

# SURVEILLANCE OF INFECTIOUS DISEASES IN ANIMALS AND HUMANS IN SWEDEN 2019

Chapter excerpt -  
Shigatoxin producing *Escherichia coli*



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**Reporting guidelines:** Reporting guidelines were introduced in 2018 for those those chapters related to purely animal pathogens. The guidelines build on experiences from several EU projects, and have been validated by a team of international experts in animal health surveillance. The aim is to develop these guidelines further in collaboration within the global surveillance community and they have therefore been made available in the form of a wiki on the collaborative platform GitHub (<https://github.com/SVA-SE/AHSURED/wiki>). Feel free to contribute!

**Layout:** The production of this report continues to be accomplished using a primarily open-source toolset. The method allows the source text, produced by authors, to be edited independently of the template for the layout which can be modified and reused for future reports. Specifically, the chapter texts, tables and captions are authored in Microsoft Word and then converted using pandoc and R to the LaTeX typesetting language. Most figures and maps are produced using the R software for statistical computing. Development for 2019 has further improved the importing of content from Word to LaTeX. The method can now import text, tables and figure captions from Word, as well as the newly designed 'IN FOCUS' sections of some chapters. The tool is available as an R-package at GitHub (<https://github.com/SVA-SE/mill/>). This year the report was also built with a continuous integration pipeline on Microsoft's Azure DevOps platform, allowing every committed change to the content to be built and tested automatically. The report generation R-package and process was designed by Thomas Rosendal and Stefan Widgren. In 2019, figures and the final typesetting were done by Wiktor Gustafsson and Thomas Rosendal with contributions from the report authors.

**Print:** TMG Tabergs AB.

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**Suggestion citation:** Surveillance of infectious diseases in animals and humans in Sweden 2019, National Veterinary Institute (SVA), Uppsala, Sweden. SVA:s rapportserie 64 1654-7098.

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# Shigatoxin producing *Escherichia coli*

## BACKGROUND

Shigatoxin producing *Escherichia coli* (STEC) or, synonymously, verotoxin producing *Escherichia coli* (VTEC), may cause serious intestinal infections in humans. The toxin can be divided into two main groups, shigatoxin 1 (Stx1) and shigatoxin 2 (Stx2), and then the genes can be further divided into several subtypes, for example, *stx1a*. Often the strains associated with severe disease carry the *stx2* gene.

STEC was only sporadically detected in Sweden before 1995, when 114 human cases of STEC O157:H7 were notified. In 1996, STEC O157 was isolated in Swedish cattle for the first time and human STEC O157 infection was traced to a cattle herd. Cattle are the main reservoir of STEC associated with human disease although other animal species may also carry the organism. Not only foods of bovine origin but also vegetable food items and drinking water have been implicated in outbreaks. The infection can also be transmitted through direct or indirect animal contact, via the environment or person-to-person contacts.

Since 2005, between 230–890 cases (2.4–8.7 cases per 100 000 inhabitants) of STEC infections have been reported in Sweden annually, of which 50%–80% are domestically acquired. Most of the domestic cases are reported during the period July to September.

## DISEASE

### Animals

Animals do not develop clinical disease.

### Humans

The clinical picture can vary from asymptomatic infection to non-haemorrhagic or haemorrhagic diarrhoea associated with abdominal cramps. Most patients fully recover. However, a severe complication of the disease is haemorrhagic uremic syndrome, HUS. HUS is characterised by acute renal failure, thrombocytopenia, and microangiopathic haemolytic anaemia; a condition that may lead to death. In recent years, approximately 3% of the cases in Sweden have developed HUS. A large proportion of the patients are young children, and severe complications are most common in this age group, as well as among elderly people.

During 2015 to 2019, 112 cases with STEC were reported to develop HUS. When analysing which serotypes and stx profiles that have been associated with HUS during 2005 to 2019 the most prevalent serotype was the domestic serotype O157:H7 clade 8 with 39 (34%) cases, followed by O26 with 15 (13%) cases and O121 with 6 (5%) cases (Table 24). Almost 30 percent of the HUS cases did not have an isolate for typing.



