



Epidemiological Alert:

Haemolytic Uraemic Syndrome (HUS) and infection by Enterohaemorrhagic *E. coli* (EHEC)

(Published on 3 June 2011)

The objective of this alert is to provide an update on cases of Haemolytic uraemic syndrome (HUS) and on cases of infection by enterohaemorrhagic *Escherichia coli* (EHEC) (or Shiga toxin-producing *E. coli* (STEC)) in Germany and other countries.

Included are the Pan American Health Organization (PAHO) recommendations to Member States in relation to this theme.

Current Situation

On 22 May, Germany reported a significant increase in the number of patients with haemolytic uraemic syndrome (HUS) and bloody diarrhoea caused by Shiga toxin-producing *E. coli* (STEC).

Since 2 May 2011 and as of 3 June a total of 551 cases of HUS have been reported from European Union Member States, with 520 of the cases detected in Germany. In this outbreak the great majority of cases are adults, with more than two thirds of which are women. Twelve of the cases resulted in deaths due to HUS.

Laboratory results indicate that STEC serogroup O104:H4¹ is the causative agent.

The source of the outbreak is under investigation, but contaminated food seems to be the most likely vehicle of infection. There is currently no indication that raw milk or meat is associated with the outbreak.

Most cases are from, or have a history of travel to the North of Germany. Within the EU cases related to the ongoing outbreak have been reported from

Description

Haemolytic uraemic syndrome (HUS):

It is a life-threatening disease characterized by acute renal failure (uraemia), haemolytic anaemia, and a low platelet count (thrombocytopenia). It results from EHEC infection, and it is estimated that up to 10% of EHEC-affected patients may develop HUS. The mortality rate has decreased during the last few years and with appropriate treatment is between the 3% and 5%.

It can cause neurological complications (such as seizure, stroke and coma) in 25% of HUS patients and chronic renal sequelae, usually mild, in around 50% of survivors.

EHEC or STEC is a severe strain of *E. coli* bacterium that is commonly found in the gut of animals, mainly ruminants. EHEC produces toxins, known as verotoxins or Shiga-like toxins because of their similarity to the toxins produced by *Shigella dysenteriae*. They can cause severe foodborne disease. STEC is transmitted to humans primarily through consumption of contaminated foods, such as raw or undercooked ground meat products and raw milk, contaminated water, direct contact with animals or contact with infected people.

Symptoms of disease include abdominal cramps and diarrhoea, which may be bloody. Fever and vomiting may also occur.

¹ Stx2-positive, eae-negative, hly-negative, ESBL, aat, aggR, aap. PFGE results shows indistinguishable pattern of 7 human O104:H4 outbreak strains in Germany and 2 strains of O104:H4 in Denmark.

Sweden, United Kingdom, the Netherlands, Denmark and Spain.

The Center for Disease Control and prevention reported on 1 June 2011, that no confirmed cases of STEC O104 infections have been reported in U.S. travelers to Europe. Two cases of HUS in the United States have been reported in persons with recent travel to Hamburg, Germany².

Haemolytic uraemic syndrome (HUS) case definition (used by Robert Koch Institute to be applied to HUS-cases associated with the current EHEC/HUS outbreak)³

HUS Clinical criteria:

A clinical picture of acute enteropathogenic HUS is defined by the presence of at least two of the following three criteria:

1. Hemolytic anemia.
2. Thrombocytopenia $\leq 150,000$ cells/mm³.
3. Renal dysfunction.

Laboratory confirmed cases:

Positive result in at least one of the following tests:

Detection of Shigatoxin

1. Culture of the pathogen and isolation only from stool **AND** detection of Shigatoxin Stx2 using ELISA on the *E. coli* culture.
2. Mixed culture of the pathogen, enriched stool cultures or isolation of *E. coli* **AND** nucleic acid amplification test (e.g. PCR) for detection of the shigatoxin gene stx2 from the same sample.

Indirect (serological) detection

1. Detection of ant-LPS-IgM-antibodies against *E. coli* Serogroups (once markedly increased titre/concentration, e.g., using ELISA, Western Blot).
2. Marked change between two consecutive samples in titre/concentration of anti-LPS-IgG-antibodies against *E. coli* Serogroups e.g.; using ELISA).

² http://www.cdc.gov/media/releases/2011/s0601_ecoligermany.html

³ This case definition was developed by the Robert Koch Institute to be applied to HUS-cases associated with the current EHEC/HUS outbreak. It is based on the case definition for "haemolytic uraemic syndrome (HUS), enteropathogenic" defined in the 2007 edition of the Case definitions for reporting communicable diseases of the Robert Koch Institute", modified to reflect features of the current outbreak.

http://www.rki.de/clin_178/nn_217400/EN/Home/HUS_Case_definition,templateId=raw,property=publicationFile.pdf/HUS_Case_definition.pdf (Source obtained on 2 June, 2011)

Suspect HUS case:

Case with a clinical picture of acute enteropathogenic HUS as assessed by the attending physician, but not formally meeting the clinical criteria (at least two of three) identified above, are classified as suspect cases regardless of laboratory confirmation.

Recommendations

The Organization is not making any new recommendations for treatment.⁴

Normal hygiene measures should be observed. Hand washing after toilet use and before touching food, are highly recommended, as the bacterium can be passed from person to person, as well as through food, water and direct contact with animals. The bacteria is destroyed by thorough cooking of foods until all parts reach a temperature of 70 °C or higher.

Anyone who has developed bloody diarrhoea and abdominal pain and who has recently had contact with northern Germany should seek medical advice urgently. The HUS complications can cause acute kidney failure and can develop after the diarrhoea has resolved.

Travel and international trade

The World Health Organization does not recommend any restrictions in travel to or trade related to this outbreak.

Technical Information

Daily updates respecting the number of Haemolytic uraemic syndrome (HUS) cases are published on the WHO website available via the following link:

<http://www.who.int/csr/don/en/index.html>

Laboratory Protocols

WHO Global Salm Surv. Manual of Diagnostic Procedures and characteristics of Escherichia coli O157 producer of the Shigatoxin based on clinical specimens starting in 2007. The guide is available in Spanish via the following link:

<http://fos.panalimentos.org/gfn/ManualesdeProcedimiento/tabid/783/language/en-US/Default.aspx>

The standard laboratory protocols for molecular subtyping of the pathogens under surveillance by PulseNet laboratories (One-Day (24-28 h) Standardized Laboratory Protocol for Molecular Subtyping of Escherichia coli O157:H7, Salmonella serotypes, Shigella sonnei, and Shigella flexneri by Pulsed Field Gel Electrophoresis (PFGE)) is available via the following link:

http://www.pulsenetinternational.org/SiteCollectionDocuments/pfge/5%201_5%202_5%204_PNetStand_Ecoli_with_Sflexneri.pdf

⁴ <http://www.euro.who.int/en/what-we-do/health-topics/emergencies/international-health-regulations/news2/news/2011/06/ehc-outbreak-rare-strain-of-e.-coli-unknown-in-previous-outbreaks>