The guidance aims to:

- Reduce morbidity and mortality in STEC cases, by addressing the early recognition and clinical management of clinically suspected or confirmed STEC infection.

- Assist in the prevention of STEC infection, occurring either as a result of continuing exposure to a primary source, the environment or secondary spread from person to person (see the Guidance for the public health management of *Escherichia coli* O157 and other Shiga toxin-producing (STEC) infections available here).

Objectives

The objectives are to provide guidance to primary and acute care clinicians on the assessment and management of clinically suspected or confirmed STEC infection. The guidance covers:

1. Initial assessment and management of a patient with a diarrhoeal illness where STEC infection is clinically suspected or confirmed.

2. Initial assessment and management of a patient with clinically suspected or confirmed STEC associated Haemolytic Uraemic Syndrome (HUS).

3. Advice on circumstances where urgent specialist advice should be sought.

4. An outline of infection control and prevention measures and the requirement to notify local public health teams (see the Guidance for the public health management of *Escherichia coli* O157 and other Shiga toxin-producing (STEC) infections available here).

Acknowledgements

We wish to express appreciation to all whose efforts made this guidance possible. In particular, to the members of the Guidance Development Group and their constituencies, PHI Digital Support at HPS, stakeholders and external reviewers, who contributed and reviewed the content of this guidance.

Feedback on the guidance

Comments on this guidance should be sent to the SHPN Guidance Group by emailing NSS.SHPN@nhs.net.

Summary of Recommendations

Acute bloody diarrhoea requires **urgent clinical assessment** especially in a child under 16 years of age.

STEC infection should always be **suspected** in **a child or adult** with **acute bloody diarrhoea** even if only **one episode** contains blood.

STEC infection should also be **considered** in a child or adult with non-bloody diarrhoea and epidemiological risk factors for STEC infection.

Most STEC infections are sporadic and STEC infection should still be considered even in the absence of known epidemiological risk factors.

Clinically suspected cases of STEC infection should be discussed **urgently** with the local public health team who will advise on the appropriate public health management.

All patients with clinically suspected STEC infection should urgently:

- Be assessed in primary or acute care
- Have a stool sample submitted for culture indicating bloody diarrhoea on the request form
- Have recommended bloods and urinalysis performed
- Be notified to the local public health team
- Be considered infectious and have infection control measures discussed and implemented with the individual and their carers

Patients with clinically suspected or confirmed STEC infection should be admitted to hospital if they:

- are unwell or dehydrated
- are at risk of dehydration due to frequent loose stools and/or persistent vomiting
- have laboratory features associated with HUS

Patients admitted to hospital should be treated with early intravenous fluids, rather than oral rehydration.

Patients with evidence of HUS should be discussed with the relevant nephrology department.

The frequency of repeat blood tests should be determined by clinical progress and the results of the baseline investigations.

Anti-diarrhoeal drugs are not recommended in symptomatic treatment of STEC infection.

Pain should be managed with simple analgesia where possible. NSAIDs should be avoided and opiate analgesia should be restricted to circumstances where other pain control measures have failed.

Antibiotics are not recommended in the treatment of clinically suspected or confirmed STEC infection.

Plasma exchange is not recommended in the treatment of STEC associated HUS.

Eculizimab cannot currently be recommended for rescue therapy of STEC associated HUS as evidence is lacking for benefit in severe disease.

Where STEC infection is confirmed, patients require monitoring for potential development of HUS for 14 days following the onset of diarrhoea.

Introduction

In all patients presenting with diarrhoea the need for vigilance in detecting STEC infection is paramount because of the significant risk of developing haemolytic uraemic syndrome (HUS) particularly in children and older adults.

STEC infection, although uncommon overall, is more likely in patients with bloody diarrhoea and therefore acute bloody diarrhoea requires urgent clinical assessment, especially in a child under 16 years of age.

Clinically suspected cases of STEC infection should be discussed **urgently** with the local public health team. Advice will be provided on the appropriate public health management.

This clinical guidance was developed to provide clear principles of assessment of clinically suspected or confirmed *Escherichia coli* O157 (STEC positive and negative) and non-O157 STEC infection in patients of different age groups presenting to primary care and acute care.

Clinical Features of STEC

Symptoms of STEC infection range from asymptomatic infection, to mild non-bloody diarrhoea, through to bloody diarrhoea, abdominal pain and occasionally fever. Around one third of patients require to be admitted to hospital[9].

STEC infection may be complicated by the development of haemolytic uraemic syndrome (HUS)[1]. Mortality from STEC infection is largely associated with HUS and its renal and neurological complications although severe gastrointestinal complications are also reported.

Haemolytic Uraemic Syndrome

Definition

Haemolytic Uremic Syndrome comprises a triad of:

- microangiopathic haemolytic anaemia
- thrombocytopaenia
- acute kidney injury

Incidence

Approximately 10-15% of cases of STEC infection overall will develop HUS[2]. Children under 16 years and older adults are more likely than other age groups to develop HUS, particularly children under 5 years and adults over the age of 65 years[3]. In England between 2009 and 2012, three quarters of STEC-HUS cases occurred in children (0-14 years)[4].

Clinical Features of HUS

Features on clinical assessment associated with more severe illness and increased risk of HUS include [1, 2, 3, 5, 15, 16, 17, 18, 19, 20, 21]:

- Dehydration
- Frequent bloody stools
- Severe abdominal pain/cramps
- Vomiting
- Pallor
- Petechiae
- Oilguria
- Blood and protein on urine dipstick.

Laboratory Features of HUS

Laboratory indicators of established HUS include:

- Anaemia (dehydration with subsequent haemoconcentration may obscure anaemia)
- Fragmented red cells on blood film
- Thrombocytopenia
- Rising urea and creatinine
- Elevated LDH
-

Disease Progression to HUS in Children

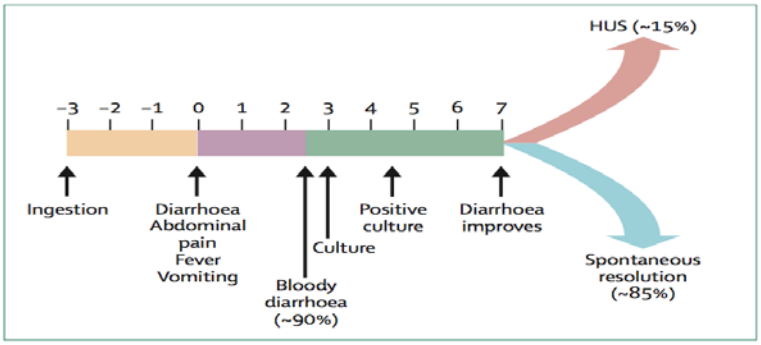
Approximately 15% of children with STEC infection will develop HUS[1, 2].

HUS predominantly affects the kidneys but other organ systems are also affected and HUS may present with neurological features such as irritability, encephalopathy, seizures and focal neurological signs and features.

HUS typically develops 6-8 days after the onset of diarrhoea, often as diarrhoeal symptoms are improving, but an interval of up to 14 days has been reported [Figure 1][1,22]. HUS has also been reported after apparent recovery from the initial diarrhoeal illness[21].

Figure 1 Timeline of STEC infection and duration of symptoms in children

Comment [e1]: This will be redrawn with "Time in days" as the legend to avoid confusion



Epidemiological risks for STEC

In a patient presenting with diarrhoea, particularly bloody diarrhoea, clinicians should have a high index of suspicion that STEC infection is present if:

1. the patient has been in recent close contact with or had potential exposure to:
    a. ruminant animals (principally cattle, goats, sheep), their faeces, and faecally contaminated environments (such as at open farm visits or during outdoor activities in rural areas)
    b. untreated water from rivers, streams and lochs or private water supplies
    c. a clinically suspected or confirmed or case of STEC
    d. high risk food (such as undercooked meat, unpasteurised milk/milk products or raw vegetables/salad)
2. the patient gives a history of recent travel out with the UK. STEC is endemic in the UK, however, cases also occur in people with a recent history of travel. Of the STEC cases in 2016, 15% were reported to have travelled outside the UK in the 14 days prior to the onset of symptoms.
3. an outbreak of STEC infection is known, or suspected, to be present locally or nationally.

