

EFSA/ECDC JOINT RAPID RISK ASSESSMENT

Cluster of haemolytic uremic syndrome (HUS) in Bordeaux, France

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Source and date of request

ECDC internal decision.

Public health issue

Cluster of haemolytic uremic syndrome (HUS) due to *Escherichia coli* (*E. coli*) O104:H4 in Bordeaux, France.

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Disease background information

Shiga toxin-producing *E. coli* (STEC) is a type of pathogenic *E. coli* strain capable of producing Shiga toxins. The strains are also known as verotoxin- or verocytotoxin-producing *E. coli* (VTEC). Virulent strains among this pathotype are also called enterohaemorrhagic *E. coli* (EHEC) and can cause illness ranging from mild intestinal disease to severe kidney complications. There are around 250 different *E. coli* O serotypes producing Shiga toxin, of which over 100 have been associated with human disease. While the serotype O157:H7 is considered as clinically the most important, up to 50% of STEC infections are caused by non-O157 serotypes.

The incubation period ranges from three to eight days. The typical presentation of infections with STEC is acute gastroenteritis, including bloody diarrhoea, often accompanied with mild fever and sometimes vomiting. The 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 haemolytic uremic syndrome (HUS). This proportion is usually much lower among adults. HUS is a serious and sometimes deadly complication. The complete clinical picture of HUS is characterised by acute renal failure, haemolytic anaemia and thrombocytopenia. The severity of disease caused by STEC is determined by several factors, including the *E. coli* serotype, the patient's age and the infecting dose. Children under the age of 5 years and elderly persons are at higher risk of developing HUS when infected, and infants are at increased risk of death from dehydration and septicaemia.

Transmission of STEC infection mainly occurs through contaminated food, water or contact with animals, even though person-to-person transmission is also possible among close contacts (families, childcare centres, nursing homes, etc).

The treatment of STEC infections is mainly based on rehydration. Antibiotic treatment is controversial as certain antimicrobial drugs may activate Shiga toxin release and, therefore, cause clinical deterioration with a potential evolution to HUS, but in some specific clinical situations antibiotic treatment could be used.

STEC infections in humans are under epidemiological surveillance in the EU. In 2009, there were 3 573 reported cases of STEC infections, of which about half were caused by the *E. coli* O157:H7 serotype. A total of 242 HUS cases were reported in 2009.

Event background information

On Friday 24 June, France reported a cluster of eight patients presenting with bloody diarrhoea or HUS in the Bordeaux area. By 28 June, 15 cases of HUS or bloody diarrhoea have been identified in this area. Eleven of them have participated in an event in the commune of Bègles, in Bordeaux, on 08 June. Of these, eight have developed HUS, a severe complication of *E. coli* infection. Seven of the patients are women between 31 and 64 years of age, and four are men, between 34 and 41 years of age. The date of onset of disease for these 11 patients was between 15 and 20 June. In three of the patients, infection with *E. coli* O104:H4 has been confirmed. The isolated strain characteristics are similar to that of the strain isolated in the German outbreak with a similar antibiotic resistance profile.

Nine of the cases reported having eaten sprouts (fenugreek, mustard and rucola) at the event on 08 June, and for two the information is not yet available. Leftover seeds of the sprouts are currently being analysed. These suspected sprouts were locally produced, and were not imported from the farm implicated in the outbreak in Germany [1]. Initial investigations suggested that the seeds used for the sprouts in France were distributed by a UK-based company. Further investigations are now being carried out to determine the origin of the suspected sprout seeds from this French cluster and to establish if there is any link between that cluster and the large outbreak reported from Germany. An analytical epidemiological study is underway with the persons that attended the event on 08 June.

On 28 June, Sweden reported the existence of a confirmed case of *E. coli* O104:H4 in southern Sweden in an adult male who had no history of recent travel to Germany and did not immediately recall the consumption of sprouts during his incubation period, but this is being further investigated.

