Hamburg University of Applied Sciences
Department Health Sciences

Hamburg Open Online University
Hamburg University of Applied Sciences

Bernhard Nocht Institute for Tropical Medicine
Department Infectious Disease Epidemiology

Epidemic
Disease
Detective
Hamburg

An Epidemic of Haemolytic Uraemic Syndrome in Hamburg

Modified by Juliane Boenecke, Ralf Reintjes, Ranjeet Dhonkal,
Norbert Georg Schwarz and Dewi Ismajani Puradiredja

Based on a true event

Objectives

Through this scenario-based teaching activity, the participants

a. learn about the steps involved in an epidemiological investigation and the roles that different stakeholders play
b. learn to describe, analyze, and interpret epidemiological data using descriptive and analytical epidemiological tools and methods
c. discuss and determine epidemic evidence suggestive of an infectious disease outbreak and appropriate measures of control and prevention

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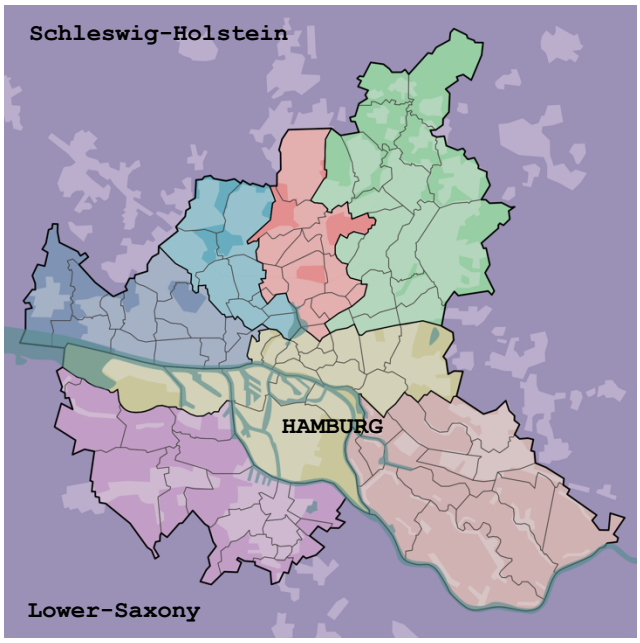
BACKGROUND

Hamburg – "The Gateway to the World"

The *Free and Hanseatic City of Hamburg* is Germany's second-largest city and the biggest port. It is also one of Germany's wealthiest cities. Besides its maritime spirit, it is portrayed by vibrant neighbourhoods with multicultural eateries, seaward-facing architecture, the unmistakable cry of seagulls and the unique Reeperbahn entertainment district.



Roughly 5 million people live in Hamburg's metropolitan region, located in the North of Germany. The city comprises seven boroughs subdivided into 104 quarters (see Hamburg Map and Material *M1*). It is surrounded by the federal states Schleswig-Holstein to the north and Lower Saxony to the south. Hamburg's main waterway, the Elbe river, connects the city and the North Sea.

M1. *Detailed Hamburg map – boroughs and districts (p.I)*

Besides being a major European science, research and education hub, Hamburg is a popular international tourist destination. Among its most notable cultural venues are the *Elbphilharmonie* and *Laeiszhalle* concert halls.

PART I: A CLUSTER OF HUS OCCURRING IN HAMBURG

Wednesday, May 19

It is Wednesday, May 19, almost 5 p.m. You are the epidemiologist on call at the Hamburg Public Health Department. Your work is nearly finished when Professor Stats, the chief of the Internal Medicine Department at the Elbe Health Centre, calls you over the phone.

Five paediatric patients with an illness characterized by dehydration, weakness, bloody diarrhoea, and renal insufficiency were admitted to the Elbe Health Centre. The clinical picture has been classified as **Haemolytic Uraemic Syndrome (HUS)**. All children showed initial symptoms of spasmodic pain of the lower abdomen, nausea, and vomiting, with only low or absent fever. A few hours to three days after the onset of the initial symptoms, the five children experienced bloody diarrhoea.

Initial blood tests show high white blood cell counts, abnormally low levels of thrombocytes (< 150/nl), presence of schistocytes in blood, and signs of haemolysis with anaemia, all of which may indicate severe blood disease. Moreover, all children have a mild elevation of C-reactive protein levels (CRP 35.7±7.2 mg/l) and leucocytosis (12.3±0.7/nl), both signs of infection and inflammation. With the onset of HUS, serum creatinine levels were rising above > 0.5mg/dl, indicating impaired kidney function.

