Improving Food Safety Through a One Health Approach: Workshop Summary

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WORKSHOP SUMMARY

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Forum on Microbial Threats

Board on Global Health

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The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

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"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

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Appendix A

Contributed Manuscripts

A1

EHEC O104:H4 IN GERMANY 2011: LARGE OUTBREAK OF BLOODY DIARRHEA AND HAEMOLYTIC URAEMIC SYNDROME BY SHIGA TOXIN–PRODUCING *E. COLI* VIA CONTAMINATED FOOD

Reinhard ***Burger***[1,2]

In the summer of 2011 Germany experienced one of the largest outbreaks of a food-borne infection caused by enterohaemorrhagic *Escherichia coli* (EHEC) with the serotype O104:H4. A large number of cases with bloody diarrhea and haemolytic uraemic syndrome (HUS) occurred. Never before was such a high rate of HUS cases observed in an outbreak caused by a food-borne pathogen. The events in Germany caused by EHEC O104:H4 in the summer of 2011 show dramatically how rapidly an infectious agent is able to develop into a major health threat for a whole country. The outbreak caused widespread concern among the population, turning soon into fear. People expecting safe and healthy food felt threatened. It changed the eating habits of the majority of the population, and it had enormous economic consequences, particularly for farmers producing salad ingredients. It resulted in a large number of seriously ill patients and in a substantial number of deaths. The burden of disease and the economic consequences

[1] For the HUS investigation team of the Robert Koch Institute.
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have made it a tragedy for many. It is important to analyse this outbreak scientifically in order to learn from this unique event and to be prepared for comparable infections in the future. In particular, all the steps regarding detection of cases, diagnostic procedures, identification of vehicle and origin, and infection control measures, all the way to therapy, should be reflected carefully. Usually, even experienced physicians encounter only a few cases of EHEC-induced HUS in adults in their whole career. Therefore, the large number of cases in Germany represents a valuable source of information for future epidemics.

This manuscript summarises the work of the HUS investigation team of the Robert Koch Institute (RKI) and gives an overview of the work done by the colleagues in the Department of Infectious Disease Epidemiology at the RKI (G. Krause, C. Frank, D. Werber, K. Stark, and U. Buchholz), the Department for Infectious Diseases (M. Mielke and A. Fruth), and the RKI-Consultant Laboratory for HUS/EHEC at the University of Münster (H. Karch). Many additional colleagues were involved.

Epidemic Profile and Development of the Outbreak

The extent of the outbreak becomes apparent by comparison with the average annual numbers of EHEC cases or HUS in Germany. In previous years about 1,000 patients per year were identified, with a median age of about 5 years. Of these patients about 70 per year developed HUS, with a median age of about 2 years (Frank et al., 2011a). In the outbreak from May to September 2011, approximately 3,000 EHEC cases were observed with a median age of 46 years, 58 percent of those patients were female, and 18 deaths were observed among the EHEC patients (0.6 percent). An additional 855 EHEC patients who developed HUS were identified (Frank et al., 2011b). This represents more than 20 percent of the total number of patients (3,842). The large majority of these patients were adults, the average age was 42 years, 68 percent of the HUS cases were female, and 35 deaths were observed among the HUS patients (4.1 percent). The total death toll was 53 patients (Figure A1-1).

Analysis of the incidence of HUS by the likely county of infection revealed that northern Germany was mainly affected. The same is true for cases with travel history; also for these patients the county of residence at the time of infection was northern Germany. Most cases were observed in the states of Schleswig-Holstein, Mecklenburg-Western Pomerania, Hamburg, Bremen, and Lower Saxony. Later in the epidemic, cases were found in all of the 16 German states. The incidence in the five northern German states varied from 1.8 to 10 cases per 100,000 persons. All other states had incidence rates with less than 1 case per 100,000 persons (Frank et al., 2011b; Wadl et al., 2011).