Most STEC infections are sporadic and STEC should still be considered even in the absence of known epidemiological risk factors.

Incubation period of STEC Infection

The incubation period for diarrhoeal illness caused by infection with STEC is usually three to four days, with a range of one to ten days, but has been occasionally recorded as long as 14 days [5, 6, 7] However, longer incubation periods have also been noted[8].

Diagnosis of STEC

- Microbiological diagnosis of STEC infection is by stool culture, or PCR followed by culture or serology (serum samples) in cases with HUS whose stools are culture and PCR negative[9].

- Stool samples from patients with clinically suspected STEC infection should be collected and processed urgently.

- Submitted stool specimens will be tested routinely for the presence of *E. coli* O157 at the local diagnostic laboratory. Indicate on the request if bloody diarrhoea is present. If the clinical information on the request is suggestive of STEC infection, *E. coli* O157 culture negative stool samples are referred to the Scottish *E. coli* O157/ STEC Reference Laboratory (SERL) for PCR testing, which detects both *E. coli* O157 and non-O157 STEC.

- Culture confirmation of *E. coli* O157 at the local diagnostic laboratory will take 24-48 hours from sample receipt. Following local confirmation isolates are referred to SERL for confirmation of identity and typing.

- Rapid referral of samples from diagnostic laboratories to SERL is important to improve the probability of culture confirmation.

- Positive PCR results will be telephoned immediately to the referring diagnostic laboratory and culture results will follow.

- The local diagnostic laboratory will inform the clinical team and the local public health team of positive PCR and culture results.

- Do not delay appropriate clinical and public health management while awaiting Reference Laboratory results.

STEC Infection in Children

Bloody diarrhoea is rare in children and STEC infection should always be suspected in a child with acute bloody diarrhoea even if only one episode contains blood.

Almost one third of STEC cases occur in children under 16 years[10] and rates of infection in Scotland are highest in children under 5 years, therefore it is important to have specific paediatric clinical pathways for clinically suspected or confirmed STEC infection. Complications such as HUS are also most common in children. In England between 2009 and 2012, three quarters of STEC-HUS cases occurred in children (0-14 years)[4].

STEC is also important because of the risk to public health. Large outbreaks have occurred and person-to-person spread of infection with STEC is common and has caused, on average, 20% of cases in outbreaks[11]. Therefore acute bloody diarrhoea in a child under 16 years of age requires urgent public health action, even before microbiological confirmation of STEC infection.

Overall, STEC is an uncommon infection. In a child presenting with acute bloody diarrhoea a

there should also be consideration of more common gastrointestinal infections such as campylobacter, shigella and salmonella. A travel history should always be taken. Non-infective pathology, particularly intussusception and inflammatory bowel disease, should be in the differential diagnosis.

Initial Assessment of Clinically Suspected STEC Infection in Children (in Primary or Secondary Care)

STEC infection should be suspected where children and young people present with:

- acute bloody diarrhoea even if only one episode contains blood
- a diarrhoeal illness and epidemiological risk factors for STEC infection (Box 1-page 18)

Initial assessment should include the assessment of:

- features of more severe illness (vomiting, frequent bloody diarrhoea, severe abdominal pain, oliguria[12 13 14 15])
- dehydration
- the presence of epidemiological risk factors for STEC (Box 1-page 18)
- the probability of an alternative diagnosis particularly one requiring surgical intervention

Initial Management of Children in Primary Care

Where STEC is considered possible on the basis of clinical features or epidemiological risk factors:

- Send a stool sample for culture (www.nice.org.uk/Guidance/CG84).
- Provide relevant clinical history, particularly any history of bloody diarrhoea, on the stool culture request. If the clinical information is suggestive of STEC infection, *E. coli* O157 culture negative stool samples are referred to the SERL for PCR testing, which detects both *E. coli* O157 and non-O157 STEC.

Where STEC is clinically suspected or confirmed:

- Refer urgently to paediatric department for assessment of potential for HUS.
- Notify the local public health team on first suspicion of STEC infection, even pending test results.
- Consider risk to household contacts and give advice on personal hygiene, especially where young children are involved (see appendix 1). The local public health team can provide additional advice and support to patients/parents on control measures.
- Assess any cases of diarrhoea arising in close contacts promptly.

- Advise that all symptomatic people should remain off nursery/school/work until they have been symptom free for at least 48 hours and that some groups such as young children, food handlers, those with inadequate hygiene procedures or people working with vulnerable groups will be required to remain off nursery/school/work for a longer period of time. This also usually applies to people in high risk groups living in the same household as those infected. The local public health team will provide guidance in these circumstances (see the guidance for the public health management of *Escherichia coli* O157 and other Shiga toxin-producing (STEC) infections available here).

- Advise parents that public health/environmental health will be in contact with the family to try to determine the source of infection and to give advice on prevention of onward spread and returning to nursery/school/work.

Investigations recommended in the diagnosis of HUS are documented in **Table 1**.

Evidence grade B

Table 1

Microbiology	**Comments**
Stool culture	Indicate bloody diarrhoea on request form
Stool PCR	If stool culture negative
Blood (serum sample) for STEC Antibody (HUS only)	If stool culture or PCR negative or stool sample not available
Urine	**Features of HUS**
Dipstick testing	Haematuria and proteinuria
Blood	**Features of HUS**
FBC and **film** • Film • WBC • Haemoglobin • Platelets	Fragmented RBC Neutrophilia [4,14,16,17,18] Anaemia or a falling Hb Low or falling platelet count for age
Urea and electrolytes	Rising urea or creatinine
Liver function tests	Bilirubin elevated due to haemolysis. Transaminitis is not uncommon
Lactate dehydrogenase	Elevated due to haemolysis

C-Reactive protein	Any increase in CRP is associated with increased risk of HUS, even if a small rise [20, 19]
Coagulation Screen	Check in confirmed cases

Management of Children with clinically suspected STEC infection in Secondary Care

- Patient should be assessed and monitored for dehydration. Send bloods and test urine to look for evidence of dehydration or HUS (Table 1).
- Urgently send a stool sample for culture if STEC is not already confirmed.
- Provide relevant clinical history, particularly any history of bloody diarrhoea, on the stool culture request. If the clinical information is suggestive of STEC infection, *E. coli* O157 culture negative stool samples are referred to the SERL for PCR testing, which detects both *E. coli* O157 and non-O157 STEC.
- Implement mandatory infection control measures immediately (Appendix 2)
- Intravenous Fluid Therapy
  In children who develop HUS there is evidence that the administration of intravenous saline in the four days from the onset of diarrhoea or at the first sign of HUS reduced the need for dialysis in up to 50% of patients[20,21,22,23,24,25]. Therefore in contrast to NICE clinical guidance on gastroenteritis (www.nice.org.uk/Guidance/CG84), consider early intravenous fluid therapy in clinically suspected cases of STEC infection where there is:
  - clinical dehydration
  - clinical features associated with HUS (Flowchart 1)
  - early features of HUS on bloods (Table 1)

  For these patients, give isotonic intravenous solution (0.9% sodium chloride or 0.9% sodium chloride with 5% dextrose) for both fluid deficit replacement and maintenance.

