

# SURVEILLANCE OF INFECTIOUS DISEASES IN ANIMALS AND HUMANS IN SWEDEN 2020

Chapter excerpt -  
Shigatoxin producing *Escherichia coli*



**Editor:** Karl Ståhl

Department of Disease Control and Epidemiology  
National Veterinary Institute (SVA), SE-751 89 Uppsala, Sweden

**Authors:** Charlotte Axén, Mia Brytting, Ioana Bujila, Erika Chenais, Rikard Dryselius, Helena Eriksson, Eva Forsgren, Malin Grant, Gittan Gröndahl, Gunilla Hallgren, Kristina Hammarén Busch, Anette Hansen, Marika Hjertqvist, Mia Holmberg, Cecilia Hultén, Helena Höök, Cecilia Jernberg, Jerker Jonsson, Oskar Karlsson Lindsjö, Ulrika König, Elina Lahti, Emelie Larsdotter, Moa Lavander, Mats Lindblad, Anna Lundén, Margareta Löfdahl, Oskar Nilsson, Maria Nöremark, Anna Ohlson, Ylva Persson, Karin Persson-Waller, Thomas Rosendal, Karl Ståhl, Lena Sundqvist, Robert Söderlund, Magnus Thelander, Karin Troell, Henrik Uhlhorn, Anders Wallensten, Per Wallgren, Stefan Widgren, Ulrika Windahl, Joakim Wistedt, Beth Young, Nabil Yousef, Siamak Zohari, Erik Ågren, Estelle Ågren, Elina Åsbjer

**Cover:** Juvenile mink in hand. Photo: Elina Kähkönen

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**Reporting guidelines:** Reporting guidelines were introduced in 2018 for 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 and the LaTeX library pgfplots. Development for 2020 has further improved the importing of content from Excel files to automatically build figures in the pgfplots LaTeX library. The tool is available as an R-package on GitHub (<https://github.com/SVA-SE/mill/>). The report generation R-package and process was designed by Thomas Rosendal, Wiktor Gustafsson and Stefan Widgren. In 2020, final typesetting was done primarily by Wiktor Gustafsson with contributions from the report authors.

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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 the genes encoding the toxins 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 2020, 122 cases with STEC were reported to develop HUS. When analysing which serotypes and *stx* profiles that have been associated with HUS during 2015 to 2020 the most prevalent serotype was the domestic serotype O157:H7 clade 8 with 42 (34%) cases, followed by O26 with 16 (13%) cases and O121 with 7 (8%) cases (Table 23). Almost 30 percent of the HUS cases did not have an isolate for typing.

## 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.

Table 23: Serotypes and shigatoxin (stx) profiles for reported cases with haemorrhagic uremic syndrome (HUS), 2015–2020.

Serotype	stx1	stx1+stx2	stx1a	stx1a+stx2a	stx1c+stx2b	stx2	stx2a	stx2a+stx2c	stx2a+stx2d	stx2b	stx2b+stx2d	stx2c	Unknown stx	Total
Untyped	-	-	-	-	-	1	-	-	-	-	-	-	33	34
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	-	-	-	-	-	-	7	-	-	-	-	-	-	7
O26	-	1	3	5	-	-	7	-	-	-	-	-	-	16
O157:H7, clade 8	-	-	-	-	-	-	5	37	-	-	-	-	-	42
ONT:H6	-	-	-	-	-	-	-	-	-	1	-	-	-	1
Total	2	1	5	7	3	2	25	39	1	2	1	1	33	122

## 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.

### Molecular surveillance

Isolates from human cases, food and animals are investigated by the national authorities using whole genome sequencing (WGS) to determine the molecular serotype, relevant virulence genes and for cluster detection. As a conventional nomenclature tool, the Multi Locus Sequence Typing (MLST) type, i.e. ST-type, is also defined by WGS. Single nucleotide polymorphism (SNP) analysis is used to compare human isolates to those recovered from suspected sources during outbreak investigations and traceback activities. WGS data is also used to monitor long-term trends, e.g. the population structure of STEC among Swedish animals and the types of STEC causing severe cases of illness among humans.

## RESULTS

### Animals

#### Passive - Traceback from human cases

See section “Investigations of outbreaks and single cases of infection of STEC” below.

### Active

A one-year prevalence survey of STEC O26 and O157 in cattle at abattoirs was started in the fall 2020. In total, 1200 samples will be collected from 13 abattoirs.

### Food

In 2020, 37 samples were taken by national and local authorities from different types of food and analysed for STEC. STEC was not found in any of these samples. Most samples (n=35) were taken at border control from bovine meat. The two other samples were taken to investigate complaints or suspected food poisonings.