A substantial number of EHEC or HUS cases occurred also internationally during this time, particularly in the European Union, but also a few cases in the United States and Canada. Particularly affected was Sweden with 35 EHEC

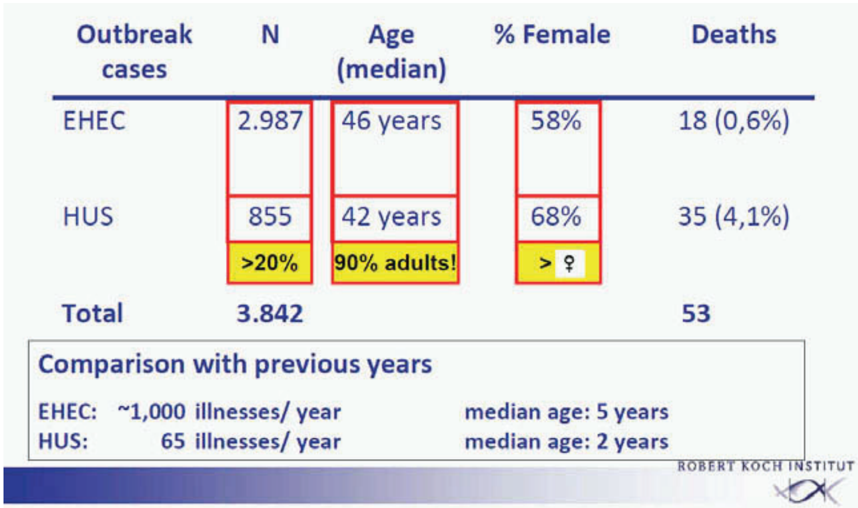

FIGURE A1-1 Total number of EHEC and HUS cases and associated deaths during the outbreak of EHEC O104:H4 in summer 2011 in Germany and comparison to an average year.

and 18 HUS cases including one fatality, Denmark with 15 EHEC and 10 HUS cases, and France with 10 EHEC and 8 HUS cases. Single cases were found in 12 additional European countries. In the United States 2 EHEC and 4 HUS cases were identified with one fatality, and Canada had a single EHEC case. An epidemiological analysis revealed that—with two exceptions—all cases in this outbreak of EHEC or HUS found internationally were directly or indirectly associated with a visit to Germany during the weeks of the outbreak. Most of these patients visited northern Germany for a shorter or longer period of time during the peak of the outbreak.

The RKI was notified about the outbreak by a phone call from the local health authority of the state of Hamburg on May 19, 2011. Immediately (i.e., the next day), the RKI sent a substantial team of experts to Hamburg in support of the local colleagues. The subsequent epidemiological analysis revealed in retrospect that the outbreak had in fact started at the beginning of May and reached the peak of cases on May 22, 2011 (Figure A1-2). Thus, there was an obvious and substantial notification delay (Altmann et al., 2011). Up to the moment of notifying the RKI, a large proportion of the infections had already occurred. After May 22 both the reported number of EHEC gastroenteritis and the number of HUS cases decreased (Wadl et al., 2011).

The team of epidemiological specialists sent to Hamburg started right away with initial explorative interviews. The team size was enlarged in the next days

