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REGIONAL OFFICE FOR **Europe**

**PUBLIC HEALTH REVIEW OF THE
ENTEROHAEMORRHAGIC *ESCHERICHIA*
COLI OUTBREAK IN GERMANY**

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INTRODUCTION

Enterohaemorrhagic *Escherichia coli* (EHEC) is a human pathogenic *E. coli* bacterium that is able to cause haemorrhagic colitis (bloody diarrhoea), which sometimes develops into haemolytic uraemic syndrome (HUS). HUS is a life-threatening disease that causes kidney damage and is a severe complication of EHEC infection. EHEC belongs to the so-called Shigatoxin-producing *E. coli* (STEC), also known as verocytotoxin-producing *E. coli* (VTEC). Animals can carry other types of STEC/VTEC in their intestines that are not necessarily pathogenic for humans.

Every year there are EHEC outbreaks in different parts of the world including Europe, sometimes involving HUS and even deaths, but the number of affected people is normally very much lower than what Germany is now experiencing. In 1996, the world's biggest recorded outbreak was registered in Japan and included over 8 000 reported cases.

EHEC OUTBREAK: CURRENT EPIDEMIOLOGICAL SITUATION

Germany informed WHO about an outbreak of EHEC infections in Germany through the European Union Early Warning and Response System (EWRS) on 22 May 2011. In accordance with the International Health Regulations, a formal notification from Germany to WHO was received the following day.

Epidemiological situation in Germany

From 1 May to 9 June 15:00 CET, Germany has reported 759 cases of HUS, including 21 fatal cases; 68% of cases are female and 88% adults aged 20 years or older, with the highest attack rates per 100 000 population in the 20–49 age groups.

From 1 May to 9 June 15:00 CET, Germany has reported 2229 cases of EHEC infections without HUS, 9 of which were fatal; 60% of cases are female and 88% adults aged 20 years or older.

Most patients are from northern Germany and the area around Hamburg is especially affected.

According to the Robert Koch Institute, as of 9 June the number of notified HUS/EHEC cases reported to it has declined over the past few days. The daily absolute and relative numbers of patients presenting to hospital emergency departments with bloody diarrhoea have also decreased. It is still uncertain whether this decline in outbreak activity is due to changes in consumption of raw vegetables and/or the waning of the source of infection.

Epidemiological situation in other countries

As of 9 June, 36 HUS (one fatal) and 63 EHEC cases (none fatal) had been reported from 13 other European countries. The European Union (EU) countries are reporting their cases using a common EU case definition, which has been coordinated by the European Centre for Disease Prevention and Control (ECDC). This EU case definition can be found at:

http://ecdc.europa.eu/en/healthtopics/escherichia_coli/epidemiological_data/Pages/EU_case_definition.aspx.

In addition, as of 9 June 2011 the Centers for Disease Control and Prevention (CDC) in Atlanta, United States of America, have published information about 3 HUS cases (1 confirmed and 2 suspected) and 1 suspected EHEC case (without HUS) linked to this outbreak. On 7 June, the Public

Health Agency of Canada reported one suspected case of *E. coli* O104 infection (without HUS), with travel history to Northern Germany and with links to a confirmed case of *E. coli* O104 infection in Germany. The confirmation of the serotype O104 is still pending as of 10 June.

All except two of the above HUS and EHEC cases had travelled to or from Germany during the incubation period for infection, typically 3 to 4 days post-exposure (range 2–10 days). The EHEC case reported by Norway gave no travel history to Germany, but had a visitor from Hamburg during the incubation period. The visitor is currently hospitalized in Germany with EHEC infection. The first fatal HUS case outside Germany was reported by Sweden on 31 May. Another case from Denmark has now known link to Germany.

Globally, therefore, 798 cases of HUS (22 fatal) and 2294 cases of EHEC without HUS (9 fatal) have been officially reported as of 7 June 2011, making the total number of reported cases 3092, out of which 31 (1%) have been fatal.

The table shows totals for all affected countries.

Country	HUS		EHEC		Comments
	Cases	Deaths	Cases	Deaths	
Austria	1	0	3	0	
Canada	0	0	1	0	
Czech Republic	0	0	1	0	A tourist from the United States who had travelled in Germany
Denmark	8	0	12	0	
France	0	0	2	0	+7 cases of bloody diarrhoea not yet confirmed as EHEC
Germany	759	21	2229	9	
Greece	0	0	1	0	A German tourist
Luxembourg	0	0	1	0	
Netherlands	4	0	4	0	
Norway	0	0	1	0	Contact with a German national in Norway
Poland	2	0	0	0	
Spain	1	0	1	0	
Sweden	17	1	30	0	
Switzerland	0	0	5	0	
United Kingdom	3	0	2	0	All 5 cases confirmed
United States of America	3	0	1	0	3 HUS cases (1 confirmed and 2 suspected) and 1 suspected EHEC case
Total	798	22	2294	9	

Note

As EHEC and HUS have exclusive notification categories, the case numbers should not overlap. However, the figures in any rapidly evolving outbreak, however, are provisional and subject to change for a variety of reasons.

