

ECDC RAPID RISK ASSESSMENT

Outbreak of Shiga toxin-producing *E. coli* (STEC) in Germany

27 May 2011

Source and date of request

Request from the European Commission's Directorate-General for Health and Consumers (DG SANCO, Unit C3) on 24 May 2011. Initial Rapid Risk Assessment on 25 May 2011.

Public health issue

Unusual increase of Shiga toxin-producing *Escherichia coli* (STEC) infections in Germany, with patients presenting with haemolytic uremic syndrome (HUS) and bloody diarrhoea.

Consulted experts

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Disease background information

Shiga toxin-producing *E. coli* (STEC) is a group of pathogenic *Escherichia coli* strains capable of producing Shiga toxins, with the potential to cause severe enteric and systemic disease in humans. The full serotype is usually defined by determining both O and H antigens. There are around 200 different *E. coli* O serotypes producing Shiga toxin, of which over 100 have been associated with human disease. Two major Shiga toxin types (Stx1 and Stx2) have been associated with strains causing human disease. While the serotype O157:H7 is considered as clinically the most important, it is estimated that up to 50% of STEC infections are caused by non-O157 serotypes. STEC is of public health concern because of the potential for outbreaks and the risk of serious complications. Haemolytic uremic syndrome (HUS) is considered as the most common cause of acute renal failure in European children. Even if the clinical presentation of non-O157 STEC infections may vary, they can be as virulent as O157:H7 infections.

Transmission of STEC infection mainly occurs through contaminated food or water and contact with animals. Person-to-person transmission is also possible among close contacts (families, childcare centres, nursing homes, etc.). A wide variety of food has previously been implicated in outbreaks as suspected sources, including raw (unpasteurised) raw milk and cheese, undercooked beef, a variety of fresh produce (e.g. sprouts, spinach, lettuce), unpasteurised apple cider, etc. Recently an outbreak of STEC O157 infections in Canada and the USA was linked to walnuts, thus new sources continue to be identified. Various types of animals, in particular cattle and other ruminants, can be healthy carriers of human-pathogenic STEC that can be spread to humans through faecal contamination.

The infective dose is very low. The incubation period ranges from three to eight days. The typical presentation of infections with STEC is acute gastroenteritis, often accompanied with mild fever and sometimes vomiting. The typically bloody diarrhoea is in most cases mild and self-limiting and most people recover within five to seven days. Around 15% of children diagnosed with STEC O157 infection develop the severe complication of HUS; this proportion is much lower among adults, and this proportion in outbreaks of non-O157 outbreaks is not well documented. The severity of STEC diarrhoea is determined by several factors, including the *E. coli* serotype, the type of Shiga toxin produced and other virulence characteristics of the bacteria. The patient's age and the infecting dose also play an important role. Children under the age of 5 years are at higher risk of developing clinical disease when infected, and infants are at increased risk of death from dehydration and septicaemia.

While the confirmation methods of O157 STEC infection are well established, this is not always the case for infections caused by STEC non-O157 serotypes. Therefore, underreporting of non-O157 STEC infections is very likely, and their importance for clinical disease in humans is insufficiently understood.

The treatment of STEC infections is mainly based on rehydration, while antibiotic treatment is often contraindicated as it may activate Shiga toxin release and therefore cause clinical deterioration with a potential evolution to HUS.

STEC infections in humans are under epidemiological surveillance in the EU and in 2009 there were 3 573 reported cases of which about half were caused by the STEC O157:H7 serotype.

Since 2008, eight cases of STEC O104 have been reported in the EU, by Austria (one case in 2010), Belgium (two cases in 2008), Denmark (one case in 2008), Norway (three cases in 2009), and Sweden (one case in 2010); three of these cases were imported. In addition, between 2004 and 2009, Austria and Germany reported some positive findings of STEC O104 in food or animals. However, the suggested outbreak strain of serotype STEC O104:H4 has been rarely reported worldwide.

Event background information

On 22 May 2011, Germany posted a EWRS message reporting a significant increase in the number of patients with HUS and bloody diarrhoea caused by STEC. An urgent inquiry was launched through the EPIS platform on 24 May.

The update provided by Germany on 27 May reports 276 cases of HUS since 25 April. While HUS cases are usually observed in children under 5 years of age, in this outbreak 87% are adults, with a clear predominance of women (68%). Cases in children of school age are also reported. Two people affected by HUS have died. The onset of disease relating to the latest reported case was 25 May. New cases are still being reported.

Laboratory results from samples taken from patients have identified STEC strain of serotype O104:H4 (Stx2-positive, *eae*-negative). A German study has shown that *eae*-negative STEC strains generally affect adults more than children. Two strains isolated from patients from Hesse and Bremerhaven were shown to be highly resistant against third-generation cephalosporins (ESBL) and resistant to trimethoprim/sulfonamid and tetracyclines.