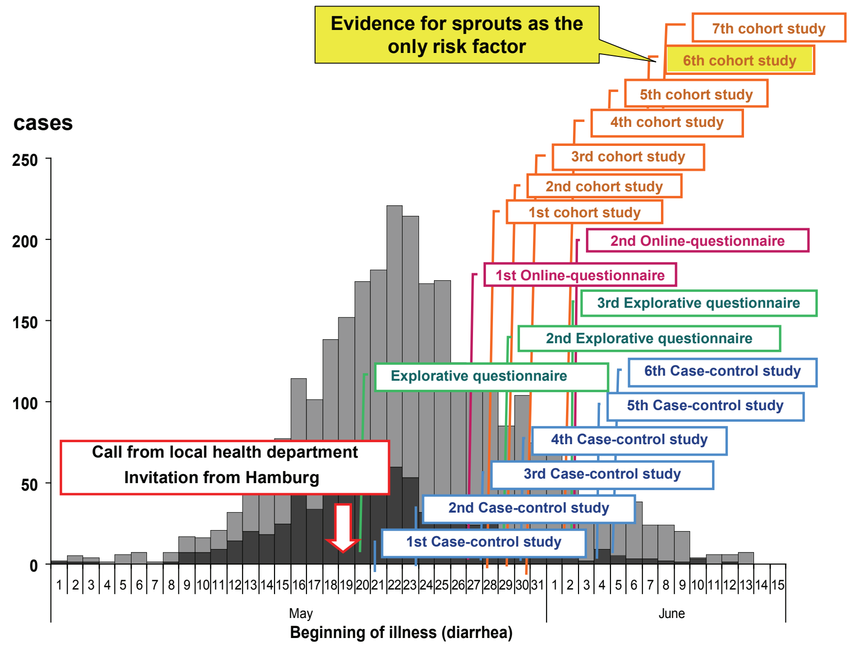

FIGURE A1-2 Epidemiological curve of EHEC (gray) and HUS cases (dark) and overview of epidemiological studies performed by the Robert Koch Institute for identification of sprouts as the vehicle of transmission.
SOURCE: Robert Koch Institute.

(up to 15 members), and a substantial number of case-control studies, additional explorative interviews, and cohort studies were started. As early as May 21 (i.e., 2 days after the RKI was notified), the first qualitative evidence for the role of vegetables was obtained. Raw milk products or products from raw meat, which frequently represent a source of infections with EHEC, had already been ruled out as the origin of infection in this outbreak. On May 22 the corresponding information was submitted to the European Early Warning and Response System and to the World Health Organization. Local public health authorities were warned, and initial interviews were given to the German press. During the next few days, information was provided on the website and in a series of press conferences and interviews. On May 25 (i.e., 5 days after the outbreak), the pathogen was identified from patient samples as EHEC O104:H4 by the RKI-Consulting Laboratory for HUS in Münster and the National Reference Centre laboratory for bacterial enteric pathogens at the RKI (Buchholz et al., 2011).

After a number of telephone conferences, the RKI together with the Federal Institute for Risk Assessment and the Federal Office of Consumer Protection and Food Safety conducted a press conference advising on food consumption. Advice was given not to consume raw tomatoes, cucumbers, and salad *in* northern Germany. This recommendation was based on the increased risk of illness after consumption of these raw salads in northern Germany. Unfortunately, the majority of the press reported this advice as warning against salad *from* northern Germany.

Once the magnitude of the outbreak became apparent, the RKI immediately established a website providing all details about the infectious agent, updated as they developed, both for the medical specialists and microbiological laboratories in Germany and abroad and for the general public. Data sheets on the infectious agent and frequently asked questions, sometimes updated several times a day, proved to be an important source of information.

After mid-June 2011 only single cases of HUS occurred. On July 26 the RKI declared in a press conference the end of the outbreak because no new cases clearly associated with the outbreak had been reported for 3 consecutive weeks since the last newly reported illness on July 4.

Identification of the Infection Vehicle

In addition to the explorative interviews and case-control studies, cohort studies in disease clusters proved to be particularly helpful. Beginning on June 1, more than 30 cohorts were investigated in order to identify the vehicle of infections and to identify further cases. Particularly useful were cohort studies of travel groups that included international visitors or tourist groups from abroad. Here a close cooperation with foreign health authorities was instrumental. For a number of travel groups the length of stay, the particular location, and food consumption could be reconstructed in detail. Also, cluster analysis of patients associated with food consumption in different restaurant-associated outbreaks provided information. An analysis of billing data of guests at an affected canteen provided further data. In these studies a detailed investigation was performed using ordering information and additional details documenting the consumption as revealed by the corresponding bills. The most substantial evidence regarding the vehicle of infection was obtained by a so-called recipe-based restaurant cohort study (Buchholz et al., 2011).

Sprouts as the Responsible Vehicle of Infection

In the course of the epidemiological analysis it became obvious that patient memory is not a reliable source of information. This proved to be particularly true because in these EHEC/HUS patients not only symptoms of gastrointestinal infection and impaired kidney function were observed but also major neurological symptoms, preventing reliable interviews. Therefore, the recipe-based restaurant cohort study was designed to obtain information independent of a functioning patient memory (Figure A1-3).

Table 3. Relative Risk of Infection Associated with Sprouts and Other Raw Food Items in Univariable Analysis.