The French cluster and the Swedish case have been reported in the existing context of an ongoing large outbreak of *E. coli* O104:H4 since May 2011 in northern Germany with a likely association to the consumption of sprouts from a local producer. Characterisation of the German strain shows that it is multidrug resistant and that it produces a CTX-M-15 extended spectrum beta-lactamase (ESBL). In Germany, between 01 May and 27 June 2011, 838 HUS cases and 3 063 STEC cases were reported, of which 47 persons have died. The last date of onset of disease in a case with a STEC O104 confirmation reported from Germany was 12 June; the last date of onset of disease for an HUS case was 22 June. Up to 28 June, 12 EU/EEA countries reported cases associated with the outbreak in Germany for a total of 878 HUS and 3 134 non-HUS STEC cases, with one additional death in Sweden.

There is no link between this current cluster in Bordeaux and a cluster of HUS in children in northern France reported earlier in June, caused by a different serotype of STEC and linked to the consumption of beef burgers [2].

ECDC threat assessment for the EU

E. coli O104:H4 is a very rarely isolated pathotype from humans in Europe. Therefore, it is unlikely that the French HUS cluster is an isolated event unrelated to the recent German outbreak. The currently available information on the French cluster is in favour of a link between these two health events for several reasons. The clinical picture of the French HUS cases in Bordeaux is similar to that of the cases reported from Germany: the cases are adults, the majority are women and the majority are presenting with HUS. The microbiological characteristics of the isolated strain of *E. coli* O104:H4 from three of the French HUS patients seem similar to the isolated strain in the German outbreak, including the antibiotic

resistance profile. Finally, preliminary investigations in Bordeaux show that all cases with microbiological evidence of *E. coli* O104:H4 infection attended the same social event on 08 June, consuming sprouts (fenugreek, mustard and rucola) as part of several of the dishes offered at that event.

Therefore, the occurrence of the French cluster, considering the elements outlined above, might support one of the initial hypotheses on the cause of the German outbreak, i.e. that the seeds used for sprouting and distributed to local producers or retail outlets contained a level of *E. coli* O104:H4 contamination, ultimately leading to contaminated sprouts destined for human consumption.

Following this hypothesis, contamination of the seeds could have occurred at any stage in the long and complex supply chain between seed production, transport, packaging and distribution. This would also mean that other batches of potentially contaminated seeds are still available within the EU and perhaps outside. Currently ongoing intensive epidemiological, microbiological and food trace-back and trace-forward investigations will therefore be vital to further confirm (or discard) this current hypothesis.

Based on the available information, the French HUS cluster is limited to persons that attended a social event on 08 June. A recent study by the German outbreak team shows that the median incubation period of *E. coli* O104:H4 is eight days with a maximum duration of 15 days [3]. Therefore, it would seem unlikely that new cases would appear as a direct result of exposure of the 08 June event. However, as with other *E. coli* infections, person-to-person transmission is possible, and therefore new cases can also be expected in persons that had close contact with already identified cases in this part of Bordeaux.

However, pending the confirmation of the source of this cluster and whether it is linked to contaminated seeds or sprouts, new cases or clusters might still be identified in the near future both in France and elsewhere in the EU, such as the case in Sweden, or beyond.

Current efforts are targeted to four main areas:

Food source identification

Preliminary information on the French HUS cluster and detailed information from the German outbreak investigations suggest that the consumption of sprouts is the source of infection of *E. coli* O104:H4 in both countries. The planned analytical epidemiological studies in Bordeaux and the microbiological studies on leftover seeds and food items, and on seeds from the retail outlet, may provide further evidence for this hypothesis of infection. However, *E. coli* contamination is difficult to identify in food items, including seeds, and it is possible that microbiological evidence cannot be established.