Figure 24: Incidence (per 100 000 inhabitants) of notified human STEC cases in Sweden, 1997–2019. Prior to 2005, only O157 was required to be reported. In 2005, all serogroups of STEC including PCR findings became subject for notification. In 2005, 2016 and 2018, the number of cases increased due to one or more domestic outbreaks.

Table 24: Serotypes and stx-profiles for reported cases with HUS, 2015–2019.

Serotype	stx1	stx1+stx2	stx1a	stx1a+stx2a	stx1c+stx2b	stx2	stx2a	stx2a+stx2c	stx2a+stx2d	stx2b	stx2b+stx2d	stx2c	UNK	Total
Untyped	-	-	-	-	-	1	-	-	-	-	-	-	29	30
ONT:H29	-	-	-	-	-	-	-	-	-	-	1	-	-	1
ONT:H2	-	-	-	-	-	-	1	-	-	-	-	-	-	1
O182:H25	-	-	1	-	-	-	-	-	-	-	-	-	-	1
O175:H21	-	-	-	1	-	-	-	-	-	-	-	-	-	1
O165:H25	-	-	-	-	-	-	-	1	-	-	-	-	-	1
O156	1	-	-	-	-	-	-	-	-	-	-	-	-	1
O153	-	-	-	-	-	1	-	-	-	-	-	-	-	1
O146:H21	-	-	-	-	-	-	-	-	-	1	-	-	-	1
O130:H11	-	-	-	-	-	-	1	-	-	-	-	-	-	1
O117:H7	-	-	1	-	-	-	-	-	-	-	-	-	-	1
O113:H21	-	-	-	-	-	-	-	-	1	-	-	-	-	1
O112ac:H19	-	-	-	-	-	-	-	-	-	-	-	1	-	1
O103	1	-	-	-	-	-	-	-	-	-	-	-	-	1
O77:H41	-	-	-	-	-	-	1	-	-	-	-	-	-	1
O145:H28	-	-	-	-	-	-	2	-	-	-	-	-	-	2
O113:H4	-	-	-	-	3	-	-	-	-	-	-	-	-	3
O157:H7	-	-	-	1	-	-	1	1	-	-	-	-	-	3
O121:H19	-	-	-	-	-	-	6	-	-	-	-	-	-	6
O26	-	1	2	5	-	-	7	-	-	-	-	-	-	15
O157:H7, clade 8	-	-	-	-	-	-	4	35	-	-	-	-	-	39
Total	2	1	4	7	3	2	23	37	1	1	1	1	29	112

## LEGISLATION

### Animals

Since 1999, STEC O157 findings in animals are notifiable when associated with human infection (SJVFS 2013:23).

### Food

Detection of STEC in food is not notifiable.

### Humans

STEC O157 has been notifiable for both clinicians and laboratories under the Swedish Communicable Disease Act since 1996. All EHEC serotypes have been notifiable since 1 July 2004 (SFS 2004:168 with the addition of SFS 2013:634). A laboratory confirmed case can also include cases that are only positive by PCR i.e. where no isolate has been obtained.

## SURVEILLANCE

### Animals

Surveillance of STEC in animals is both enhanced passive (i.e. traceback investigations from human STEC cases) and active, which consists of planned prevalence surveys of STEC in abattoirs.

#### Passive - Traceback from human cases

If a County Medical Officer suspects an association between a human case of STEC infection and animals, or a farm with animals, the County Veterinary Officer will be informed. A request will be made to the Swedish Board of Agriculture for a trace back investigation and sampling of suspected animals, and/or the environment of the animals.