Food Item	Total Subjects Evaluated	Subjects Exposed (Percent of Cohort)	Cases among Subjects Exposed (Attack Rate)	Subjects Not Exposed (Percent of Cohort)	Cases among Subjects Not Exposed (Attack Rate)	Relative Risk (95% CI)	P Value
	no.	*no. (%)*					
Sprouts	152	115 (76)	31 (27)	37 (24)	0	14.23 (2.55–∞)	0.001
Tomatoes	152	50 (33)	14 (28)	102 (67)	17 (17)	1.68 (0.77–3.62)	0.18
Cucumbers	152	50 (33)	14 (28)	102 (67)	17 (17)	1.68 (0.77–3.62)	0.18
Chinese cabbage	152	45 (30)	13 (29)	107 (70)	18 (17)	1.72 (0.77–3.71)	0.17
Radicchio	152	45 (30)	13 (29)	107 (70)	18 (17)	1.72 (0.77–3.71)	0.17
Lettuce	152	45 (30)	13 (29)	107 (70)	18 (17)	1.72 (0.77–3.71)	0.17

Source: Buchholz U, Bernard H, Werber D, et al. German outbreak of Escherichia coli O104:H4 associated with sprouts. N Engl J Med 2011. DOI: 10.1056/NEJMoa1106482.

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FIGURE A1-3 Recipe-based restaurant cohort study of the Robert Koch Institute reveals risk for infection associated with the consumption of sprouts.
SOURCE: Taken from Buchholz et al., NEJM, 365, 1763 (2011).

Ten cohorts with a total of 168 guests of a given restaurant in the city of Lübeck in Schleswig-Holstein were identified. All persons had dinner at the same restaurant between May 12 and 16. Eighteen percent of the guests consuming food at this restaurant showed bloody diarrhea or EHEC/HUS within 14 days (31 persons). All persons were questioned about which meals they ordered, using photos of the dishes as a reminder. Booking details and billing documents were utilized. Using these consumption data from the individual guests, the chef of the restaurant was interviewed about the detailed ingredients of each dish ordered by the guests. This included not only the major ingredients of each dish itself but also elements used for decoration of the dish or of the salad served separately. This approach provided reliable information about which food ingredients each guest had actually ordered and eaten. This interview technique and analysis had the major advantage that it was no longer necessary to depend on the memory of the guests to find out what they had eaten. Additional verification was obtained through photos taken at the table by a number of groups. These photos confirmed the details given for the nature of the ordered dish and its contents.

In univariate analysis the relative risk of disease was 14.2 times higher for persons eating sprouts compared to that of persons not eating sprouts (Buchholz et al., 2011). All 31 patients with EHEC/HUS had consumed sprouts. None of the guests who did not consume sprouts became ill. Based on these cohort studies, in a joint press conference of the RKI with the food safety authorities on June 10 the public announcement was made that sprouts were the vehicle of infection. The earlier warning against the consumption of salad was now focused on a warning against consumption of the salad ingredient sprouts.

Origin of Bacterial Contamination of the Sprouts

The more than 40 clusters within this outbreak were analyzed for a common denominator. The federal authorities responsible for food safety in Germany (the Federal Institute for Risk Assessment and the Federal Office of Consumer Protection and Food Safety) performed an intensive forward-backward tracing of the food supply chain of the various cluster locations (Figure A1-4). Through one or several distributors and intermediates, all clusters turned out to be connected to a specific food enterprise producing sprouts commercially. All infections within this outbreak in the state of Lower Saxony had in common that originally the supply of sprouts came from this single food enterprise.

Two clusters of infection independent of the outbreak in Lower Saxony provided information on the origin of the sprout contamination (Appel et al., 2011). Both clusters had definitely no connection to the sprout producer in Lower Saxony. One cluster consisted of so-called self-sprouters (i.e., consumers who grow their