Three children live in Hamburg Altona, and two in Hamburg North. Three of them are members of the same family. None had travelled outside Germany.

Q1. What could be the cause of this illness? What would be the next thing to do? Please discuss in your group.

Because various pathogens could cause the given symptoms, you suggest that stool cultures be obtained from all affected patients to screen for pathogenic viruses or bacteria, including *Clostridium*, *Salmonella*, *Shigella*, Shiga-toxin-producing *Escherichia coli* (*E.coli*), *Noro-/Adenovirus*, among others. You contact your colleagues from the Hamburg Institute of Hygiene and Environment (HU) to support laboratory diagnostics.

Time to catch up on the basics: you decide to revisit the epidemiology of HUS and its occurrence in Germany to assess the current situation.

M2. *Epidemiology of HUS / Epidemic profile of HUS in Germany (p.II)*

You learn that HUS cases usually occur in small numbers throughout the year without being attributable to an unusual cluster or event. But what does that mean?

Q2. Is this an outbreak? What would you do next? Please discuss in your group.

According to *M2.*, the cluster of five paediatric cases exceeds the average number of HUS cases per day usually reported in Germany. You wonder if there are any more cases... You are asking for a report on all hospitalized patients with bloody diarrhoea and HUS complications recorded at the Elbe Health Centre and start to survey all HUS cases reported in Hamburg since May 1 via the National Electronic Health Reporting System.

Given this unusual event, you decide to inform the National Public Health Institute, the *Robert Koch Institute* (RKI), about the incident and ask for their support. In addition, the national government authorities responsible for consumer protection – the *German Federal Institute for Risk Assessment* (BfR), the *German Federal Office of Consumer Protection and Food Safety* (BVL), and the *German Federal Ministry of Health* (BMG) – shall be notified about the current HUS cluster to assist in diagnostics and risk communication.

Thursday, May 20
Total Case Counts: HUS=70

Before the arrival of the RKI team, you receive the health centre's report.

M3. *HUS Summary report from the Elbe Health Centre since May 1 (p.III)*

You learn that a total of 59 patients with symptoms of bloody diarrhoea, most of them aged 20 years or older, had been hospitalized since May 1. Just yesterday, 11 new patients were admitted to the hospital. You recall that in previous outbreaks, children have been found to be at the highest risk for HUS complications. Yet, this cluster seems to be different:

In total, 70 cases of HUS could be identified in Hamburg by the evening of May 19. Seeing such a high number of HUS in one place, especially in adults, is very unusual…

Together with your colleagues from the HU and RKI, you form an interdisciplinary team to investigate the outbreak cluster – the **Epidemic Disease Detectives "EDDi"**.

Q3. Who are you going to involve in your outbreak investigation team?

Later in the day, you receive a report from the reference laboratory. The stool test results of the 59 patients who have been hospitalized at the Elbe Health Centre with symptoms of diarrhoea, bloody diarrhoea and HUS are available.

M4. *Laboratory findings from the HU lab in Elbe Health Centre patients (p.IV)*

Microbiological testing revealed the growth of enterohemorrhagic *Escherichia coli* (*EHEC*) bacteria in 11 of 12 paediatric patients. Forty-six of 47 adult patients also tested positive for EHEC infection. Of the 59 patients, 36 developed HUS, occurring mainly in female adults. Further screening identified *Shiga-like toxin* (stx2) associated with the onset of HUS complications. The BfR, the national reference laboratory investigating the outbreak, was asked to obtain a more specific characterization of the pathogen to inform guidelines for the treatment and management of the outbreak.

As for HUS, you start summarizing the background information on EHEC, both notifiable diseases in Germany. In addition, you review all case reports on confirmed EHEC infection in Hamburg since May 1 using the National Electronic Health Reporting System.

M5. *Epidemiology of EHEC / Epidemic profile in Germany (p.V)*

You learn that a total of 325 cases of suspected EHEC infection had been reported as of May 19. That's quite a high number! Immediate action is now needed to prevent the outbreak from spreading further. The EDDi team starts to work on a case definition informed by the most recent findings. By defining a case more accurately in the context of the outbreak, infected individuals potentially linked to the outbreak cluster may be identified more effectively, aiming for a better understanding of the outbreak situation.