### Active

Prevalence studies of STEC O157 in cattle at abattoirs have been conducted annually between 1997 and 2002, and then every third year. The next study will be performed during 2020–2021. In these conducted studies, STEC O157 has predominantly been isolated from cattle originating from southern Sweden but rarely from the northern two thirds of the country. The collected samples during 2011–2012 were also analysed for STEC O26 and STEC O103. STEC O26 was detected in 8 of 1308 faecal samples (0.6%) and in 15 of 336 cattle ear samples (4.5%). STEC O103 was detected in three of 1000 faecal samples (0.3%) and in three of 500 ear samples (0.6%). Results from a slaughter prevalence survey from 1998 showed that 0.1% of the pigs were positive for STEC O157:H7.

### Food

No official control programme exists for STEC. National and local authority may perform sampling as a part of extended official controls or targeted projects.

### Humans

The surveillance in humans is based on identification of the disease by the treating physician and/or by laboratory diagnosis (i.e. passive surveillance). Both treating physicians and laboratories are obliged to report to the regional and national level to enable further analyses and adequate intervention measures.

Isolates from human cases are sent to the Public Health Agency of Sweden for typing using whole genome sequencing (WGS) to verify molecular serotype, relevant virulence

### IN FOCUS: Tracing STEC cases back to farms

When a link between a sporadic human case of STEC and a farm is suspected, a traceback investigation is often performed to find the source of infection. Examples of typical connections leading to a traceback are contact with animals and/or their excrements and consumption of raw milk.

The investigation is initiated by the county medical officer and the county veterinary officer who inform the Swedish Board of Agriculture, and the Board of Agriculture decides whether the farm should be sampled. The farm will not always be sampled, it will depend on the severity and number of cases affected. Any recovered isolates from the farm will be compared to human isolates by whole genome sequencing. If the isolates match, the farm is considered as the likely source of infection.

During 2019, the authorities investigated several minor clusters and sporadic cases of STEC that could be linked to farms and food producing animals. The most commonly found STEC type was O157:H7 clade 8, a domestic subtype known for its potential to cause severe disease. It carries the shigatoxin gene *stx2a*, or more often *stx2a* in combination with *stx2c* and is today the most common subtype to cause domestically acquired HUS. The strain was first established in the 1990s in the county of Halland, situated along the west coast of Sweden and has further spread over the years to the southern parts of the country and to the east coast. In recent years, clade 8 has mainly been found in the regions of Skåne, Blekinge, Småland and on the islands Öland and Gotland (Figure 25). It was not until 2004 that other serotypes of STEC than O157 became mandatory to report, and therefore only O157 was traced to farms before this year.

Tracebacks to farms is a valuable tool for preventing further spread by providing advice to farm owners. They also serve as a basis for monitoring the occurrence and geographical spread of STEC variants capable of causing severe illness in infected humans and serve as an early warning system for introduction of new STEC variants in ruminant populations.