  Evidence grade B
- Discuss further management with paediatric nephrology services.
- Notify the local public health team on first suspicion of STEC infection, even pending test results.
- Consider risk to household contacts and give advice on personal hygiene, especially where young children are involved (see appendix 1). The public health/infection prevention and control team can provide additional advice and support to patients/parents and clinical teams on control measures.

Comment [e2]: For paediatric colleagues to consider:
Should this stay in this section? Would you want to discuss all STEC cases or just HUS cases? If all cases then would need an explanation as to why.

- Advise parents that public health/environmental health will be in contact with the family to try to determine the source of infection and to give advice on prevention of onward spread and returning to nursery/school/work.

Management of Symptoms in Children

Anti-motility drugs are not recommended because an association with developing HUS or neurological complications of STEC infection has been reported with the use of anti-motility agents[3, 26].

Evidence grade C

Where possible opiates should be avoided[27] and simple analgesia is advised however, in patients with severe pain, opiates may be required and in such cases surgical assessment (including abdominal imaging) is advised.

Evidence grade D

Treatment with non-steroidal anti-inflammatory drugs (NSAIDs) is not recommended because NSAIDs may have adverse effects on renal blood flow and increase the risk of kidney injury [28].

Role of Antibiotics in Children with Clinically Suspected or Confirmed STEC Infection

In children with clinically suspected or confirmed STEC infection antibiotics are not recommended.

Evidence grade B

There is evidence that antibiotic treatment, particularly exposure to bactericidal antibiotics such as β-lactams (penicillins, cephalosporins, monobactams and carbapenems), may also be a risk factor for HUS and although this finding is not consistent across clinical reports, trials and meta-analyses, there is no clear evidence to recommend antibiotics in the treatment of STEC infection[12,13,15,25,29, 30, 31, 32].

Evidence grade C

The use of antibiotics should, therefore, be governed by good paediatric practice as indicated by clinical needs other than the management of STEC infection itself.

Ongoing monitoring for the development of HUS in Children with STEC Infection

Where STEC infection is confirmed, vigilance for the onset of HUS should be maintained for at least two weeks following the date that diarrhoea first occurred[1].

Children confirmed to be STEC positive, who are well and discharged, should have paediatric review until 14 days after the onset of diarrhoea.

Blood tests should be repeated every 1-3 days depending on clinical presentation, initial test results and clinical progress.

Blood and protein in urine is associated with HUS. Urine should be tested by dipstick on a daily basis for 14 days from the onset of diarrhoea. The detail of how this is achieved will be determined by local service provision.

Evidence grade D

Children with evidence of HUS

If features of HUS are present, the patient needs to be managed in conjunction with the paediatric nephrology service.

The principles of management are determined by renal function and urine output.

Ongoing intravenous fluid therapy should be used for those with a good urine output, but once oligoanuria is identified fluid restriction should be considered to avoid fluid overload[33].

Evidence grade D

Further management of confirmed HUS in Children

HUS is associated with an acute mortality of between 2-5% and approximately 50% of children will require renal replacement therapy[34,35].

Children with established HUS should therefore be managed in conjunction with paediatric nephrologists. In Scotland it is probable that such children will be transferred to the Royal Hospital for Children (RHC), Glasgow.

In most cases renal function recovers although long-term renal sequelae such as hypertension and chronic kidney disease can develop[36, 37, 38].

Role of Plasma Exchange in Children with STEC Associated HUS

There is insufficient evidence to recommend treatment of STEC associated HUS with plasma exchange.

In STEC associated HUS, the recently published evidence in support of or against plasma exchange remains contradictory in outbreak reports, case comparison studies and expert opinion. A Cochrane review of interventions for HUS published in 2009 concluded that supportive therapy (including blood transfusion, control of fluid and electrolyte imbalance, dialysis when indicated and control of hypertension) remains the preferred management for patients with post-diarrhoeal HUS. The review identified only a small number of studies, however treatment of STEC associated HUS with plasma exchange is not recommended[39, 40]. Cases of clinical or diagnostic uncertainty can be discussed with the regional apheresis unit.

Evidence grade B

Role of Eculizimab in Children with STEC Associated HUS

Eculizimab cannot currently be recommended for rescue therapy of STEC associated HUS as evidence is lacking for benefit in severe disease.

Eculizimab was frequently administered in patients with typical HUS in the large EHEC O104:H4 multi-region outbreak in Europe in 2011. Results from retrospective analyses of this outbreak are mixed with both no definite positive effect of eculizumab on the clinical course of patients and rapid and efficient recovery following early treatment with eculizumab[41, 42,43,44].

Eculizumab therapy was often given when there was severe neurological involvement or persistence of HUS despite plasmapheresis therapy. There was some evidence that in children with typical HUS and CNS involvement, early use of eculizumab was associated with good neurological outcome, but in patients with rapidly progressing HUS and multiple organ involvement, eculizumab seemed to be less beneficial.

Ongoing clinical trials may be beneficial in answering the question about the benefit of eculizimab over best supportive care.

Evidence grade C

Information for Parents of Children with clinically suspected or confirmed STEC Infection

Give parents and families the STEC Patient Information Leaflet (see Appendix 1)

The parents should be made aware of signs and symptoms that require them to return for further medical reassessment:

- Bloody diarrhoea, if this was not present before.
- Repeated vomiting.
- Abdominal pain/cramps.

- Passing urine less often or in smaller amounts.
- Increasingly weak and tired.
- Cold hands and feet.
- Looking very pale.
- Petechiae.
- Oedema, especially around the eyes or legs and feet.
- Headache.

Emergency healthcare contact details should be provided.

Information for Parents of Children with HUS

Parent and patient information is available on the Infokid Website
http://www.infokid.org.uk/STEC-HUS

Public Health and Infection Control Advice in Children

All cases of clinically suspected or confirmed STEC infection should be immediately notified to public health and infection prevention and control teams if an acute care setting.

Public health/environmental health will then contact the case/family to try to determine the source of infection, to provide infection control advice in the community setting and to advise on exclusion from nursery/school/work where necessary.

In order to prevent the onward transmission of infection, all symptomatic people should remain away from nursery/school/work until they have been symptom free for 48 hours.