In providing the above information, WHO wishes to recognize the contribution of its Member States, and technical partners such as the European Commission, the European Centre for Disease Prevention and Control and a number of WHO collaborating centres.

Groups at highest risk

Although in previous EHEC outbreaks young children have been identified as the group at highest risk of severe disease, the current outbreak is unusual as it is affecting adults (88% are 20 years or older), mainly women (currently 60% of the EHEC cases and 69% of the HUS cases). Cases have also occurred in school-aged children.

Causal agent

An increasing number of cases are laboratory confirmed as EHEC serotype O104:H4. This is a rare serotype that does not seem to have been documented in outbreaks before, although a few sporadic cases with EHEC O104:H4 have been reported previously. The outbreak strain is shigatoxin (stx2a)-positive, intimin-negative (*eae*) and enterohaemolysin (*hyl*)-negative. It is noteworthy that the outbreak strain is also an enteroaggregative *E. coli* (EAggEC). Thus it possesses genetic characteristics that could explain its virulence, with an unusual combination of virulence factors, being both shigatoxin-producing and enteroaggregative. More information about the outbreak strain is available on the Robert Koch Institute web site (http://www.rki.de/cln_109/nn_217400/EN/Home/E0HEC_O104_H4.templateId=raw.property=publicationFile.pdf/EHEC_O104_H4.pdf).

At this stage the outbreak strain should be classified both as an EAggEC and STEC as it has both enteroaggregative and shigatoxin-producing characteristics.

Laboratory criteria

According to the outbreak case definition used by the Robert Koch Institute, laboratory criteria applied in an EHEC/HUS outbreak must have a positive result in at least one of the following tests.

Detection of toxin

- Culture of the pathogen and isolation only from stool and detection of Shigatoxin (stx2) using enzyme-linked immunosorbent assay (ELISA) on the *E. coli* culture.
- Mixed culture of the pathogen, enriched stool cultures or isolation of *E. coli* and nucleic acid amplification test e.g. Polymerase Chain Reaction (PCR) for detection of the Shigatoxin gene *stx2* from the same sample.

Indirect (serological) detection

- Detection of anti- Lipopolysaccharides(LPS)-IgM-antibodies against *E. coli* serogroups (with markedly increased titre/concentration, e.g. using ELISA, Western-Blot).
- Marked change between two consecutive samples in titre/concentration of anti-Lipopolysaccharides(LPS)-IgG-antibodies against *E. coli* serogroups (e.g. using ELISA).

More information about the case definition for HUS cases associated with the EHEC outbreak in Germany is available on the Robert Koch Institute web site

(http://www.rki.de/cln_109/nn_217400/EN/Home/HUS_Case_definition.templateId=raw.property=publicationFile.pdf/HUS_Case_definition.pdf).

Syndromic surveillance

Cases with bloody diarrhoea and with a history of consumption of raw vegetables and/or raw/undercooked meat and/or of travelling to northern Germany should be referred for confirmation through laboratory investigation.

Severity of the outbreak

The current EHEC outbreak is the biggest ever seen in Europe, and the second biggest ever reported worldwide. It is the most deadly EHEC outbreak ever reported, due to its size and virulence.

The implicated strain seems to be very virulent. There are delays in reporting, particularly of the less severe cases, but the percentage of patients that develop HUS and later neurological complications seems to be higher than that observed during previous EHEC outbreaks.

Treatment

Most people recover without any specific treatment in 5–10 days. The WHO recommends that in general, treatment with antibiotics and antidiarrhoeals is not recommended for patients infected with EHEC. Such treatments have been reported to actually increase the likelihood of complications. WHO recommends people who are experiencing symptoms to seek medical attention and not self medicate. Treatment will probably include fluids. For patients with severe HUS, blood transfusions and dialysis might be needed to support failing kidneys.

EPIDEMIOLOGY OF EHEC

E. coli are normal intestinal bacteria of animals or humans. *E. coli* can range in behaviour from relatively harmless commensals to being fully pathogenic for humans and/or animals. *E. coli* bacteria are usually transmitted by the faecal/oral route.