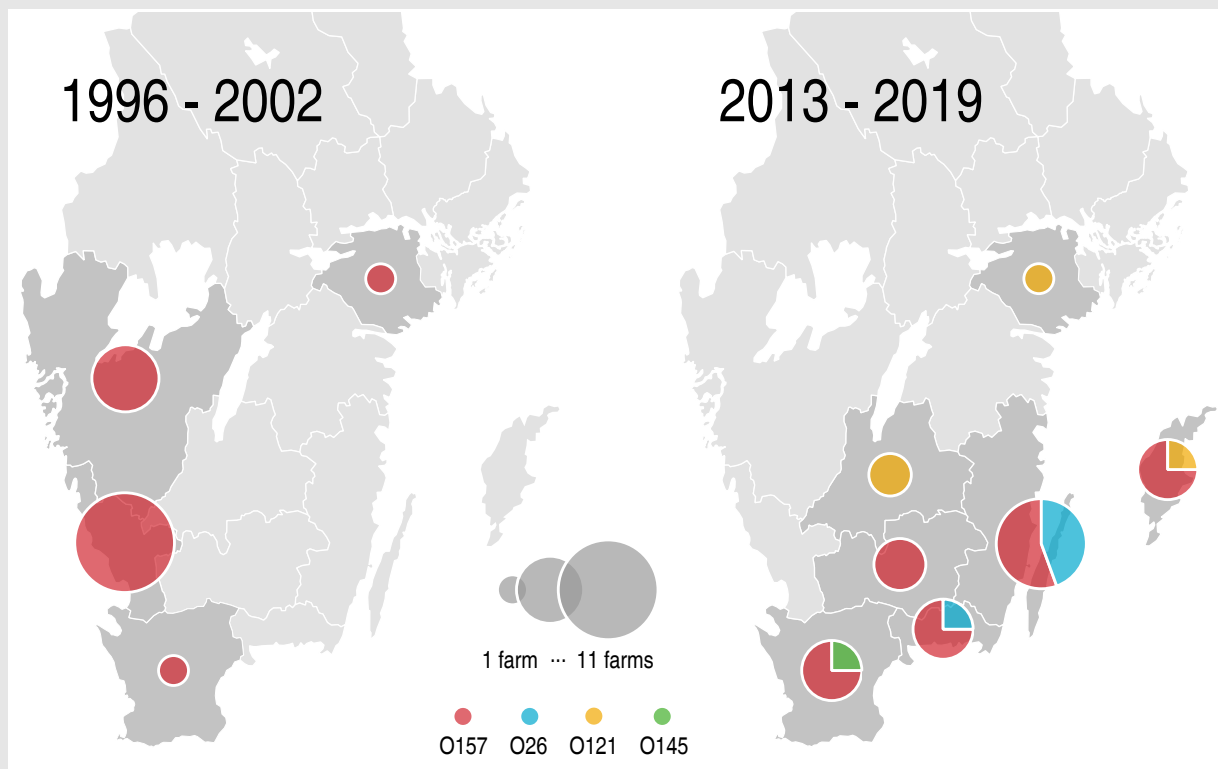


Figure 25: Cattle farms confirmed by genotyping as the source of human infection 1996–2002 (left) and 2013–2019 (right). Serotypes are shown as colors and the size of circles show the number of farms identified during the period, aggregated to county level. Spread of the clade 8 variant of O157 in cattle on the west coast in the late 90's led to a number of farm-associated human cases as well as outbreaks. Since then a notable shift has occurred and clade 8 is now mostly found in the southeastern part of the country. Other serogroups (O26, O121, O145) appear to have become more common as the cause of farm associated human STEC infections over the years. This could reflect improved laboratory capacity and reporting routines for non-O157.

Table 25: Number of reported human cases in comparison to number of cases where an isolate could be retrieved 2019.

Origin of infection	Number of reported cases	Number of isolates typed (%)
Domestic infection	412	237 (58%)
Travel associated infection	331	118 (36%)
Unknown country of infection	13	3 (23%)
Total	756	358 (47%)

genes and for cluster detection. As a conventional nomenclature tool, not only the serotype but also the Multi Locus Sequence Typing (MLST) type, i.e. ST-type, is defined by WGS.

## RESULTS

### Animals

#### Passive - Traceback from human cases

During 2019, 12 investigations were performed where cattle or sheep farms were suspected as sources for human infection, see the “in focus” box. An epidemiological association was established on four occasions of STEC O157:H7 stx2a, stx2c (cattle farms), one occasion of O26:H11, stx2a (cattle farm) and one occasion of O121:H19 stx2a (sheep farm). The other farms were either negative or, in two investigations, had non-identical variants.

#### Active

During 2019 no active surveillance was performed.

### Food

In 2019, 75 samples were taken by national and local authorities from different types of food, and analysed for STEC (6 of these only for STEC O157). Most samples (n=60) were taken at border control from bovine meat. STEC was not found in any of these samples. The rest of the samples were mainly taken to investigate complaints or suspected food poisonings and STEC was found in four of these 15 samples. Three of the positive samples (two samples of meat from wild boar and one sample of cevapcici) were collected at the home of a family with two human cases with EHEC infection. The fourth positive sample was a fresh cheese made from unpasteurised milk.