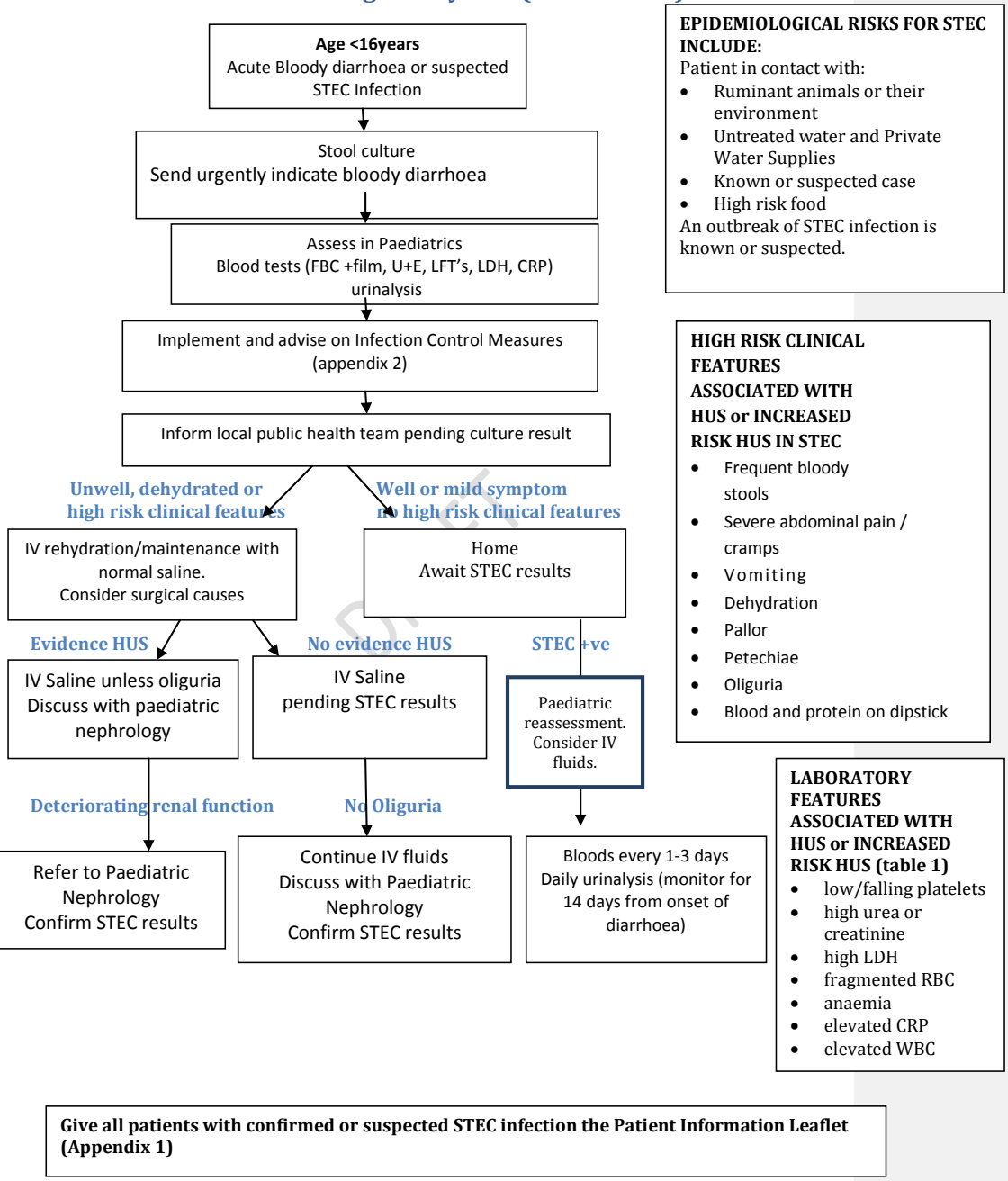
Also, certain groups of people such as food handlers, young children, those with inadequate hygiene procedures or people working with vulnerable groups will be required to be remain off nursery/school/work for a longer period of time. This also usually applies to people in high risk groups living in the same household as those infected. Public health will provide guidance in these circumstances.

More information on STEC infection including infection control advice within the home can be found in the Patient Information Leaflet (Appendix 1).

Infection Control advice for patients in hospital is available in Appendix 2.

Full details on the public health response can be found in the 'Guidance for the public health management of *Escherichia coli* O157 and other Shiga toxin-producing (STEC) infections' (available here).

Management of Acute Bloody diarrhoea or Clinically Suspected STEC Infection in children age< 16 years (Flowchart 1)



STEC Infection in Adults

The diagnostic assessment of bloody diarrhoea in adults is complicated by a higher incidence of non infectious causes.

The differential diagnosis in an adult presenting with acute bloody diarrhoea includes:

- infection (camplylobacter, shigella, salmonella and STEC)
- inflammatory bowel disease
- diverticular disease
- ischaemic colitis
- malignancy

STEC is an uncommon cause of bloody diarrhoea in adults out with outbreaks, however specific clinical guidance on the management of STEC is required because of the risk of HUS which in turn is associated with high mortality in adults[3,45,46].

Recognition of STEC is also important because of the risk to public health. Large outbreaks have occurred and person-to-person spread of infection with STEC is common and has caused, on average, 20% of cases in outbreaks[11].

Initial Assessment of Clinically Suspected STEC Infection in Adults (in Primary or Secondary Care)

STEC infection should be suspected where an adult presents with:

- acute bloody diarrhoea even if only one episode contains blood
- a diarrhoeal illness and epidemiological risk factors for STEC infection (Box 1-page 27)

Initial assessment should include the assessment of:

- clinical severity
- hydration
- the presence of epidemiological risk factors for STEC (Box 1-page 27)
- the probability of alternative diagnosis particularly one requiring surgical intervention

If there is a high index of suspicion for STEC infection the case should be discussed urgently with an Infection Specialist.

Initial Assessment of Adults in Primary Care

Where STEC is considered possible on the basis of clinical features or epidemiological risk factors:

- Urgently send a stool sample for culture if STEC is not already confirmed.

- Provide relevant clinical history, particularly any history of bloody diarrhoea, on the stool culture request. If the clinical information is suggestive of STEC infection, *E. coli* O157 culture negative stool samples are referred to the SERL for PCR testing, which detects both *E. coli* O157 and non-O157 STEC.

Where STEC is clinically suspected or confirmed:

- Refer for admission patients who are dehydrated, systemically unwell or with severe abdominal pain.

- Send bloods and test urine to look for evidence of dehydration or HUS (Table 2).

- Notify the local public health team on first suspicion of STEC infection, even pending test results.

- Consider risk to household contacts and give advice on personal hygiene (Appendix 1). The local public health team can provide additional advice and support to patients on control measures.

- Assess any cases of diarrhoea arising in close contacts promptly

- Advise that all symptomatic people should remain off work until they have been symptom free for at least 48 hours and that some groups such food handlers, those with inadequate hygiene procedures or people working with vulnerable groups will be required to remain off work for a longer period of time. This also usually applies to people in high risk groups living in the same household as those infected. Public health will provide guidance in these circumstances (see the Guidance for the public health management of *Escherichia coli* O157 and other Shiga toxin-producing (STEC) infections available here).

- Advise that public health/environmental health will be in contact to try to determine the source of infection and to advise on prevention of onward spread and returning to work.

Adults managed at home should be provided with information on:

- rehydration
- symptoms that indicate concern (Flowchart 2)
- the expected clinical course of their illness
- good personal hygiene to reduce the risk of transmission in household contacts
- how to get immediate help from appropriate healthcare professionals should their symptoms worsen or fail to settle

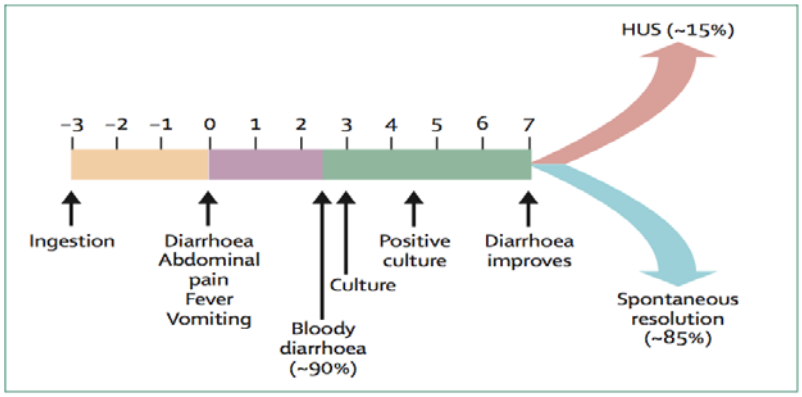
Disease progression to HUS in Adults

Less than 5% of adults with STEC infection will develop HUS[47]. Patients of older age or with comorbid illness or any laboratory abnormalities associated with increased risk of HUS require to be monitored most closely[48].

HUS typically develops 6-8 days after the onset of diarrhoea but an interval of up to 14 days is reported [Figure 2] [11, 22]. HUS has also been reported after apparent recovery from the initial diarrhoeal illness[21].

