SURVEILLANCE OF INFECTIOUS DISEASES

IN ANIMALS AND HUMANS IN SWEDEN 2022

Chapter excerpt:
Shigatoxin producing Escherichia coli

SVA NATIONAL VETERINARY INSTITUTE
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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 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 to the LaTeX typesetting language using a custom package written in the R software for statistical computing. The package uses the pandoc document conversion software with a filter written in the lua language. Most figures and maps are produced using R and the LaTeX library pgfplots. Development for 2022 has focused on generalising the R package to accommodate conversion into formats other than LaTeX and PDF, with a focus on markdown files which can be published as HTML websites using the Quarto publishing system. The report generation R package and process was designed by Thomas Rosendal, Wiktor Gustafsson and Stefan Widgren.

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Shigatoxin producing *Escherichia coli*

BACKGROUND

Shigatoxin producing *Escherichia coli* (STEC) 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 cases, both domestic and travel-associated, 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 laboratory-confirmed 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 2022, 162 of a total of 5339 cases with STEC were reported to develop HUS (3.0%). When analysing which serotypes and stx profiles that have been associated with HUS during 2015 to 2022 the most prevalent serotype was the domestic serotype O157:H7 clade 8 with 53 (33%) cases, followed by O26 with 23 (14%) cases, O157:H7 with 9 cases (6%) and O121 with 8 cases (5%). (Table 24). 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 as described in SJVFS 2021:10.

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 2022:217). 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 last study was performed during 2020–2021. In these conducted studies, STEC O157 has predominantly been isolated from cattle originating from southern Sweden and rarely from the northern two thirds of the country.

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.

IN FOCUS: Whole genome typing data provides support for source tracking

The most obvious use of whole genome typing data is event-driven comparison of isolates from cases and suspected sources to confirm routes of transmission. However, as WGS has now been in use for some time at Swedish national authorities, analysing cumulative data over time can give even more interesting information. Figure 49 shows a single nucleotide polymorphism (SNP) tree of all available sequence data from domestically acquired human cases of STEC O157:H7 between 2018 and 2021, compared to all isolates from cattle and sheep collected 2014–2021. The animal data include multiple nationwide slaughterhouse prevalence studies and is therefore likely to contain all variants commonly occurring among Swedish ruminants.

Notably, the diversity among the ruminant isolates is low, and for example clade 8 isolates are homogenous which is consistent with the theory of them being present as the consequence of a single introduction event in the 90s (Franz et al 2019). All ruminant clusters are linked to human cases of STEC infection, but certain clusters are very common among ruminants while causing few infections among the human population, e.g., the cluster marked with an asterisk. As evident in the tree, the diversity among human isolates is far higher, likely reflecting infection from diverse imported foodstuffs and perhaps unexplored animal reservoirs.

This type of reference data from historical isolates can suggest likely sources for investigation early in an outbreak, as illustrated by the clade 8 outbreak 2022 which was identified as likely to be of domestic origin based on genome comparison. One limiting factor, however, is that reference data from animals is only available for the more common serotypes due to the difficulty and high cost of large-scale sample collection and analysis.