Table 26: Distribution of serotypes and shigatoxin-subtypes in HUS cases in 2019.

Serotype	stx1a+stx2a	stx2a	stx2a+stx2c	stx2b	stx2c	Unknown stx
O157:H7, clade 8	-	2	8	-	-	-
O157:H7	-	-	1	-	-	-
O26	2	2	-	-	-	-
O112ac:H19	-	-	-	-	1	-
O146:H21	-	-	-	1	-	-
O175:H21	1	-	-	-	-	-
Untyped	-	-	-	-	-	4
Total	3	4	9	1	1	4

### Humans

In 2019, 756 human cases were reported of which 415 were domestic (55%). The domestic incidence in 2019 was 4 (cases per 100 000 inhabitants), and over a longer period of time an increasing trend is seen (Figure 24). As in previous years, the incidence was highest in children.

STEC-associated HUS was reported in 22 cases of which 18 were domestically acquired infections. Eleven of the HUS cases were children under the age of 10. For 18 of the HUS cases an isolate could be retrieved and thereby serotyped. Ten of the domestic HUS cases belonged to serotype O157:H7, clade 8 (Table 26)

For 58% of the domestic STEC cases, an isolate could be retrieved and thereby serotyped. However, for the travel associated cases only 37% were typed. (Table 25). The reason for the low isolation frequency is not known. It can be influenced by regional analysis algorithms, unusual serotypes that are difficult to isolate or that cases who are infected abroad are seeking care in a later stage of the infection where the concentration of the pathogen is too low for isolation. In total 80 different serotypes were identified. The most common serotypes were O157:H7, O26:H11 and O103:H2. 32 cases were diagnosed with the domestic clade 8 of O157:H7, stx2a and stx2c, 10 (31%) of which developed HUS. The third most common serotype in Sweden, O103:H2, normally carries stx1a and gives milder symptoms. However, during 2019 several cases were infected with the more unusual variant that carried both stx1a and stx2a. This variant was detected for the first time in 2012. The fourth most common serotype 2019 was O91:H14, stx1a, a type associated with mild symptoms. This serotype is another example of STEC serotypes that can carry different variants of *stx* genes. In a retail study 2017–2018 by the Swedish Food Agency, O91:H14 carrying both *stx1a* and *stx2b* was the most common type of STEC isolated from lamb meat. This variant has also been identified in a retail study on Swedish beef meat in 2015. Five cases had co-infections of STEC where two different serotypes were detected.

### National outbreak investigations

No national outbreak investigations were performed during 2019.

## DISCUSSION

The long-term trend for human cases of STEC infection in Sweden is rising. One known factor contributing to the higher incidence in some regions in Sweden is an increased use in multiplex PCR panels where a higher number of faecal samples are screened for STEC. Thereby, more STEC cases

are identified. The isolation frequency of PCR positive human samples however decreased in 2019, especially for the travel associated cases. Without characterization of isolates, outbreak investigations, identifying highly pathogenic types and comparison with animal, food and environmental isolates is challenging.

In 2019, an unusually high number of farms, 12 in total, were investigated following suspicion of STEC infection spreading e.g. to visitors. All of these farms were located in southern Sweden (see further discussion regarding this type of investigation in the “in focus” box). The repeated occurrence of STEC O26 among farms in recent years is notable, including strains carrying *stx2a* which have historically been rare or absent among Swedish ruminants while being a common cause of severe STEC cases in other countries. This echoes a trend of increasing numbers of human O26 cases in Sweden caused by strains carrying *stx2a*. To further investigate this, a nationwide cattle slaughterhouse prevalence study targeting O26 as well as O157 will be conducted during 2020–2021. The most common cause of HUS cases in Sweden remains the O157:H7 variant known as clade 8, which is endemic in the southeast.

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National guidelines: Infektion med EHEC/VTEC Ett nationellt strategidokument. Available from: [www.folkhalsomyndigheten.se](http://www.folkhalsomyndigheten.se)