Q4. How would you define a case? Please try to describe the following: (a) A suspected case, (b) a probable case, (c) a confirmed case

PART II: SUMMARIZING THE DETAILS

After successfully developing a case definition for further investigation (see *M6*.), you and your team recap what you have uncovered about the outbreak cluster.

M6. *Case definition in the context of the outbreak (p.VI)*

Between May 1 and 19, 164 confirmed EHEC cases and 70 confirmed HUS cases were reported in Hamburg. Based on reports from hospitals and laboratories, information has been gathered on the demographic characteristics, clinical signs and symptoms, and the date of illness onset and duration. Following the participants' residence addresses, cases could be mapped out at the Hamburg district level. In addition, the statistician of your team prepared an epidemiological curve. Both are helpful tools to describe the incidence of EHEC gastroenteritis and HUS in time and space.

M7. *Outbreak Details Hamburg 1st – 20th May (p.VII-VIII)*

Q5. What information can you derive from the descriptive outputs? Interpret the findings in your group.

The descriptive outputs revealed that the outbreak had already started at the beginning of May, almost two weeks before you received notification from the Elbe Health Centre. Moreover, there seems to be a significant reporting delay, and the case numbers may only represent the tip of the iceberg. Most infections seem to occur in the North-West of Hamburg, mainly Hamburg-Nord, Eimsbuettel, Altona and Wandsbek. Overall, young adults aged 20-50 years, primarily females, seem at the highest risk of EHEC infection and HUS complications. The mean age of EHEC patients is 40.2 years, with 61% of them being female. The mean age in HUS patients is 39.2 years, of which 75% are female.

You prepare an investigation plan to study further the foodborne outbreak.

Q6. What steps would you follow in investigating the outbreak?
Find the correct sequence and number each step of the outbreak investigation process.

[ ] Deciding the outbreak is over

[ ] Verifying a possible outbreak

[ ] Testing hypotheses through analytical studies and laboratory testing of samples

[ ] Application of control measures, including
(a) recall of products,
(b) removing the source of contamination,
(c) revision of the production process

[ ] Defining and finding cases

[ ] Generating hypotheses through interviews and surveys

The EDDi team decides to release the first official report on the EHEC outbreak in Hamburg via the RKI to raise awareness among hospitals, laboratories, and health practitioners in Germany.

PART III: THE OUTBREAK INVESTIGATION

Friday, May 21

Total Case Counts: Susp. EHEC=393; Conf. HUS=91; Conf. EHEC=198

Following the investigation plan, the EDDi team contacts hospitals and healthcare facilities in Hamburg to interview hospitalized patients about the possible source of the EHEC outbreak and to determine local treatment capacity.

You visit the Elbe Health Centre and meet Professor Stats, who reported the cluster of paediatric HUS patients two days ago. You start interviewing the Professor about the outbreak situation and learn about the complications that occur in patients as a result of HUS. Some of them, for instance, experience severe neurological symptoms and are treated with plasmapheresis. However, since treatment capacity is limited, the hospital has begun urging healthy people to donate blood. As of May 21, a total of 61 patients were admitted to the Elbe Health Centre due to EHEC-associated HUS syndrome. Ten different departments manage patient care, including nephrology, gastroenterology, hygiene, microbiology, emergency and intensive care, transfusion medicine, neurology and psychology. As new cases are increasing rapidly, the hospital management initiated a crisis task force to consolidate capacities.

Using investigative interviews with hospitalized patients, you want to find out what types of food they have consumed in the past 25 days, given that HUS tends to occur 2-14 days after the onset of diarrhoea and after an incubation period of a maximum of ten days.

At the Elbe Health Centre, you could talk to eight patients:

M8. *Interviews with hospitalized patients at the Elbe Health Centre (p.IX)*

Q7: Which hypotheses can you draw from the qualitative results?

In addition to the interviews, your colleagues collect information on the food choices of a larger sample of hospitalized patients using a food questionnaire. The results are expected to be available soon.

By Friday evening, **May 21**, the number of hospitalized EHEC and HUS cases went up to 353. The EDDi team also learns about the first case that died from complications at the Elbe Health Centre.

Early Saturday, you receive the results of the food survey. Based on these findings, you and your team design a first case-control study to determine the food exposure that could explain the infection among the cases now being treated at the Elbe Health Centre.