Figure 2 Timeline of STEC infection and duration of symptoms in adults

Comment [DS(IUC3]: This needs a legend that says "Time in days" and to change % who develop HUS to less than 5% and spontaneous resolution 95%to match the text



HUS typically affects the kidneys but can also affect organ systems and adults may present with neurological features such as reduced consciousness, seizures or focal neurological signs and symptoms . Myocardial ischaemia and pancreatitis are also reported[3].

Investigations recommended in the diagnosis of HUS are documented in Table 2

Evidence grade B

Table 2

Microbiology	**Comments**
Stool culture	Indicate bloody diarrhoea on request form
PCR	If stool culture negative
Blood(serum sample) for STEC Antibody (HUS only)	If stool culture or PCR negative or stool sample not available
Urine	**Features of HUS**
Dipstick testing	Haematuria and proteinuria
Blood	**Features of HUS**
FBC and **film** • Film	 Fragmented RBC

• WBC • Haemoglobin • Platelets	Neutrophilia [4, 14,23, 24, 25,48] Anaemia or a falling Hb Low or Falling platelet count
Urea and electrolytes	Rising urea or creatinine
Lactate	Elevation may indicate alternative diagnosis such as severe sepsis or ischaemic colitis
Liver function tests	Bilirubin elevated due to haemolysis. Transaminitis is not uncommon
Lactate dehydrogenase	Elevated due to haemolysis
C-Reactive protein	Any increase in CRP is associated with increased risk of HUS [20, 48]
Coagulation Screen	Confirmed cases

Management of Adults in Secondary Care

- Patient should be assessed and monitored for dehydration
- Send bloods and test urine to look for evidence of dehydration or HUS (Table 1).
- Initiate intravenous fluids if the patient is dehydrated, at risk of dehydration with frequent diarrhoea or where there are laboratory features that indicate HUS or increased risk of HUS.

  For these patients, give isotonic intravenous solution (0.9% sodium chloride, PlasmaLyte or Hartmanns solution) for both fluid deficit replacement and maintenance.

  Evidence grade B
- Implement mandatory infection control measures immediately.
- Send stool sample for culture and PCR if STEC is not already confirmed.
- Provide relevant clinical history, particularly any history of bloody diarrhoea, on the stool culture request. If the clinical information is suggestive of STEC infection, *E. coli* O157 culture negative stool samples are referred to the SERL for PCR testing, which detects both *E. coli* O157 and non-O157 STEC.
- Notify the local public health team on first suspicion of STEC infection, even pending test results.

- Consider risk to household contacts and give advice on personal hygiene (Appendix 1). The public health/infection prevention and control team can provide additional advice and support to patients and clinical teams on control measures.

- Advise patients that public health/environmental health will be in contact to try to determine the source of infection and to give advice on preventing onward transmission and returning to school/work.

- Pending a definitive diagnosis continue the investigation and management of other causes of colitis.

Management of Symptoms in Adults

Anti-motility drugs are not recommended because an association with developing HUS or neurological complications of STEC infection has been reported with the use of anti-motility agents[3, 49].

Evidence grade C

Where possible opiates should be avoided[50] and simple analgesia is advised, however, in patients with severe pain, opiates may be required and in such cases surgical assessment (including abdominal imaging) is advised.

Evidence grade D

Treatment with non-steroidal anti-inflammatory drugs (NSAIDs) is not recommended because NSAIDs may have adverse effects on renal blood flow and increased risk of kidney injury [51].

Role of Antibiotics in Adults with Clinically Suspected or Confirmed STEC Infection

In adults with clinically suspected or confirmed STEC infection antibiotics are not recommended.

Evidence grade B

There is evidence that antibiotic treatment, particularly exposure to bactericidal antibiotics such as β-lactams, may also be a risk factor for HUS and although this finding is not consistent between clinical reports, trials and meta-analysis there is no clear evidence to recommend antibiotics in the treatment of STEC infection[12,13,15,25,30,,31,32,33].

Evidence grade C

The use of antibiotics should, therefore, be governed by good infection management, as indicated by needs other than the management of STEC infection itself.

Ongoing monitoring for HUS in Adults with STEC Infection

Where STEC infection is confirmed, vigilance for the onset of HUS should be maintained for at least two weeks following the date that diarrhoea first occurred[21].

Adults, who are well but confirmed to be STEC positive, should have ongoing review until 14 days after the onset of diarrhoea.

Urine should be tested for blood and protein by dipstick on a daily basis for 14 days after the onset of diarrhoea. The detail of how this is achieved will be determined by local service provision.

Bloods should always be repeated if any clinical deterioration occurs.

Refer for admission any adult who develops clinical features of concern (see flowchart 2).

Discuss with a nephrologist any adult who has clinical or laboratory evidence of HUS.

Evidence grade D

Adults with Evidence of HUS

STEC associated HUS in adults affects predominantly older patients and is associated with acute mortality of 30%, which is ten-fold that of other age groups[47]. Approximately 50% of adult patients will require renal replacement therapy[43, 44].

In most cases renal function recovers although long-term renal and/or extra-renal sequelae such as hypertension can develop[37, 38, 39].

Further management of established HUS should be delivered and directed by a nephrologist.

Evidence grade D

Role of Plasma Exchange in Adults with STEC Associated HUS

There is insufficient evidence to recommend treatment of STEC associated HUS with plasma exchange.

In STEC associated HUS, the recently published evidence in support of or against plasma exchange remains contradictory in outbreak reports, case comparison studies, case reports and expert opinion. A Cochrane review of interventions for HUS published in 2009 concluded that supportive therapy (including blood transfusion, control of fluid and electrolyte imbalance, dialysis when indicated and control of hypertension) remains the preferred management for patients with post-diarrhoeal HUS. However, the review identified only a small number of studies. Therefore, treatment of STEC associated HUS with plasma exchange is not recommended[52, 53]. Cases of clinical or diagnostic uncertainty can be discussed with the regional apheresis unit.

Evidence grade B

Role of Eculizimab in Adults with STEC Associated HUS

Eculizimab cannot currently be recommended for rescue therapy of STEC associated HUS as evidence is lacking for benefit in severe disease.

Evidence grade C

Eculizimab was frequently administered in patients with typical HUS in the large EHEC O104:H4 multi-region outbreak in Europe in 2011. Results from retrospective analyses of this outbreak are mixed with both no definite positive effect of eculizumab on the clinical course of patients and rapid and efficient recovery following early treatment with eculizumab[42,43,44,45].

Eculizumab therapy was often given when there was severe neurological involvement or persistence of HUS despite plasmapheresis therapy and there was some evidence that in patients with typical HUS and CNS involvement, early use of eculizumab was associated with good neurological outcome, but in patients with rapidly progressing HUS and multiple organ involvement, eculizumab seemed to be less beneficial.

Information for Adults with clinically suspected or confirmed STEC Infection

Give patients the STEC Patient Information Leaflet (see Appendix 1). The patient should be advised to report any signs and symptoms of concern, particularly:

- Bloody diarrhoea, if this was not present before.
- Repeated vomiting
- Severe abdominal pain/cramps.
- Passing urine less often or in smaller amounts.
- Increasingly weak and tired.
- Cold hands and feet.
- Looking very pale.
- Petechiae.
- Oedema, especially around the eyes or legs and feet.
- Headache

Emergency healthcare contact details should be provided.

Public Health and Infection Control Advice in Adults

All cases of clinically suspected or confirmed STEC infection should be immediately notified to public health and infection prevention and control teams if an acute care setting.

Comment [e4]: The wording of this section currently being checked by Kenny Douglas so it may change slightly based on his expertise.

Public health/environmental health will contact the case/family to try to determine the source of infection, to provide infection control advice in the community setting and to advise on exclusion from school/work, where necessary.

In order to prevent the onward transmission of infection, all symptomatic people should remain away from work until they have been symptom free for 48 hours.

