Case definition for HUS-cases associated with the outbreak in the spring 2011 in Germany

The following case definition should be applied to HUS-cases associated with the EHEC/HUS outbreak in the spring of 2011 in Germany. 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.

Important modifications are:

1. Limitations of time, place and person concerning exposure,

2. Limitations regarding the serotype,

2. Omission of epidemiological confirmation as a basis for case classification,

3. Inclusion of suspected cases in the definition.

Cases of HUS that are not associated with this outbreak should be defined according to the case definition of 2007.

Detailed definitions of terms marked with the sign „►" are provided below.

Exclusion Criteria

A1. Identification of a non-infectious cause,

A2. Detection of a Serotype other than O104.

Exposure

The relevant exposure period is defined as the period from (and including) April 21, 2011 to the date of ►illness onset. "During the exposure period" is defined as any time-period that overlaps with the relevant exposure period.

Symptomatic patients are identified as associated with this outbreak if they meet at least one of the following criteria:

E1. Residence or permanent stay in Germany during the exposure period; except patients are known to have been outside of Germany during the entire exposure period,

E2. Temporary stay in Germany at any time during the exposure period,

E3. Consumption of a food item that was acquired in Germany during the exposure period,

E4. Close contact (e.g., in a household) with a HUS case belonging to case category Cat 1 or Cat 2 who meets at least one of the criteria E1 to E3.

Clinical criteria

►Illness onset on or after **Mai 1, 2011** and a clinical picture of acute enteropathogenic HUS defined by the presence of at least two of the following three criteria:

C1. Hemolytic anemia,

C2. Thrombocytopenia ≤ 150,000 cells/mm^3,

C3. ►Renal dysfunction.

Laboratory criteria

Positive result in at least one of the following four tests:

[Detection of toxin:]

L1. Culture of the pathogen and isolation only from stool AND detection of Shigatoxin Stx2 using ELISA on the *E. coli* culture,

L2. 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:]

L3. Detection of anti-LPS-IgM-antibodies against *E.coli* Serogroups (once ► markedly increased titre/concentration, e.g., using ELISA, Western-Blot),

L4. ►Marked change between two consecutive samples in titre/concentration of anti-LPS-IgG-antibodies against E.coli Serogroups (e.g., using ELISA).

Cases are classified into the following categories:

Cat 1. Clinically confirmed HUS case

Clinical picture of acute enteropathogenic HUS without laboratory confirmation.

Cat 2. Clinically and laboratory confirmed HUS case

Clinical picture of acute enteropathogenic HUS with laboratory confirmation.

Cat 3. Suspected HUS case

Cases with a clinical picture of acute enteropathogenic HUS as assessed by the attending physician, but not formally meeting the clinical criteria (at least 2 of C1 to C3) identified above, are classified as suspected cases regardless of laboratory confirmation.

When reporting without specifying exact case categories, cases from the category 1 and 2 will be classified as „**confirmed HUS cases**" and cases from the categories 1 to 3 - as „**HUS cases including suspected cases"**.

Further definitions

Outbreak specific

Bloody diarrhea*,* defined as unformed stool admixed with blood considered to be bloody diarrhea by the patient, his/her caretaker or attending medical staff. The frequency criterion for ►diarrhea of ≥ 3 unformed stools in 24 hours need not be fulfilled.

Illness onset, defined as date of onset of ►diarrhea or ►bloody diarrhea, if either of these are part of the patient's clinical picture, otherwise earliest date of onset of any of the clinical criteria C1 to C3.

If illness onset as defined here is unknown, the earliest date on which any one of these criteria are documented to be present should be used instead.

General

Markedly increased titre/concentration, defined as sufficiently exceeding the cut-off value as set by the test manufacturer and the laboratory to indicate the presence of acute infection as judged by the laboratory

Marked change between two consecutive samples, defined as a sufficient increase (or in some cases, decrease) of the relevant laboratory value in two consecutive samples taken within an appropriate time interval to indicate the presence of acute infection (e.g. negative result, followed by a positive result (e.g., ELISA) or an at least fourfold increase in antibody titer (e.g., CFT)).

Diarrhea, defined as ≥ 3 unformed stools in 24 hours. A history obtained from the patient, his caretaker, or the attending medical staff may be considered equivalent.

Renal dysfunction, defined as at least one of the four following criteria:

- Reduced renal function (e.g. increased serum creatinine, oliguria (reduce urinary excretion, under 500 ml/24 h))
- Renal failure (e.g., anuria (urinary excretion under 100 ml/24 h))
- Proteinuria (protein excretion in the urine)
- Haematuria (blood in the urine)

Nucleic acid amplification test (e.g., PCR) defined as gene amplification, followed by an appropriate specificity control (e.g., sequencing)