Recap: Case-control studies compare a group with a disease or outcome of interest (case) with a group that does not present the outcome (control). Such studies trace back retrospectively to compare how frequently the exposure to a risk factor is present in each group. It determines the association between a risk factor / exposure and the disease / outcome of interest. The measure of association is called Odds Ratio (OR): With OR >1, the exposure may be a risk factor in the case group. With OR <1, exposure may be a protective factor in the case group.

The case group includes 15 hospitalized patients following your case definition. The control group holds 17 individuals with no signs of HUS or EHEC infection, who are members of the same family or who usually had food together with the affected cases. Each participant is interviewed about their most common food choices. The following results could be gathered to determine the exposure associated with the ongoing outbreak.

M9. *Results from the first case-control study from Elbe Health Centre (p.X)*

You try to draw a preliminary conclusion from the findings of the exploratory interviews at the Elbe Health Centre and your first case-control study.

Q8: How do you interpret the results? Which conclusions can you draw from the interviews and case-control study?

Raw milk or meat products do not seem to be a source of transmission in the current outbreak. Instead, all patients consumed fruits and vegetables more frequently than non-affected study participants. More specifically, the hospital-based case-control study suggests a health risk related to consuming raw vegetables, including salads.

And there's more news! You have been given the latest outbreak report:

M10. *Outbreak Details Hamburg and Germany May 1 – 21 (p.XI-XII)*

The situation is critical, with case numbers increasing significantly in Hamburg and beyond. As of May 22, 56 new confirmed cases of HUS and EHEC gastroenteritis have been hospitalized in Hamburg. More than 550 suspected EHEC cases had been identified in Hamburg only. In total, 1857 confirmed cases of EHEC gastroenteritis and HUS had been reported from other states in Germany, including Bremen, Schleswig-Holstein, Lower Saxony and North Rhine-Westphalia, indicating the further spread of the outbreak.

Q9: Which statements can you draw from the report?

Although the outbreak affects several federal states in Germany, most reported cases seem connected and share exposure in Northern Germany. You and your team update all evidence to issue an alert to the *Early Warning and Response System* (EWRS) of the *European Centre for Prevention and Disease Control* (ECDC), the *European Food Safety Authority* (EFSA) and the *World Health Organization* (WHO) to be better prepared in case of further spread.

Sunday, May 23

Total Case Counts: Susp. EHEC=566; Conf. HUS=124; Conf. EHEC=285; Death=1

Even though you could gather promising evidence on the possible source of the outbreak, your analyses could not narrow down any specific vegetable vehicle. Further epidemiological studies are needed to take your investigation and management of the outbreak forward.

Recap: The EDDi team revisits different outbreak investigation methods to identify the most effective approaches. A good choice seems to be an observational analytical study design, which allows the team to evaluate the association between a disease or the outcome of interest and different exposures.

M11. *Recap: Overview of epidemiological study designs in outbreak investigation (p.XIII-XIV)*

Q10: In general: Which of the study designs is best suited to test your hypotheses? Can you give more specific suggestions on how to plan the investigation?

The EDDi team is preparing further investigative measures focusing on two canteens and one local restaurant in Hamburg. All facilities are potentially linked to the occurrence of HUS and EHEC gastroenteritis cases.

And this is your plan: A second case-control study shall be conducted in two canteens of a Hamburg-based company associated with infected cases to track down the source of the outbreak. According to your definition, the case group includes 28 employees who purchased food in the canteen and eventually developed bloody diarrhoea, HUS or EHEC gastroenteritis. The control group includes 81 non-affected employees who bought food in the same canteen but showed no signs of illness. In addition, food samples shall be collected from the patients' kitchen refuse and sent for microbiological testing at the reference laboratory at BfR.

Monday, May 24

Total Case Counts: Susp. EHEC=638; Conf. HUS=134; Conf. EHEC=322; Death=3

Five days after you were informed about a cluster of HUS patients in Hamburg, you learn about the identification of the EHEC outbreak strain. This is important news! The RKI, together with the Institute of Hygiene at the University Clinic Muenster, identified the outbreak strain *O104:H4*. Compared to other EHEC serotypes that caused previous outbreaks, this serotype has many unique properties and does not seem to have been documented in any outbreaks before. *O104:H4* is a rare pathogen, with a distinct pathogenic potential due to an unusual combination of virulence factors (produces *Shiga-toxin* yet is enteroaggregative) while being difficult to detect via laboratory testing. Consistent with Professor Stats' description of the health complications observed in his HUS patients, this serotype primarily affects adults, with a higher proportion of women developing complications such as renal failure with obligatory dialysis and progressing neurological complications, possibly leading to death. Compared to previous outbreaks, significantly more patients developed HUS. Even more concerning, all isolates of the outbreak strain showed resistance to several common antibiotics, except for carbapenems antibiotics.