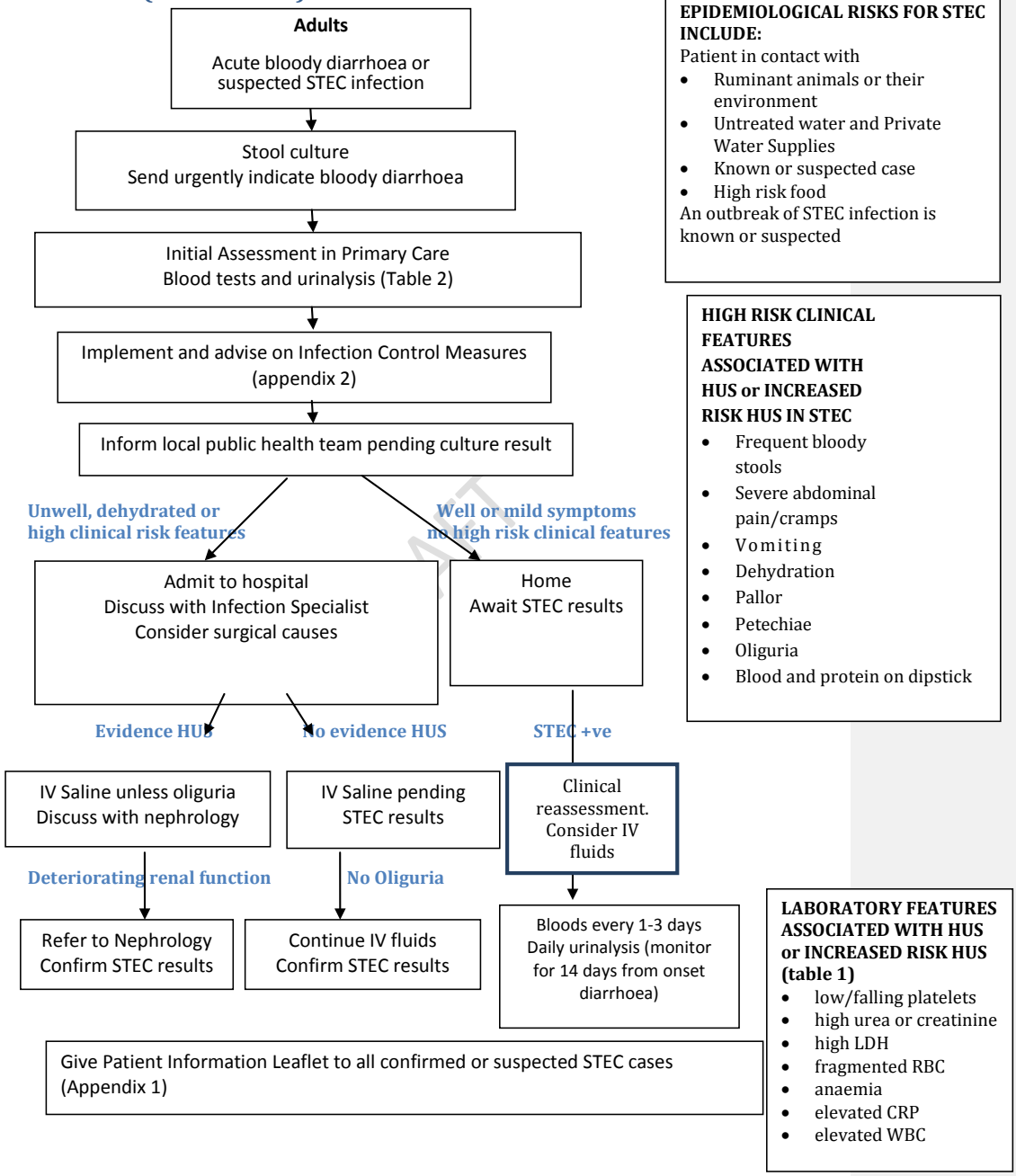
Also, certain groups of people such as food handlers those with inadequate hygiene procedures or people working with vulnerable groups will be required to remain off work for a longer period of time. This also usually applies to people in high risk groups living in the same household as those infected. Public health will provide guidance in these circumstances.

More information on STEC infection including infection control advice within the home can be found in the Patient Information Leaflet (Appendix 1).

Infection Control advice for patients in hospital and care homes is available in Appendix 2.

Full details on the public health response can be found in the 'Guidance for the public health management of *Escherichia coli* O157 and other Shiga toxin-producing (STEC) infections' (available here)

Management of Adults with Clinically Suspected or Confirmed STEC Infection (Flowchart 2)



EPIDEMIOLOGICAL RISKS FOR STEC INCLUDE:

Patient in contact with

- Ruminant animals or their environment
- Untreated water and Private Water Supplies
- Known or suspected case
- High risk food

An outbreak of STEC infection is known or suspected

HIGH RISK CLINICAL FEATURES ASSOCIATED WITH HUS or INCREASED RISK HUS IN STEC

- Frequent bloody stools
- Severe abdominal pain/cramps
- Vomiting
- Dehydration
- Pallor
- Petechiae
- Oliguria
- Blood and protein on dipstick

LABORATORY FEATURES ASSOCIATED WITH HUS or INCREASED RISK HUS (table 1)

- low/falling platelets
- high urea or creatinine
- high LDH
- fragmented RBC
- anaemia
- elevated CRP
- elevated WBC

Appendix 1

***E. coli* O157 and other STEC infections – Patient Information Leaflet**

Essential Information – a summary

STEC can cause diarrhoea (which may contain blood), and stomach cramps for up to 14 days.
It is important to drink lots of fluids.
There may be serious complications of this infection such as kidney failure. It is important that you return for the tests and check ups we have told you about.
If any of the following signs or symptoms develop, then you should return for further prompt medical assessment:

- Bloody diarrhoea, if this was not present before.
- Severe tummy pain/cramps.
- Passing urine less often or in smaller amounts.
- Increasingly weak and tired.
- Cold hands and feed.
- Looking very pale.
- Pink or purple spots appearing on the skin.
- Swelling (oedema), especially around the eyes or legs and feet.
- Headache.

STEC is infectious to other people so follow strict hygiene measures.
At home, you must be very careful about hand washing with liquid soap and running warm water. Do not share towels and clean the bathroom regularly.
Stay off nursery/school/work until you have had no diarrhoea or other symptoms for at least 48 hours. Some people such as food handlers, nursery school children and those who work with vulnerable people will be required to stay away from nursery/school/work and some community activities for longer than this. Public health/environmental health will advise.

What are *E. coli* O157 and STEC?

Escherichia coli (*E. coli*) is a bacterium commonly found in the gut (intestines) of humans and animals. It makes up part of the normal gut flora - the bacteria living in the intestine.

Shiga toxin-producing *E. coli* (STEC) are a particular type of *E. coli*, one of which is known as 'O157'. These are **not** usually found in the intestines of healthy humans and can cause serious illness in humans.

Why is it important?

STEC causes diarrhoea (around half of people infected will have bloody diarrhoea), stomach cramps and occasionally fever. Symptoms may last up to 14 days. However, the bacteria can still be present in the faeces for longer than this.

Some people who are infected may not show any symptoms. Others may go on to develop very serious complications such as haemolytic uraemic syndrome (HUS) which causes kidney failure.

Young children are at higher risk of STEC infection and along with older adults, are at greater risk of serious complications. Almost half of STEC cases in Scotland are in children under 16 years of age.

Can STEC be treated?

Specific treatment is not usually needed for STEC infection. It is important to drink plenty of fluids to replace the water lost through diarrhoea.