Most cases are from, or have a history of travel to, northern Germany (mainly Hamburg, Northern Lower Saxony, Schleswig-Holstein). Clusters of cases were reported from Hesse and linked to a catering company that supplies cafeterias. These most likely constitute a satellite outbreak.

The source of the outbreak has not yet been confirmed and intensive investigations are ongoing. German health authorities suspect that contaminated food is the vehicle of the outbreak, based on the epidemiological description (e.g. age and geographical distribution) of the cases. Current investigations are focused on raw vegetables. Preliminary results of a case-control study (with 25 cases and 96 controls) conducted by the Robert Koch Institute (RKI) and the health authorities in Hamburg demonstrate a significant association between disease and the consumption of raw tomatoes, fresh cucumbers and lettuce. Considering that the ongoing outbreak included many cases with a severe course of disease, the RKI and the Federal Institute for Risk Assessment (BfR) recommend people in Germany to abstain from consuming raw tomatoes, fresh cucumbers and leafy salads, especially in the northern part of the country, until further notice. Regular food hygiene rules remain in effect.

On 26 May, the Hamburg authority for health and consumer protection isolated STEC from two samples of cucumbers originating from Spain. The German and Spanish authorities are in contact and further investigating the situation.

Through the EPIS forum of the Food- and Waterborne Diseases and Zoonoses network, 10 Member States (Austria, Czech Republic, Finland, France, Hungary, Ireland, Italy, Norway, Poland and Slovenia) confirmed they did not see any unusual increases of STEC cases in the past weeks.

Sweden has reported 10 HUS cases, all of which have travelled to northern Germany between 5 and 15 May. Overall eight of the 10 HUS cases are laboratory confirmed; non-O157 and/or Stx 2-positive and/or *eae*-negative. One of the strains isolated is STEC O104.

Other Member States have also reported HUS cases: UK (2), Denmark (3) and Netherlands (1). One of the UK cases has been confirmed as STEC O104. Both of the UK cases are German nationals. The Danish HUS cases have yielded isolation of STEC strain, which is *eae*-negative and Stx1/Stx2-positive. One of the Danish cases is a German national, and both cases have travelled to Germany. The Dutch case had been visiting Hamburg on 15 May, three days before the onset of illness.

No case of locally acquired infection has been reported in any EU Member State other than Germany as of today.

ECDC threat assessment for the EU

The STEC outbreak reported from Germany is noteworthy considering its magnitude: 276 HUS cases and two deaths due to HUS reported in just a few weeks. The majority of cases reported are adult women. Usually, about 15% of children with STEC infection present with HUS, with this proportion being much lower among adults. This means that several hundred STEC cases with diarrhoea are likely to be occurring in the current outbreak. A further 15 HUS cases have also been identified outside Germany: in the UK, Denmark, Sweden and the Netherlands. All of these cases are related to travel in northern Germany. The exact extent of the outbreak is likely to be revealed in the coming weeks, when case definitions are harmonised and reporting challenges have been addressed.

The isolated outbreak strain STEC O104:H4 is very rare. Prior to the current outbreak, only one case has been documented in literature, and this case was a woman in Korea in 2005.

The case-control study in Hamburg revealed that raw tomatoes, fresh cucumber and leafy salad are the likely vehicles of infection. Samples of fresh cucumbers taken in Hamburg tested positive for STEC, however, the exact time and place of contamination remains unclear.

It is unclear whether the results from Hamburg can be extrapolated to the whole of Germany. Furthermore, it cannot be excluded that an alternative food item is the vehicle of infection. The definite source of the infection remains to be confirmed.

There is currently no indication that either the source of the outbreak or the vehicle of infection has been distributed outside of Germany. However, as the cases reported from Sweden indicate, increased awareness among healthcare practitioners across Europe is needed in order to rapidly identify potential cases linked to this German outbreak. In particular, patients with bloody diarrhoea and recent travel history to northern Germany need to be considered as possible cases linked to this outbreak.

Conclusions

To date, this STEC outbreak is one of the largest described outbreaks of STEC/HUS worldwide and the largest ever reported in Germany, with a very atypical age and sex distribution of the cases and the exposure being limited only to Germany.

As incident cases of HUS or suspected HUS are continuing to be reported, and consultations for bloody diarrhoea remain elevated, it can be assumed that the source of infection is still active.

Currently there is still no evidence that any potential contaminated food product would have been distributed outside of Germany. Thorough investigations ongoing in the country aim at identifying the source of infection, and are crucial to further determining the scope and magnitude of this risk.

Rapid identification of potential cases linked to this outbreak, within Germany or among persons who have travelled to Germany since mid-April/beginning of May, is essential to prevent the development of severe disease. Secondary clusters of cases from person-to-person exposure may occur and thus personal hygiene messages are important.

ECDC continues to monitor closely this event, in collaboration with the Member States, the European Food Safety Authority (EFSA), the European Commission and World Health Organization (WHO).

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