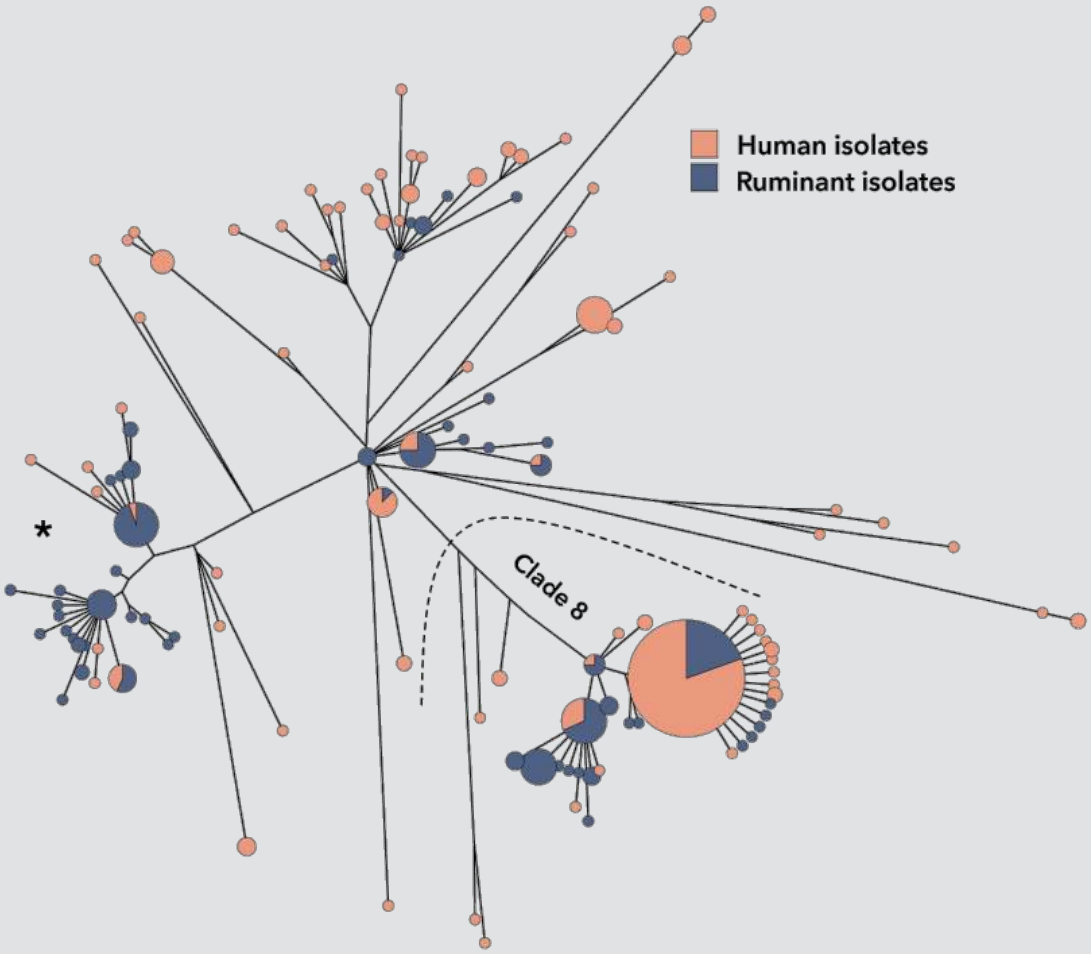

Figure 49: Single nucleotide polymorphism (SNP) tree of all available sequence data from domestically acquired human cases of STEC O157:H7 between 2018 and 2021, compared to all isolates from cattle and sheep collected 2014–2021. Created with GrapeTree.

Table 24: Serotypes and shigatoxin (stx) profiles for reported cases with haemorrhagic uremic syndrome (HUS), 2015–2022.

Serotype	*stx1*	*stx1+stx2*	*stx1a*	*stx1a+stx2a*	*stx1c+stx2b*	*stx2*	*stx2a*	*stx2a+stx2c*	*stx2a+stx2d*	*stx2b*	*stx2b+stx2d*	*stx2c*	*stx2e*	*stx2f*	*Unknown*	*Total*
O26	1	-	2	9	-	2	8	-	-	-	-	-	-	-	1	23
O111:H8	-	-	-	1	-	-	1	-	-	-	-	-	-	-	-	2
O113:H4	-	-	-	-	4	-	-	-	-	-	-	-	-	-	-	4
O121	-	-	-	-	-	1	7	-	-	-	-	-	-	-	-	8
O145:H28	-	-	-	-	-	-	2	-	-	-	-	-	-	-	-	2
O146:H21	-	-	-	-	-	-	-	-	-	2	-	-	-	-	-	2
O157:H7	-	-	-	2	-	1	5	1	-	-	-	-	-	-	-	9
O157:H7, clade 8	-	-	-	-	-	3	7	43	-	-	-	-	-	-	-	53
Other[A]	-	-	2	1	-	3	3	1	1	2	1	1	1	1	-	17
Untyped	1	5	-	-	-	20	-	-	-	-	-	-	-	-	16	42
Total	**2**	**5**	**4**	**13**	**4**	**30**	**33**	**45**	**1**	**4**	**1**	**1**	**1**	**1**	**17**	**162**