### Humans

In 2020, 491 human cases were reported of which 396 were domestically acquired (81%). The domestic incidence in 2020 was 3.8 (cases per 100 000 inhabitants), and over a longer period of time an increasing trend is seen (Figure 29). As in previous years, the incidence was highest in children.

STEC-associated HUS was reported in 10 cases of which 8 were domestically acquired infections. Six of the HUS cases were children under the age of 10. For 6 of the HUS cases an isolate could be retrieved and thereby serotyped. Three of the domestic HUS cases belonged to serotype O157:H7, clade 8 (Table 24).

For 56% of the domestically acquired 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 68 different serotypes were identified. The most common serotypes were O26:H11, O157:H7 and O103:H2. 18 cases were diagnosed with the domestic clade 8 of O157:H7, stx2a and stx2c alternatively only stx2a. Three of these cases developed HUS. The third most common serotype in Sweden, O103:H2, normally carries stx1a and gives milder symptoms. In 2020 one case was infected with the more potentially virulent variant carrying both stx1a and stx2a. In total, 19 isolates (four percent) have been identified with this type in Sweden since 2012.

Table 24: Distribution of serotypes and shigatoxin-subtypes in haemorrhagic uremic syndrome (HUS) cases in 2020.

Serotype	stx1a	stx2a	stx2a + stx2c	stx2b	Unknown stx
O157:H7, clade 8	-	1	2	-	-
ONT:H6	-	-	-	1	-
O26:H11	1	-	-	-	-
O121:H19	-	1	-	-	-
Untyped	-	-	-	-	4
Total	1	2	2	1	4

### Investigations of outbreaks and single cases of infection of STEC

In 2020, five farm investigations were carried out due to detection of human cases connected to farm animals. Three of the farms were positive for EHEC, while two were negative at sampling. At two of the farms, O26 was identified: H11, stx1a and stx2a, where one farm had sheep and the other cows and sheep. At the third farm there were goats and here the cause of infection was O157: H7 clade 8 stx2a. The most common cause of HUS cases in Sweden remains the O157:H7 variant known as clade 8, which is endemic in the southeast.

One national outbreak investigation was performed during 2020 with 7 cases of O103:H11 stx 1a. No source could be identified.

Table 25: Number of reported human cases of shigatoxin producing *Escherichia coli* (STEC) in comparison to number of cases where an isolate could be retrieved 2020.

Origin of infection	Number of reported cases	Number of isolates typed (%)
Domestically acquired infection	396	222 (56%)
Travel associated infection	78	118 (37%)
Unknown country of infection	17	3 (29%)
Total	491	256 (52%)



Figure 29: Incidence (per 100 000 inhabitants) of notified human shigatoxin producing *Escherichia coli* (STEC) cases in Sweden, 1997-2020. 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.

### IN FOCUS: It only takes two to tango – clustering of STEC isolates

Outbreaks of STEC are seldom identified and the majority of cases are considered sporadic. Microbial surveillance of STEC is a tool for cluster detection, source tracing and outbreak investigation and it captures outbreak signals that could otherwise go undetected. Epidemiological typing of STEC isolates on national level in Sweden is done using whole genome sequencing. The sequencing data is used for e.g. species determination, identification of molecular serotype, virulence genes and other relevant genes such as antibiotic resistance markers. In addition, a cluster analysis is performed for all isolates within a defined serotype where a cluster is defined as two or more isolates. When a cluster is detected, regional health authorities are informed in order to interview cases and investigate the cluster. Small clusters can for example be cases within the same family, or it can be the first signal of a continuously growing cluster that will evolve to a national outbreak investigation. Each year a number of small and large clusters are investigated. Number of clusters, number of cases involved in clusters and proportion of isolates that are part of a cluster were summarised for 2018, 2019 and 2020 (Table 26). The majority of clusters were small in regard to number of isolates and most often reported as domestically acquired. The serotypes that were most often identified in clusters during this period were O157:H7 and O26:H11, which are also the most common serotypes identified in Sweden. In 2020 there were only three small clusters identified within O157:H7. In addition, there was a farm investigation where a human isolate and an isolate identified on a farm with goats clustered (Figure 30).

The number of clusters identified during 2018–2020 varied largely between years. In the pandemic year of 2020, relatively few clusters were identified (n=18) compared to 2018 and 2019 when 53 and 33 clusters were identified respectively (Table 26). Furthermore, the proportion of isolates involved in clusters varied between years. In 2018, when there was a large outbreak with 112 cases, 52 percent of all isolates were part of a cluster. If the large outbreak is not accounted for, this proportion was 30 percent. In 2019 and 2020 the proportion of isolates in clusters were 25 and 18 percent, respectively. This shows that a considerable proportion of isolates from cases with no known epidemiological links are connected by typing data. Possible explanations include exposure to shared sources of infection as well as the regional occurrence of genetically closely related domestic strains of STEC among animals on multiple farms.