The following medications are **not** recommended for STEC infection:

- antibiotics.
- medicines to stop diarrhoea.
- non-steroidal anti-inflammatory medicines, such as ibuprofen.
- opiate-based medication, such as co-codamol or codeine phosphate.

If you are taking any of these medications, please discuss this with your GP.

When should I get help?

All people with clinically suspected or confirmed STEC infection should get prompt medical assessment.

Some people with STEC, such as young children and older adults, will require blood test monitoring to check for the development of complications.

Hospital admission may not be required, but you should be given a plan of how and when to seek further medical advice.

You may be given an appointment within 1-3 days for review, with or without further tests.

You may be shown how to test urine at home.

If any of the following signs or symptoms develop, then you should return for further prompt medical assessment:

- Bloody diarrhoea, if this was not present before.
- Severe tummy pain/cramps.
- Passing urine (weeing) less often or in smaller amounts.
- Increasingly weak and tired.
- Cold hands and feet.
- Looking very pale.
- Pink or purple spots appearing on the skin.
- Swelling (oedema), especially around the eyes or legs and feet.
- Headache.

The complications of STEC infection can develop up to two weeks after symptoms first started, even if the diarrhoea has stopped.

How might I have picked up STEC infection?

STEC are found in the intestines of animals, mainly in farmed cattle, sheep and goats including calves, lambs and kids, but also potentially in wild animals such as deer and rabbits. Although they carry the bacterium, most animals carrying STEC will show **no** signs of illness.

As well as in these animals' intestines, STEC can be found in their faeces, including anywhere their faeces may come into contact with.

STEC bacteria need to be taken in by mouth for someone to become infected.

This can happen by:

- Swallowing bacteria which are on hands after contact with animals or places/objects/clothing, where their faeces is or may have been. Hands **do not** need to look dirty to have bacteria on them.
- Drinking untreated water from lochs, rivers and streams, or from private water supplies that have not been adequately treated.
- Eating high risk foods such as undercooked meat, unpasteurised milk including dairy products made from unpasteurised milk or raw vegetables and salad.
- Eating other food items that have become 'cross-contaminated' by poor hand hygiene after handling raw meat or other contaminated foods, or by an infected person who has handled food.
- Spread from another person infected with STEC. An infected person can pass the infection on to others fairly easily when hand hygiene is poor. This can either occur through direct contact from person to person with inadequately washed hands or through the environment, such as the bathroom, if this becomes contaminated with their faeces (e.g. through touching toilet flushes, taps etc.) and is not cleaned regularly and adequately.

The time between swallowing the bacteria and symptoms starting (the incubation time) is mostly between 1 and 14 days but commonly around 3 to 4 days. Not everyone who is infected with STEC will have symptoms.

How can I avoid passing STEC onto others?

It is very important to follow strict hygiene measures if you or your child has STEC infection to help prevent others from becoming infected. STEC spreads easily within the household by accidentally passing from the faeces of an affected person to others via unwashed hands or touching contaminated surfaces such as towels, toilet flush handles, taps etc.

Measures that can be taken to reduce the risk of spreading the infection include:

- Washing and drying hands thoroughly using running warm water and liquid soap and separate towels is the **most important** way to reduce the risk of becoming infected with

STEC . **Always** wash hands after toileting (including if assisting a child to the toilet or changing nappies) and before eating or handling food and drinks or smoking. Small children should be **supervised** to wash their hands.

For detailed advice on hand washing, see http://www.washyourhandsofthem.com.

- If possible, try not to prepare food for the rest of your family until your symptoms have finished and you have not had any symptoms for a further 48 hours. If this is unavoidable then washing your hands thoroughly with warm running water and liquid soap before preparing the food is essential. People who prepare food as a job will be required to stay away from work until they are clear of infection – please see section below.
- Affected people should use their own towels which should be changed and washed daily or when visibly soiled.
- If the household has two toilets, the affected person should have their own toilet for their use.
- Bathrooms should be cleaned after use by the affected person using hot water and detergent including toilets, flush handles, taps, sinks and door handles. Cleaning with general purpose detergent should be followed by disinfection using a freshly prepared sodium hypochlorite (e.g. bleach) solution diluted following the manufacturer's instructions
- Soiled clothing and bed linen should be washed separately to other items in a washing machine on the hottest temperature possible for the fabric. Always wash your hands after handling soiled items.

People with STEC infection should avoid swimming pools until they have been completely free of symptoms for 48 hours.

Can I still go to work/school/nursery?

All people with diarrhoea or vomiting should stay away from work/school/nursery until they have been completely free of symptoms for 48 hours.

Some people with STEC infection who are more likely to pass on the infection, such as food handlers, young children or those who work with vulnerable people, will be required to stay away from school/nursery/work and some community activities as advised by the public health team. This usually means having two consecutive negative stool samples, with a minimum of 24 hours between the samples, before being allowed to return to normal daily routines. This also usually applies to people in high risk groups living in the same household as those infected. Public health will provide guidance in these circumstances.

The Food Standards Agency provides detailed advice for food handlers on fitness to work:

https://www.food.gov.uk/sites/default/files/multimedia/pdfs/publication/fitnesstoworkguide09v3.pdf

Public health/environmental health involvement

All samples which test positive for STEC infection are reported to public health and environmental health. An Environmental Health Officer or member of the public health team will contact you to ask some questions in order to try and identify where you might have picked up the infection. Questions will be about where you live, your activities, places you have visited including work/school/nursery/community activities and foods you have eaten at home or from restaurants or takeaways in the two weeks before you became ill.

The information you provide will be used locally to help understand where you have picked up STEC and the control measures needed to minimise the risk of others becoming infected. Nationally the information is used to gain a better understanding of the causes and risk factors for STEC which will inform measures to reduce the risk of these infections. The public health team can also provide information and advice on how you may have contracted the illness, how to prevent further spread and returning to work/school/ nursery.

How can I reduce my risk of contracting STEC again in the future?

Having STEC infection once does not mean you are immune from getting the infection again in the future.

Ways to reduce the risk include:

- Washing and drying hands thoroughly using running warm water and liquid soap:
    - before eating or handling food and drinks or smoking.
    - after toileting (including if assisting a child to the toilet or changing nappies).
    - after contact with animals and areas / clothing / objects that may be contaminated with animal faeces.
- Do not drink water from sources such as rivers, streams and lochs without treating it first.
- If you have a private water supply, make sure it is adequately managed and maintained. The Drinking Water Quality Regulator for Scotland provide detailed advice for owners and users of private water supplies:

  http://dwqr.scot/private-supply/information-for-pws-owners-and-users/

- Follow good food hygiene practices when handling and cooking food to prevent illness.

For further information on how you can reduce the risk, see:
https://www.hps.scot.nhs.uk/a-to-z-of-topics/escherichia-coli-o157/#guidelines
https://www.hps.scot.nhs.uk/web-resources-container/ecoli-o157-and-other-stec-infections-public-information-leaflet/

For more information on STEC infection, see:

https://www.nhsinform.scot/illnesses-and-conditions/infections-and-poisoning/escherichia-coli-e-coli-o157

Appendix 2

Action to Prevent Spread In Hospital and Care Homes

At the point at which a patient is suspected of having infectious diarrhoea, enhanced infection prevention and control precautions (i.e. transmission based precautions) should be applied as far as possible until the patient is asymptomatic for at least 48 hours. Local infection prevention and control teams should be informed and can provide additional advice on control measures in the acute setting.