Based on this evidence, recommendations for treatment and diagnostics must be developed and shared with healthcare providers and laboratories through the RKI. Moreover, the case definition underlying your investigation is to be updated in line with the new findings:

Q11: Which part of the case definition must be updated and why?

M12. *UPDATE - Case definition in the context of the outbreak (p.XV)*

Later in the day, you receive the data from the canteen-based case-control study.

Q12: *What is the measure of association for this study? Please calculate and interpret the results.*

Exposures: Consumption of salad, including cucumber, tomatoes and leaf lettuce
Consumption of dessert (not specified)
Consumption of fruits (not specified)
Consumption of asparagus

Cases: 28 employees who purchased food in one of the canteens and developed bloody diarrhoea, HUS or EHEC gastroenteritis, according to the case definition

Controls: 81 healthy employees who purchased food in one of the canteens with no signs of bloody diarrhoea, HUS or EHEC gastroenteritis

1 Contingency Table – salad, including cucumber, tomatoes and lead lettuce

		Outcome	
		+	-
Exposure	+	18	10
	-	20	61

OR =

2 Contingency Table – dessert

		Outcome	
		+	-
Exposure	+	8	20
	-	18	63

OR =

3 Contingency Table – fruits

		Outcome	
		+	-
Exposure	+	3	25
	-	13	68

OR =

4 Contingency Table – asparagus

		Outcome	
		+	-
Exposure	+	4	24
	-	19	62

OR =

M13. *Results of the canteen-based case-control study (p.XVI)*

The results reveal almost 6-fold higher odds of contracting bloody diarrhoea among employees who ate a salad from the canteen during the investigation period compared to those who did not have any salad but dessert, fruits or asparagus. Vegetable samples have been collected from the salad bar to test for EHEC contamination. To further advance your investigation, you initiate a traceback analysis to find out from which supplier the vegetables were distributed.

You take another look at the most recent case numbers: 47 new HUS and EHEC gastroenteritis cases have been confirmed in Hamburg. As of May 24, three fatal HUS cases were reported, including two younger previously healthy women.

Tuesday, May 25

Total Case Counts: Susp. EHEC=692; Conf. HUS=146; Conf. EHEC=351; Death=3

The HU laboratory results of tested food samples from the patients' kitchen refuse and the two canteens in Hamburg became available this morning. Most cucumber samples were positive for EHEC bacteria contamination, three out of four sorts of cucumber imported from Spain. Moreover, tomatoes and leaf lettuce showed proof of low-level EHEC contamination, the primary ingredients of salads in addition to cucumber. Similar findings were reported for the canteen samples.

Despite considerable progress, newly reported cases are still increasing, with a total of 497 confirmed cases of EHEC and HUS in Hamburg. Luckily, no additional fatal cases had been reported by May 25. Against this trend, the EDDi team decides to issue a first public press release, informing professionals and the public about the ongoing investigation and raising awareness about food safety and hygiene standards.

Q13: What public health recommendations can you draw from the recent findings?

Considering all circumstantial evidence, the EDDi team confirms the current EHEC outbreak could be linked to the consumption of cucumbers, mainly from Spain, as well as tomatoes and leafy greens. In addition, safety regulations are communicated to the public and food sector to prevent the epidemic from spreading further:

(a) Beyond the standard hygiene measures concerning personal hygiene and food safety (e.g., washing food, hands, counters, and cooking tools properly; if possible, cooking food products to safe temperatures), consumers are advised to refrain from eating raw tomatoes, cucumber and green salads. This advice mainly applies to the region of Northern Germany. Persons with diarrhoea should apply strict hand hygiene, particularly when interacting with infants and immunodeficient persons. Anyone experiencing bloody diarrhoea is advised to seek medical help immediately.

(b) Beyond the standard kitchen hygiene measures, food companies (including restaurants and catering businesses) are advised to consider any serving of raw cucumbers, tomatoes and green salad.