Food trace-back investigations at the EU level

The consumption of sprouts is the suspected vehicle of infection in both the French cluster and the German outbreak, and the isolated *E. coli* O104:H4 strain in human cases in both countries is the same, indicating a potential link between these two public health events. Therefore, it is opportune to strengthen trace-back and trace-forward investigations at national and EU level to identify what commonalities exist between the sprout production chains (distributor chains, distributors, retail outlets and suppliers) in Germany and France, and to identify any potentially contaminated batches of sprout seeds, so as to implement recall notifications in order to remove the vehicle of transmission quickly. Such trace-back investigations require close collaboration between national level, EU level and international public health and food safety institutions. They are currently being coordinated by the European Food Safety Authority (EFSA) taskforce established for this purpose, following a request from the European Commission.

The tracing back is progressing and has thus far shown that fenugreek seeds imported from Egypt either in 2009 and/or 2010 are implicated in both outbreaks. There is still much uncertainty about whether this is truly the common cause of all the infections as there are currently no positive bacteriological results. In particular, the 2009 lot appears to be implicated in the outbreak in France and the 2010 has been considered to be implicated in the German outbreak. Furthermore, this link does not explain the most recent case in Sweden, currently under investigation and in which, thus far, no consumption of sprouts has been implicated.

All this is being further investigated. In particular, an investigation on the distribution of seeds from these lots throughout Germany and Europe has been urgently requested. The export of some of the seeds imported from Egypt to another company in the UK (from where seeds were exported to France) demonstrates the necessity of this information.

It is also noted that seeds sold for sprouting are often sold as seed mixes and that during re-packaging cross-contamination can not be excluded. Therefore, any advice to consumers should at this time cover all seeds and raw sprouts derived thereof.

Strengthening surveillance

If it is confirmed that there is a link between the HUS cases from France and the recent outbreak in Germany, further cases or clusters of *E. coli* O104:H4 might be expected elsewhere in the EU or beyond. For this reason, increased awareness among clinical practitioners throughout the EU is encouraged to quickly identify new cases of HUS and of STEC infections that may be part of the existing outbreak in Germany and the cluster in France or potentially signal the identification of new clusters of infection. Such information should be communicated in a timely manner to public health authorities in order to timely initiate epidemiological and microbiological investigations and alert food safety authorities.

Additionally, strengthening the capacity of national reference laboratories to confirm this serotype rapidly would be crucial.

Public communication

Epidemiological, microbiological and trace-back investigations are currently ongoing to identify the origin of the contamination responsible for these outbreaks. Consumption of sprouts has been implicated as a possible source of the recent *E. coli* O104:H4 outbreaks in Germany and France. Until the investigation has been finalised, EFSA advises consumers not to grow sprouts for their own consumption and not to eat bean sprouts or other sprouted seeds unless they have been cooked thoroughly. Further preventative measures have been highlighted in the previous *ECDC-EFSA joint statement: Public health advice on prevention of diarrhoeal illness with special focus on Shiga toxin-producing Escherichia coli (STEC), also called verotoxin-producing E. coli (VTEC) or enterohaemorrhagic E. coli (EHEC)* (available from: http://ecdc.europa.eu/en/healthtopics/escherichia_coli/prevention_measures/Pages/prevention_measures.aspx).

Conclusions

Based on the available information, this HUS cluster is limited to persons that attended a social event in Bordeaux, France, on 08 June. However, a potential link to the outbreak of *E. coli* O104:H4 reported from Germany between May and June is currently being investigated, including the vehicle of transmission (germinated sprouts, sprout seeds or other food items). For the French cluster, the suspicion of sprouts as the likely vehicle of transmission, as well as the origin of the sprout contamination, will also need to be established through further microbiological and trace-back investigations. Pending the confirmation of the source of this outbreak, new cases might still be identified in the near future.

Thus far, the consumption of fenugreek sprouts has been implicated as a possible source of the recent *E. coli* O104:H4 outbreak in Germany and France. Until the investigation has been finalised, ECDC and EFSA strongly recommend advising consumers not to grow sprouts for their own consumption and not to eat sprouts or sprouted seeds unless they have been cooked thoroughly.

ECDC and EFSA will continue to closely monitor this event in collaboration with the French and other national authorities, the European Commission and the World Health Organization (WHO). ECDC will update this rapid risk assessment as necessary.

Contact

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