Comparing isolates from patients, food, animals and the environment in cluster analyses is a powerful tool for investigating outbreaks and source tracing. In the longer perspective, analysing the duration, re-occurrence and possible seasonality of clusters can provide vital clues to determine the routes of infection for STEC in Sweden. However, cluster definition remains a challenge and appropriate thresholds for inclusion in a cluster are likely to be dependent on serotype and context.

Table 26: Distribution of human clinical Shigatoxin producing *Escherichia coli* (STEC) isolates in genomic clusters in 2018, 2019 and 2020. Clusters were assessed using single nucleotide polymorphisms (SNPs) of whole genome sequencing data.

Year	Total number of isolates	Isolates in clusters (n)	Isolates in clusters (%)	Total number of clusters	Clusters >=5 isolates	Clusters 2–4 isolates
2018	510	266 <sup>A</sup>	52	53	8	45
2019	361	92	25	33	4	28
2020	256	46	18	16	2	14

<sup>A</sup>In 2018, 112 isolates were part of a large outbreak.

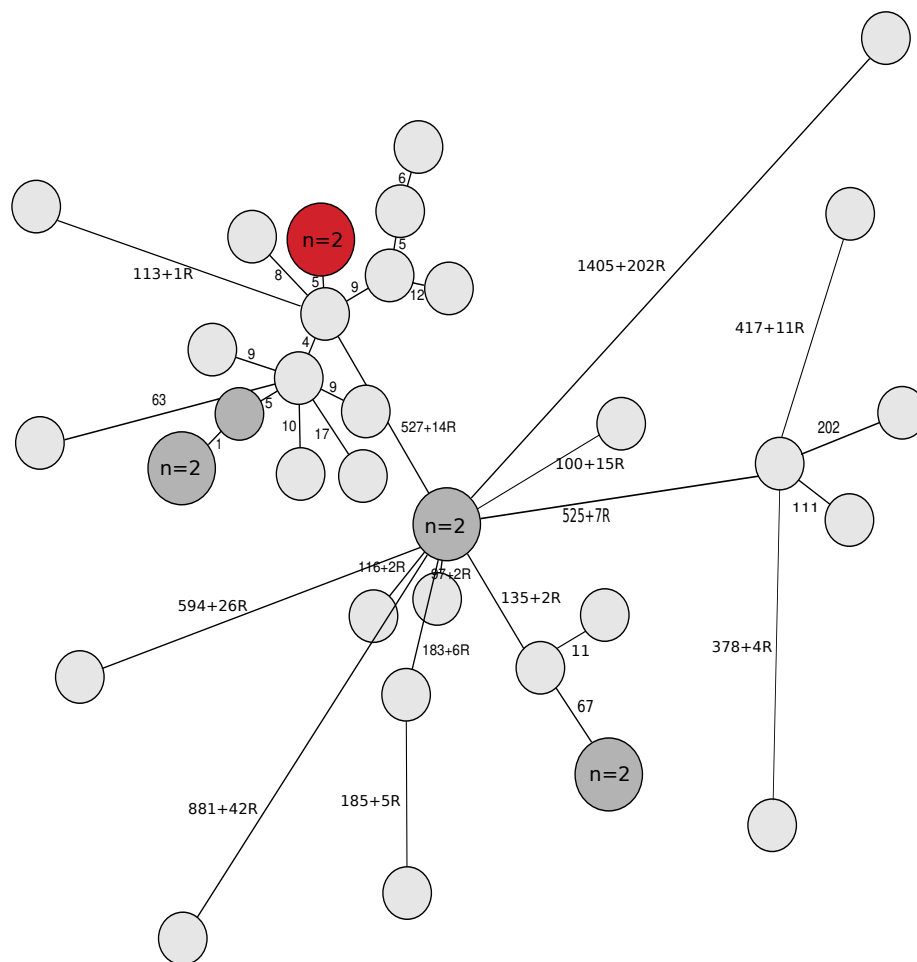


Figure 30: Minimum spanning tree of shigatoxin producing *Escherichia coli* O157:H7 isolated during 2020 in Sweden. Single nucleotide polymorphism (SNP) differences are shown next to the branches. Four small clusters are shown (2–3 isolates each). The cluster marked in red involves a trace back investigation including one human isolate and one isolate identified on a farm with goats. The lengths of the branches are not proportional to the SNP distances. Recombinations (R) were filtered by looking for SNPs with a pairwise distance of 500 nt.

## DISCUSSION

The long-term trend for human cases of STEC infection in Sweden is rising. One known factor contributing to the higher incidence of notified cases 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. It is important to type identified cases. Without characterization of isolates it is challenging to perform outbreak investigations, identify highly pathogenic types and compare animal, food and environmental isolates.

## REFERENCES

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