The WHO five keys to safer food are strongly recommended:

(1) Keep clean
(2) Separate raw and cooked
(3) Cook thoroughly (≥ 70°C)
(4) Keep food at safe temperatures
(5) Use safe water and raw materials

The current outbreak has been classified as the largest EHEC outbreak ever recorded in Germany. Considering the high number of HUS cases, it is also the largest outbreak worldwide. The good news: The public recommendations immediately affected consumer behaviour. The bad news: This also impacts the local economy and trading.

In addition to the canteen-based case-control study, a recipe-based restaurant cohort study is conducted in which diners and staff will be interviewed about their meals consumed and ordered to determine potential exposure. The cohort study includes participants who dined at the same restaurant during the investigation period (May 11 to 16), as per the case definition. Information shall be collected on the diners' ordered meals, and the ingredients used following interviews with the restaurant team. The participants have been identified by reviewing the restaurants' order books and supporting information from the local public health departments following contact tracing.

Later in the day, you receive the results of the restaurant cohort study. A total of 158 participants, allocated into eight groups, could be identified who dined at the same restaurant during the investigation period. All of them could recall the meals they had eaten at the restaurant. Among the eight groups, 34 individuals contracted bloody diarrhoea or EHEC/HUS. Based on the interview statements, you plan to determine a list of menu items associated with the outbreak.

Your task is to identify each ingredient that went into the consumed meals, their quantities, and how they were prepared. Together with your team, you visit the restaurant to interview the chef and staff that prepared the meals during the investigation period. You develop a 2x2 table listing the number of diners who consumed or did not consume the identified ingredients (exposed and non-exposed) and the number of diners who got sick (outcome-positive) and did not show any signs of illness (outcome-negative).

Q14: What is the measure of association for this study? Please calculate and interpret the results.

List of identified meals

- Garden salad with raw tomatoes, cucumber, lamb's lettuce and sprouts
- Oriental salad with Chinese cabbage, radicchio, iceberg lettuce and sprouts

Study population

- 158 participants who dined in the restaurant during the defined outbreak period from 11th till May 16th; a total of 34 restaurant guests developed bloody diarrhoea, HUS or EHEC gastroenteritis according to the case definition

Measure of association:

1 Contingency Table – tomatoes

		Outcome	
		+	-
Exposure	+	13	35
	-	18	92

RR =

2 Contingency Table – cucumbers

		Outcome	
		+	-
Exposure	+	13	35
	-	18	92

RR =

3 Contingency Table – sprouts

		Outcome	
		+	-
Exposure	+	34	84
	-	1	39

RR =

4 Contingency Table – lamb's lettuce

		Outcome	
		+	-
Exposure	+	13	35
	-	18	92

RR =

5 Contingency Table – Chinese cabbage

		Outcome	
		+	-
Exposure	+	16	37
	-	14	91

RR =

6 Contingency Table – Radicchio

		Outcome	
		+	-
Exposure	+	16	37
	-	14	91

RR =

7 Contingency Table – Iceberg lettuce

		Outcome	
		+	-
Exposure	+	16	37
	-	14	91

RR =

M14. *Results from the recipe-based restaurant cohort study (p.XVII)*

Using the cohort study design, you can calculate Relative Risks (RR) for each ingredient. The results reveal that those restaurant customers who had been served sprouts had a significantly higher risk of contracting EHEC gastroenteritis and EHEC-associated HUS than those who had not been served meals containing sprouts.

Meanwhile…

By **May 31**, the number of new cases of EHEC gastroenteritis and HUS complications in Hamburg decreased to less than ten cases for the first time, with no newly confirmed case of HUS. Finally, preventive measures and increased awareness among the population and health practitioners were taking effect.

Another 18 interviews and epidemiological studies (six case-control studies, seven cohort studies and five explorative questionnaires) were conducted in other federal states that have been significantly affected by the outbreak, including Bremen, Lübeck and Bremerhaven. All of them could confirm your findings and provide strong evidence for sprouts being the primary source of the current EHEC outbreak.

PART IV: TRACING BACK THE OUTBREAK SOURCE

Saturday, June 5

Total Case Counts: Susp. EHEC=954; Conf. HUS=175; Conf. EHEC=492; Death=11

On Saturday, you receive the results of the traceback analysis you initiated on May 24.