E. coli pathogenic for humans can be faecally shed by humans and/or animals, and can be divided into different groups.

- Enteropathogenic *E. coli* (EPEC) are associated with infantile diarrhoea.
- Enteroinvasive *E. coli* (EIEC) cause dysentery-like disease.
- Enterotoxigenic *E. coli* (ETEC) produce enterotoxins that cause diarrhoea.
- Enteroaggregative *E. coli* (EAEC) express aggregative adherence.
- Diffusely adherent *E. coli* (DAEC) adhere to the surface of epithelial cells.
- Enterohaemorrhagic *E. coli* (EHEC): produce Verocytotoxin or Shiga-like toxin (vtx, stx) which can cause haemorrhagic colitis (HC) and sometimes HUS in humans.

The primary sources of pathogenic *E. coli* contaminating foods are human shedders, which are the primary reservoir for pathogenic *E. coli* belonging to the first five groups above. The primary reservoir of EHEC are farm ruminant shedders i.e. cattle, sheep, goats. These farmed ruminants are healthy carriers of EHEC. The bacteria reside in the gut and can be intermittently faecally excreted.

EHEC is a zoonotic pathogen that can be transmitted from animals to humans via direct contact with faecally contaminated animals, or more commonly through the food chain or through water. Person-to-person faecal-oral route of transmission can also occur.

It is difficult to ascertain at this stage whether the outbreak strain is of human or animal origin as it has both enteroaggregative and shigatoxin-producing characteristics.

Foods implicated in previous EHEC outbreaks

Many types of food have been implicated in EHEC outbreaks: undercooked bovine meat products (minced meat, hamburgers, kebabs), fermented salami made from bovine and ovine meats, fresh produce such as lettuce, bean sprouts and spinach, unpasteurized apple cider, and raw milk and raw milk cheeses.

EHEC outbreaks have also been waterborne, owing to faecally contaminated drinking-water or contaminated water for swimming (such as lakes, pools and ponds).

Vehicle and source of the current outbreak

Exposure to the vehicle of the outbreak seems to have occurred in northern Germany during the last week of April and the month of May, since almost all the patients had been in northern Germany during the incubation period.

Epidemiological investigations strongly indicate a food source that has been faecally contaminated and on the market for a month. Fresh produce has been the lead hypothesis. There is increasing epidemiological and food chain evidence that implicate bean and other sprouts as the responsible vehicle. Further epidemiological and laboratory investigations are under way to confirm the source of the outbreak and to understand where how the outbreak strain contaminated the sprouts and where in the supply/food chain the contamination occurred.

TRAVEL AND TRADE RESTRICTIONS

WHO does not recommend any restrictions in travel in or to and trade with Germany and affected countries.

PUBLIC HEALTH ADVICE TO CONSUMERS

The German authorities have recommended that the public, in addition to common hygiene measures, refrain from eating raw bean sprouts and other sprouts. Households and restaurants should dispose of any sprouts they have as well as any food items that might have come in contact with them. Anyone with diarrhoea should observe strict hand hygiene, in particular when in contact with infants and immunodeficient persons. Anyone with bloody diarrhoea is advised to seek medical attention immediately.

All consumers are advised to follow strict hygienic measures with regard to personal hygiene and food safety: washing hands thoroughly before handling food and eating and after visiting the toilet, and washing fresh produce that are to be eaten without further heat treatment.

The best way to prevent infection with EHEC is to apply the good hygiene practices of the WHO five keys to safer food, but the only reliable control measure to kill the pathogen is by thorough cooking of foods until all parts reach a temperature of 70°C or higher.

The WHO five keys to safer food are:

1. Keep clean
2. Separate raw and cooked

3. Cook thoroughly ($\geq 70^{\circ}\text{C}$)
4. Keep food at safe temperatures
5. Use safe water and raw materials

Additional information on the five keys is available on the WHO web site (http://www.who.int/foodsafety/publications/consumer/en/5keys_en.pdf).

Regular updates on the outbreak and other information can be found at <http://www.euro.who.int/ehec>

SOURCES OF FURTHER INFORMATION

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- Shiga toxin/verotoxin-producing *Escherichia coli* in humans, food and animals in the EU/EEA, with special reference to the German outbreak strain STEC O104. ECDC – EFSA joint report (<http://www.efsa.europa.eu/en/supporting/pub/166e.htm>)

- Urgent advice on the public health risk of Shiga-toxin producing *Escherichia coli* in fresh vegetables EFSA (<http://www.efsa.europa.eu/en/press/news/110609.htm?wtrl=01>)