[A]ONT:H2, ONT:H6, ONT:H29, O77:H41, O103, O112ac:H19, O113:H21, O117:H7, O130:H11, O146:H21, O153, O156, O165:H25, O175:H21, O182:H25.

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, 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 prevalence survey of STEC O26 and O157 in sheep at abattoirs was performed between May and December 2022. In total, 634 samples were collected from 9 abattoirs. STEC O157 was detected in 14 samples (2.2%) of which one isolate belonged to the clade 8 variant. STEC O26 was detected in 3 samples (0.5%).

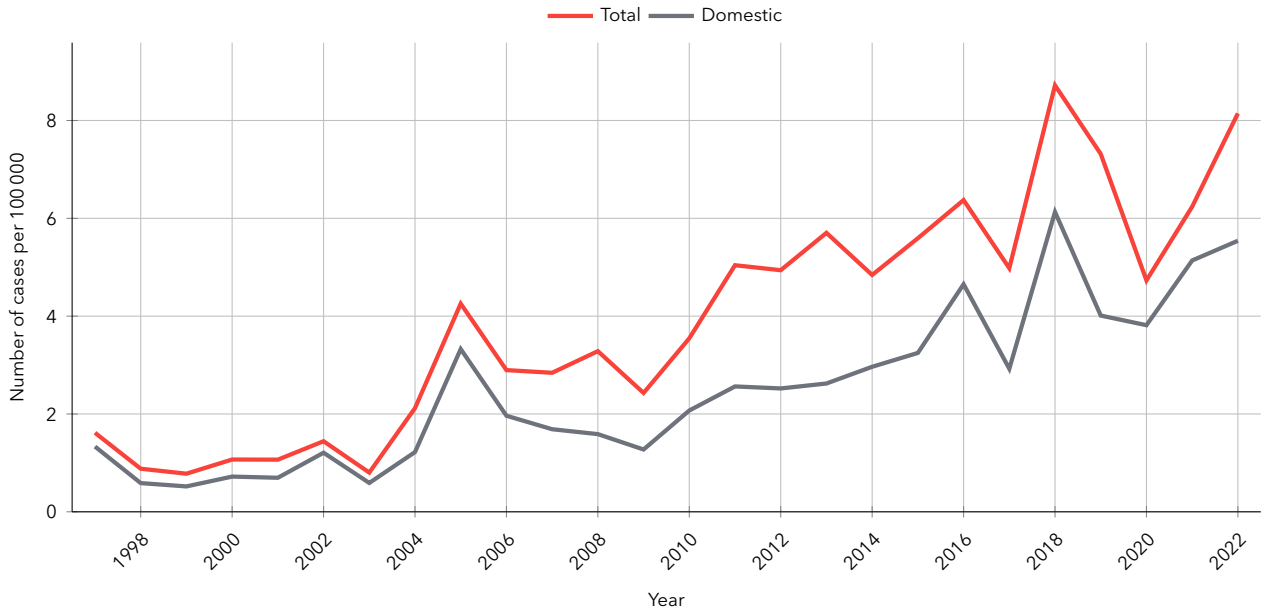

Figure 50: Incidence (per 100 000 inhabitants) of notified human shigatoxin producing *Escherichia coli* (STEC) cases in Sweden, 1997–2022. Prior to 2005, only O157 was required to be reported. In 2005, all serogroups of STEC including PCR findings became subject for notification and gradual introduction of multiplex PCR-panels has likely further led to more cases being detected with time. In 2005, 2016 and 2018, the number of cases increased due to one or more large domestic outbreaks.