M15. *Results from the traceback analysis – focus Lower Saxony (p.XVIII)*

By tracing back the food production and supply chain, one distributor could be identified that links the two affected canteens and a supplier of sprouts in Lower Saxony (Company A). Their food products – mainly vegetables, including sprouts – were served in the two canteens. You visit the company in Lower Saxony to critically assess the farm's hygiene and safety procedures and follow up on the farmers' health conditions since May 1. You learn that the farmer's wife experienced EHEC gastroenteritis-like symptoms in early May, whereas her husband did not show any signs of EHEC infection. While inspecting the farm, you and your team noticed that standard hygiene and safety measures had not been applied adequately, which most likely fueled contamination with EHEC bacteria of fenugreek sprouts and other vegetable products like tomatoes or cucumber. To confirm EHEC contamination of sprouts, amongst other vegetables, you collect various food samples from the farm and send them to the laboratory at the HU and BfR for microbiological testing.

Sunday, June 6

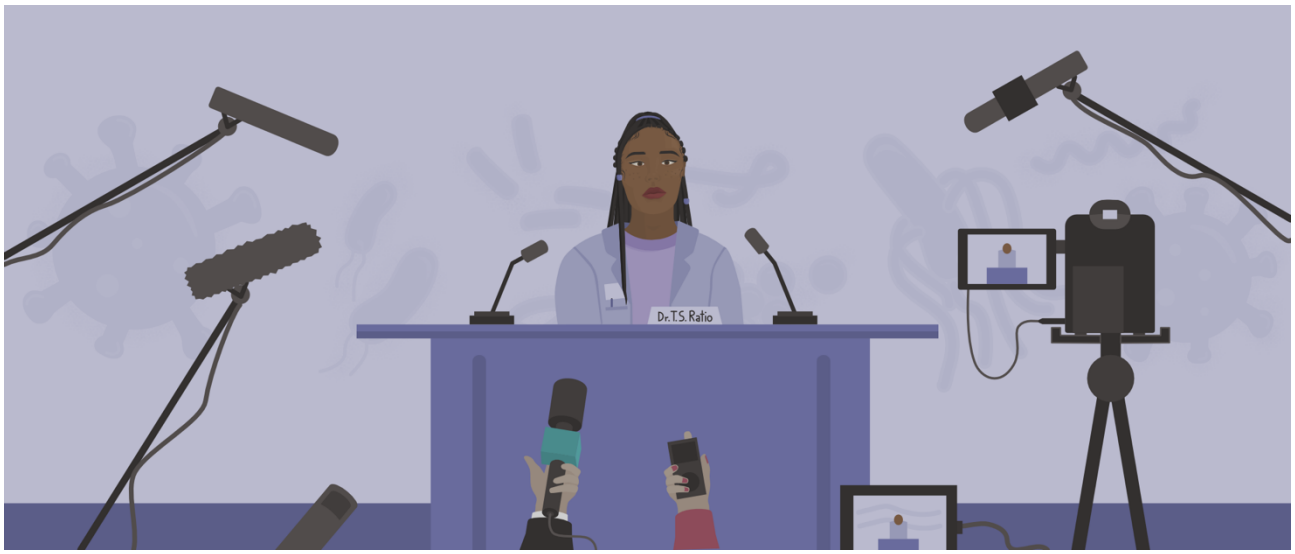
Total Case Counts: Susp. EHEC=969; Conf. HUS=177; Conf. EHEC=501; Death=11

By June 6, a total of 678 confirmed cases of EHEC and HUS had been reported in Hamburg, including only four new cases of EHEC and one new case of HUS. Since the beginning of the outbreak, a total of 11 patients have died from HUS complications.

On early Sunday morning, the results from the BfR laboratory became available. The microbiological investigation confirmed that the sprout seed samples collected from the farm in Lower Saxony tested positive for EHEC contamination. Furthermore, contamination could be detected on fenugreek sprout products from the restaurant and one canteen. Although EHEC positive, laboratory testing of cucumber, tomatoes, and leaf lettuce from the Hamburg canteens, restaurants and patients' kitchen refuse revealed a different strain not involved in the current outbreak. However, detecting the *O104:H4* outbreak strain remains challenging due to its unique microbiological properties.

Given the evidence derived from the microbiological and epidemiological studies, the outbreak event could finally be linked to consuming contaminated fenugreek sprout products and using sprout seeds. As a result, the EDDi team prompted to stop the distribution of sprouts, and the farm was temporarily closed.