These precautions include:

1. Patient placement: Place patient in a single room with ensuite facilities or own commode until they have been asymptomatic for at least 48 hours.
2. Health care equipment: Patient should have their own health care equipment which is not shared with other patients if possible. All re-usable patient care equipment should be cleaned with chlorine based detergent after each use.
3. Patient environment: The patient environment should be subject to enhanced cleaning with a chlorine based detergent to reduce risk of spread via contaminated environment.
4. Hand hygiene: Staff and visitors should be encouraged to wash their hands with liquid soap and fresh running water before and after contact with the patient or the patient's immediate environment
5. Personal Protective Equipment (PPE): Staff should wear gloves, apron, surgical mask/visor (if risk of facial contamination with aerosols). Hand hygiene should be carried out following removal of PPE.
6. Visitors should be encouraged to undertake thorough hand hygiene, before and after visiting.

Further advice can be found in the national infection prevention and control manual at:
http://www.nipcm.hps.scot.nhs.uk/

Guidance on infection prevention and control in childcare settings can be found at:
http://www.documents.hps.scot.nhs.uk/hai/infection-control/guidelines/infection-prevention-control-childcare-2015-v2.pdf

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Appendix 3

Guideline development group membership, roles and competing interests and external review

The VTEC/*E. coli* O157 – Action Plan for Scotland 2013-2017 identified key recommendations to develop clinical guidance providing advice on the early diagnosis and management of suspected STEC infection in Scotland, to identify methods for monitoring compliance with its guidance and for evaluating its effectiveness and to optimise rapid microbiological confirmation of non-O157 STEC infection.

The clinical group was established as a subgroup of the VTEC Action Plan Implementation Group, as to address these three recommendations. It consisted of different representatives across NHS Scotland who have all had a part in participating with the writing, consultation and publication of the guidance.

Name	Remit on Network	Job Title/Role	Organisation	Competing interests
Lynn Byers	Health Protection Nurse Specialist	Health protection Nurse Specialist	NHS Grampian	None
Sarah Couper	Consultant in Public Health Medicine	Consultant in Public Health	NSS, HPS	None
Stephanie Dundas	Workstream Lead and Chair	Clinical Lead Infectious Diseases	NHS Lanarkshire	None
Lindsey Guthrie	Lead Nurse Infection Prevention & Control	Lead Nurse Infection Prevention & Control	NHS Lothian	None
Mary Hanson	Consultant Microbiologist	Director of SERL and Consultant Microbiologist	NHS Lothian	None
Victoria Harkins	Paediatric Nephrologist	Specialist registrar paediatric nephrology	NHS Greater Glasgow & Clyde	None
Simon Hurding	General Practitioner Representative	Clinical Lead Therapeutics Branch	Scottish Government	None
Pamela Joannidis	Infection Prevention & Control	Nurse Consultant	NHS Greater Glasgow & Clyde	None
Lynsey MacDonald	Representative	Policy Officer	Scottish Government	None
Heather	Consultant	Consultant Paediatric	NHS Greater	None

Maxwell	Paediatric Nephrologist	Nephrologist	Glasgow & Clyde	
Stephanie McAuley	Administrator	Administrator	HPS	None
Eisin McDonald	Epidemiologist	Epidemiologist	HPS	None
Lesley McGuire	Project Manager	Project Manager	SHPN, HPS	None
Emmanuel Okpo	Consultant in Public Health Medicine	Consultant in Public Health Medicine	NHS Grampian	None
Adrian Sie	Consultant Paediatrician	Consultant Paediatrician	NHS Lanarkshire	None

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Keeping up to date

This guideline was published in 2019 and will be considered for review in three years. The review history, and any updates to the guideline in the interim period, will be noted in the review report.

External review

The guideline was sent for external feedback to the following identified stakeholders in the spring of 2018:

- Consultants in Public Health Medicine (CPHMs)
- SHPN-Coordination Group
- SHPN-Gastrointestinal and Zoonoses (GIZ) group
- SHPN-VTEC AIG Group
- Health Protection Scotland on-call consultants
- Scottish Health Protection Nurses Network
- Chief Officers of Environmental Health
- Scottish Microbiology and Virology Network (SMVN)
- Scottish Paediatrics renal and Urology Network and MCN
- Haematology
- Infectious Disease
- Primary Care
- Medical Directors

Appendix 4

Search criteria for the literature reviews

SEARCH 1

Question:

1. Antibiotics
    a. What is the evidence for increased risk of HUS?
    b. Does this risk exist for all antibiotic classes?
    c. Is the risk equal for all virulence types/ serotypes of VTEC?

Search terms [Title/Abstract]:

VTEC OR Escherichia coli OR E. coli OR Verocytotoxin OR Shiga toxin
AND Haemolytic uraemic syndrome OR HUS
AND publication date 2010 to present (February 2016)
AND English language
AND antibiotic OR antimicrobial

SEARCH 2

Question:

2. Opiate analgesia- generally recommended that this should be avoided.
    a. Is there evidence to support this recommendation? Any evidence of harm?
    b. Should they be avoided in only certain situations (e.g. HUS / VTEC / VTEC with colitis)?

Search terms [Title/Abstract]:

VTEC OR Escherichia coli OR E. coli OR Verocytotoxin OR Shiga toxin
AND Haemolytic uraemic syndrome OR HUS
AND publication date 2010 to present (February 2016)
AND English language
AND opiate OR opioid OR opiate analgesia OR morphine OR codeine OR oxycodone OR hydrocodone OR hydromorphone OR pethidine OR methodone

SEARCH 3

Question:

3. Earliest clinical signs of HUS/HUS with colitis
    a. What are these (in children, in adults)?
    b. What are prognostic factors (fever, blood tests, urine tests), and are these independent?

Search terms [Title/Abstract]:

VTEC OR Escherichia coli OR E. coli OR Verocytotoxin OR Shiga toxin
AND Haemolytic uraemic syndrome OR HUS
AND publication date 2010 to present (February 2016)
AND English language
AND risk factor OR sign OR clinical sign OR multi-variate OR multivariate OR prognostic OR biomarker

SEARCH 4

Question:

4. Recommendations for monitoring for HUS
    a. How is HUS monitored in hospitals (for children, for adults)?
    b. Does this differ the community where it is more difficult (typically for adults)?
    c. Should everyone have bloods done?
    d. Should bloods be repeated and if so when?

e. What are the recommendations for monitoring for HUS in confirmed VTEC with colitis, vs confirmed VTEC without colitis.

Search terms [Title/Abstract]:

VTEC OR Escherichia coli OR E. coli OR Verocytotoxin OR Shiga toxin
AND Haemolytic uraemic syndrome OR HUS
AND publication date 2010 to present (February 2016)
AND English language
AND volume expansion OR monitoring OR manage OR monitor OR management

SEARCH 5

Question:

5. Preferred management of HUS
    a. Is there consensus in the preferred management of HUS?
    b. What is done in each of the Health Boards?

Search terms [Title/Abstract]:

VTEC OR Escherichia coli OR E. coli OR Verocytotoxin OR Shiga toxin
AND Haemolytic uraemic syndrome OR HUS
AND publication date 2010 to present (February 2016)
AND English language
AND volume expansion OR monitoring OR manage OR monitor OR management

SEARCH 6

Question:

6. Role of eculizimab and plasma exchange in HUS
    a. When to apply these?

Search terms [Title/Abstract]:

VTEC OR Escherichia coli OR E. coli OR Verocytotoxin OR Shiga toxin
AND Haemolytic uraemic syndrome OR HUS
AND publication date 2010 to present (February 2016)
AND English language
AND eculizimab OR plasma exchange

SEARCH 7

Question:

7. Should the use of antimotility or antidiarrhoeal agents be recommended for treatment of STEC?

Search terms [Title/Abstract]:

VTEC OR Escherichia coli OR E. coli OR Verocytotoxin OR Shiga toxin
AND Haemolytic uraemic syndrome OR HUS
AND publication date 2010 to present (February 2016)
AND English language
AND anti-motility OR anti-diarrhoeal

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