Table 25: Distribution of serotypes and shigatoxin subtypes in haemorrhagic uremic syndrome (HUS) cases in 2022.

HUS serotypes 2022	*stx1a*	*stx1a+stx2a*	*stx1c+stx2b*	*stx2*	*stx2a*	*stx2a+stx2c*	*stx2b*	*Unknown*	*Total*
ONT:H2	1	-	-	-	-	-	-	-	1
ONT:H4	-	-	-	1	-	-	-	-	1
O26:H11	-	1	-	-	1	-	-	-	2
O111:H8	-	-	-	-	1	-	-	-	1
O113:H4	-	-	1	-	-	-	-	-	1
O121:H19	-	-	-	-	2	-	-	-	2
O146:H21	-	-	-	-	-	-	1	-	1
O157:H7	-	-	-	1	-	-	-	-	1
O157:H7, clade 8	-	-	-	-	-	1	-	-	1
Untyped	-	-	-	4	-	-	-	4	8
Total	**1**	**1**	**1**	**6**	**4**	**1**	**1**	**4**	**19**

Food

In 2022, 11 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.

Humans

In 2022, 857 human cases were reported of which 583 were domestically acquired (68%). The domestic incidence in 2022 was 5.5 (cases per 100 000 inhabitants), and over a longer period of time an increasing trend is seen, possibly linked to improved diagnostics (Figure 50). As in previous years, the incidence was highest in children younger than five years.

Both domestic and travel-associated infections with STEC show a clear seasonal trend with most cases being reported in summer and early autumn. In 2022, the number of domestic cases were highest between July and October. Travel-associated cases were low in the beginning of 2022, when travel restrictions still prevailed due to the COVID-19 pandemic, but eventually reached similar levels to the comparison period 2015–2019 with a peak in August (Figure 51).

STEC-associated HUS was reported in 19 cases of which 17 were domestically acquired infections. Eleven of the HUS cases were children under the age of 10. Isolates could be retrieved and serotyped from 11 of the HUS cases. No single serotype gave rise to more than two HUS-cases

