## Notes on the implementation of EHEC/HUS studies

Status 7 June 2011

RKI is carrying out a number of epidemiological studies in order to identify the source of the largest EHEC/HUS outbreak in Germany to date.

Most of the studies have been conducted in regions where especially large numbers of people have fallen ill. These have included Hamburg, Lübeck and Bremen. Teams of RKI scientists have asked affected people there about the food eaten in the period of two weeks before the onset of illness. Foodstuffs that could already be identified as causes of previous outbreaks, such as beef, vegetable sprouts or unpasteurized milk, have been explicitly asked about since the beginning of the outbreak investigations. Besides people who have fallen ill, these case control studies also include healthy control persons. This makes it possible to determine which foods are associated with an increased risk of illness. Four different case control studies involving a total of over 100 patients and more than 2000 healthy controls have so far been carried out.

Altogether, more than 10 RKI teams with a total more than 40 RKI scientists have been involved since the beginning of the outbreak. Not all patients are investigated by RKI itself; some people who have fallen ill are questioned by public health authorities or hospitals. For this purpose, a questionnaire has been made available to public health authorities, and an updated version is also used in the RKI studies.

Since groups of travellers also represent an important point of contact, those who have fallen ill with EHEC after a stay in northern Germany have also been questioned, in cooperation with authorities in Sweden and Denmark.

The information obtained by the outbreak teams and the results of further investigations are forwarded in each case to RKI, which has been working round the clock since the beginning of the outbreak. The data from outbreak investigations, as well as the extensive information provided by the general public and the notification data submitted under the Infectious Disease Control Act, are evaluated and processed there.

When evaluating the investigations – as with all epidemiological studies – a number of points must be taken into consideration: Patients have been questioned as soon as possible. At the time, some have still been seriously ill and only to a certain extent are able to remember accurately the food they have eaten in the past 2 weeks. It is also well known from earlier studies that the suspect foods discussed in public in the meantime can affect the answers of both patients and controls. In addition, patients can usually remember rare and unusual foods more accurately than healthy controls can. In that way, the differences determined can appear to be greater than the actual differences in consumption.

The current analyses show, however, that the current EHEC/HUS outbreak is clearly associated with the consumption of raw vegetables in northern Germany.

Epidemiological methods are being used to try to delimit the source as far as possible. Which food is or was exactly the carrier of the bacterium cannot be conclusively proved

epidemiologically. To this end, the results of epidemiological studies are immediately passed on to the authorities involved in the control of foodstuffs, so that they can investigate foods in a targeted way and retrace routes of transmission.

In order to be informed as quickly and fully as possible about the current situation, RKI has established several additional surveillance systems, beside the regular reporting channels. A reporting system in selected hospitals captures the number of patients with bloody diarrhoea each day. A special laboratory monitoring system compiles current laboratory findings in the responsible reference laboratories and investigation sites on a daily basis. With the network of renal treatment centres, RKI is engaged in screening HUS and EHEC patients, during which information on secondary infections and food sources, among other things, is obtained.

An overview of the ongoing and partially completed epidemiological studies is given below:

**Case control studies** (comparative investigation of healthy and ill people)

- Case control study in Hamburg; published on 25 May 2011 (RKI-BfR statement)
- Seriously affected hospitals in Lübeck, Bremen and Hamburg, using data from a population-representative survey as controls; results published on 3 June 2011 (RKI-BfR press release)
- Hospitals not previously affected but currently seeing an increased incidence of HUS
- Expanded case control studies with detailed interviews in localities in Lübeck, Bremen and Hamburg
- Case control studies of foreign cases in cooperation with ECDC
- Detailed analysis of case control studies for identification of associated sources

Meta-analysis of all case control studies (collation and analysis of the findings from single studies)

**Cohort studies** (investigation of patients who fall ill the same time and in the same situation)

- Cohort studies on groups of travellers, in cooperation with foreign authorities
- Cluster analyses of different restaurant-associated outbreaks

## **Further investigations**

- Analysis of outbreak data from visitors to an affected cafeteria; results published on 3 June 2011 (RKI-BfR press release)
- Search for possible person-to-person transmission
- Representative countrywide on-line survey to determine the disease burden
- Study to determine the secondary infection rate
- Study to determine the duration of excretion and the ratio of co-infection and subsequent infection
- Countrywide surveillance of patients with bloody diarrhoea in hospitals