In a joint press release on June 10, the BfR, the BVL and the RKI narrowed consumer recommendations to raw sprouts and withdrew previous guidance on the consumption of cucumbers, tomatoes and leaf lettuce based on the latest evidence. During the following weeks, the number of newly reported cases decreased steadily in Hamburg and Germany. Yet, advice for consumers and companies concerning food safety and hygiene measures remains essential in solving the foodborne outbreak. To eventually identify the producer of the fenugreek sprouts, the EDDi team, together with the national and European partners BfR, BVL, EFSA, and ECDC, start to further back-trace the production and supply of sprout seeds using records from the farm in Lower Saxony.



On **June 22**, you learn about the occurrence of several EHEC clusters in France, including a high number of HUS complications. Similar events have been reported in Denmark and Sweden. In these outbreaks, the same strain, *O104:H4,* could be identified. Together with the European health authorities, you further extend the traceback analysis.

On June 29, the final report becomes available. Cross-border traceback analysis has revealed that, in fact, the contaminated fenugreek sprouts can be tied to the same supplier, leading the investigation to a producer in Egypt. Accordingly, EFSA, ECDC and WHO advise European consumers to avoid eating raw and insufficiently cooked sprout products. In addition, EFSA requests that all batches of fenugreek sprouts imported into Europe from Egypt be withdrawn and destroyed. The agency also suspended all imports of sprouts until October 31.

Being the final step of the outbreak investigation, the EDDi team starts to summarize the course of the outbreak and evaluate the impact of different measures that had been applied.

M16. *Final epidemiological report on EHEC / HUS in Germany and Europe (p.XIX-XX)*

Q15: ***What conclusions can you draw from the EHEC outbreak in Hamburg? Please summarize and discuss the main findings from your investigation and try to evaluate the implemented control measures critically.***

PART V: CONCLUSION

Saturday, July 31

Total Case Counts: Susp. EHEC=1093; Conf. HUS=203; Conf. EHEC=578; Death=13

At the beginning of July, only sporadic EHEC infections occurred in Germany, and no cases of HUS had been reported since July 11. The investigation was closed eventually because no significant link to the *O104:H4* outbreak strain could be determined. On **July 14**, the farm in Lower Saxony could re-open after appropriate hygiene and food safety measure had been implemented. **On July 27**, the RKI declared the end of the EHEC outbreak in Germany.

As of **July 31**, a total of 1093 suspected EHEC cases have been reported in Germany. In Hamburg alone, 578 confirmed cases of EHEC gastroenteritis and 203 of EHEC-associated HUS had been identified. Among those, 13 individuals died from HUS complications. The total number of fatal cases in Germany was 64. The findings from the outbreak investigation in Germany revealed that the vehicle of the outbreak has been prevalent and circulating in Northern Germany between late April and the whole month of May. According to the Europe-focused investigations, different sorts of sprouts and beans have been identified as the outbreak-causing vehicle. However, no travel or trade restrictions in or to/with Germany have been recommended by the WHO.

The EDDi team publishes a final report of the outbreak investigation, summarizing the details of the investigation process:

Robert Koch Institute. Report: Final presentation and evaluation of epidemiological findings in the EHEC O104:H4 outbreak, Germany 2011. Berlin 2011. Online via: https://www.rki.de/EN/Content/infections/epidemiology/outbreaks/EHEC_O104/EHEC_final_report.pdf?__blob=publicationFile

Based on a true event

The 2011 *EHEC* outbreak was Germany's largest recorded outbreak of bacterial infection. Due to the high number of cases, it was also the largest outbreak of *HUS* worldwide. There was a 67-fold increase in *HUS* cases and a 17-fold increase in *EHEC* cases during the outbreak period in 2011 compared to previous years. No other outbreak clusters associated with the consumption of sprouts were identified.

Overall, the *EHEC* outbreak had enormous health consequences for the affected individuals, and economically due to a significant drop in the consumption and trade of lettuce and other salad ingredients, mainly imported from Spain. To date, the route of contamination of sprout seeds and the origin and reservoir of the outbreak strain in humans and/or animal species remain unclear.

The *O104:H4* EHEC outbreak vividly demonstrated how quickly a novel foodborne pathogen could spread and cause severe illness and death, even in a developed country like Germany. In addition, difficulties in the diagnostics of newly or re-emerging infectious agents, as seen in the 2011 EHEC outbreak, may delay outbreak detection and timely response, potentially leading to the exhaustion of the health care system. Yet, the *EHEC* epidemic proved the importance and success of interdisciplinary collaboration, cross-sector response and epidemic preparedness.

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