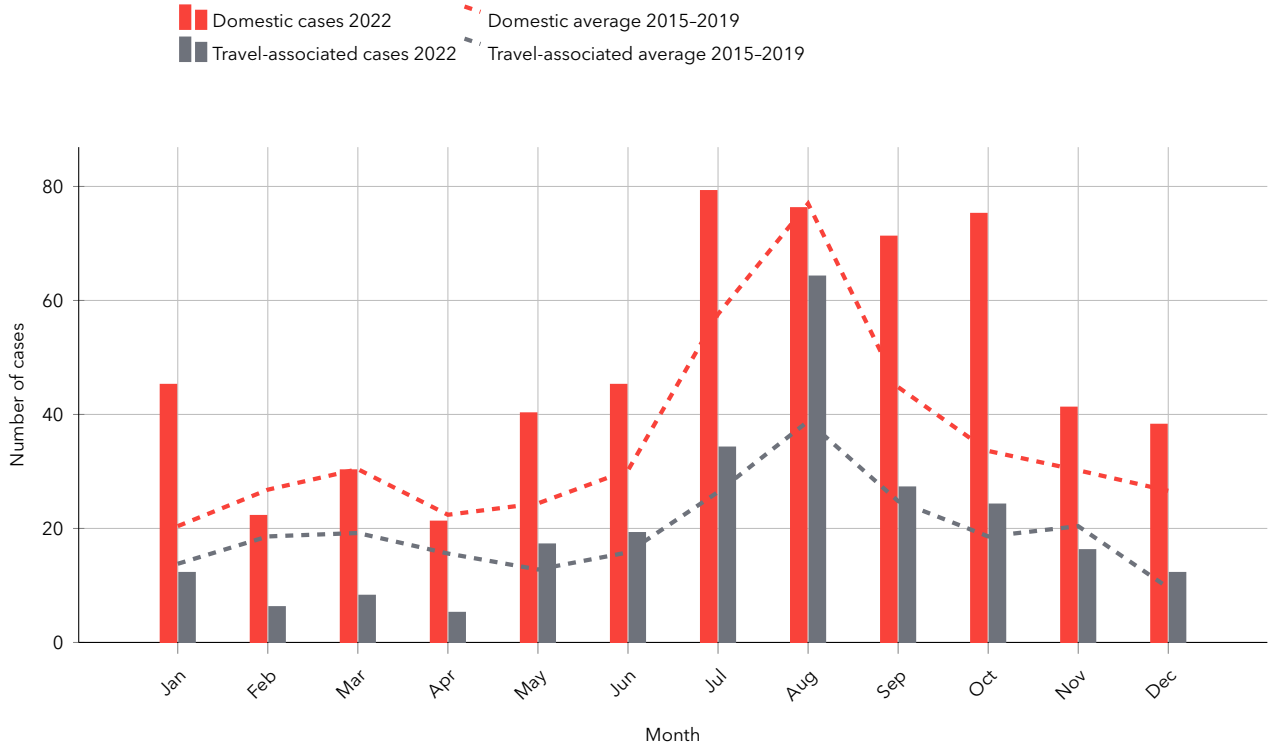

Figure 51: Monthly notifications of domestic and travel-associated human shigatoxin producing *Escherichia coli* (STEC) cases in 2022 and monthly average for domestic and travel-associated notifications in 2015–2019.

(Table 25).

An isolate could be retrieved and thereby serotyped from 53% of the domestically acquired STEC cases. However, for the travel-associated cases only 46% were typed (Table 26). 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 at a later stage of the infection when the concentration of the pathogen is too low for isolation. In total 79 different serotypes were identified, but for six of these the O type could not be identified. The most common serotypes were O157:H7 (n=79), O26:H11 (n=57) and O103:H2 (n=37). Thirty cases were diagnosed with the domestic clade 8 of O157:H7, stx2a and stx2c alternatively only stx2a. Only one of these cases developed HUS which is low compared to the seven HUS-cases with this clone reported in 2021.

Investigations of outbreaks and single cases of infection of STEC

In 2022, three joint farm investigations were carried out after human cases were detected with suspicion of connection to farm animals. Within these investigations, four animal herds were sampled. The suspicions were due to drinking of unpasteurised milk or having direct contact with cattle. All these farms were negative for STEC. The farms were examined for STEC O26 (one farm) and for O103 (three farms). In addition to the cases of suspected farm connection, three outbreaks were investigated. One outbreak was caused by O121:H19, a second by O63:H6 while a combination of the serotypes O103:H2 and O157:H7 clade 8 was behind a third outbreak. None of the investigations led to any suspected source of infection being identified, but for the outbreak in which O157:H7 clade 8 was included, the infection likely originated from a Swedish food and/or from Swedish animals as the clone is domestic.

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 of multiplex PCR panels, allowing both a broader spectrum of toxin genes to be detected and a larger number of faecal samples to be screened for STEC. Indeed, there seems to be a tendency towards a larger diversity in serotypes and toxin types identified among STEC-isolates.

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Table 26: Number of reported human cases of shigatoxin producing *Escherichia coli* (STEC) in comparison to number of cases where an isolate could be retrieved 2022.

Origin of infection	Number of reported cases	Number of isolates typed (%)
Domestically acquired	583	307 (53%)
Travel-associated	244	113 (46%)
Unknown country of infection	30	9 (30%)
Total	**857**	**429 (50%)**