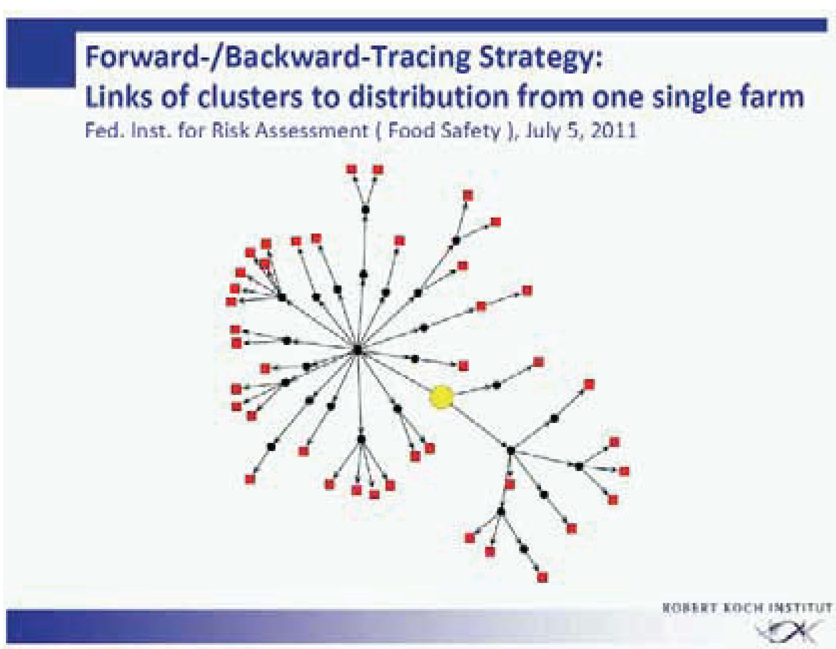

FIGURE A1-4 Trading network reveals linkage of 41 identified outbreak clusters. Supply chain of contaminated sprouts leads to one single sprout producer farm in Lower Saxony. SOURCE: Modified from Buchholz et al., NEJM, 365, 1763 (2011).

own sprouts at home from seeds provided by commercial suppliers). The second source of information was a small outbreak comprising 15 cases in the area of Bordeaux in France in mid-June. Detailed and labor-intensive tracing of the delivery channels revealed that the only common feature of the seeds used for growing sprouts in the food enterprises in Lower Saxony, in Bordeaux, and in the private households with the home-grown sprouts was a given lot of fenugreek seeds originating from Egypt. Fenugreek seeds (*Trigonella foenum-graecum*) are frequently used for the production of sprouts. The seeds are also used in many other food products (e.g., spices, cheese, and even tea) because of their very aromatic taste and intensive smell. The seeds are small (4-5 mm) and have a peanut-like colour.

Through a number of intermediates located in different countries this seed lot had been delivered to these three outbreak locations. No other common ingredient used for the production of sprouts was identified. This was clear evidence that contaminated seeds used for sprout growing were responsible for the outbreak (Appel et al., 2011). By nature, the epidemiological evidence is indirect or circumstantial but it explained the distribution of infections. The corresponding lot of fenugreek seeds was removed from the market. It is difficult to verify how complete this removal was.

"Stealth Food"

When the affected patients were interviewed initially during the first weeks of the outbreak, it became obvious that people do not remember in detail what they ate 1 or 2 weeks ago. Only in retrospect, after the second or third interview together with reports in the press, did they realize and remember that their dishes had in fact contained sprouts. Similar phenomena had been observed internationally in other outbreaks. In 2008, jalapeno chili peppers were contaminated with *Salmonella Saintpaul* in the United States. Chili peppers are used as an ingredient in tomato sauce-like salsa. The consumers were not aware that one of the spicy ingredients was chili peppers and, when interviewed, denied consumption of this food item, thereby delaying the identification of the vehicle. The identification of sprouts as a source in Germany within less than 3 weeks was quite rapid. The identification of the chili peppers took about 7 weeks. In another outbreak in 1996 with radish sprouts causing an outbreak of EHEC O157 in Japan, 7 weeks were required for the detection of the outbreak and 4 weeks to identify its source.

Microbiological Characterization of EHEC O104:H4

Once the outbreak had been recognized, EHEC O104:H4 was rapidly isolated from stool specimens of affected patients within a few days (Figure A1-5) (Askar et al., 2011, Bielaszewska et al., 2011). This is a rare serotype that had not been described previously in animals. As a rule, faecal contamination by ruminants is responsible for EHEC infections through vegetables or through

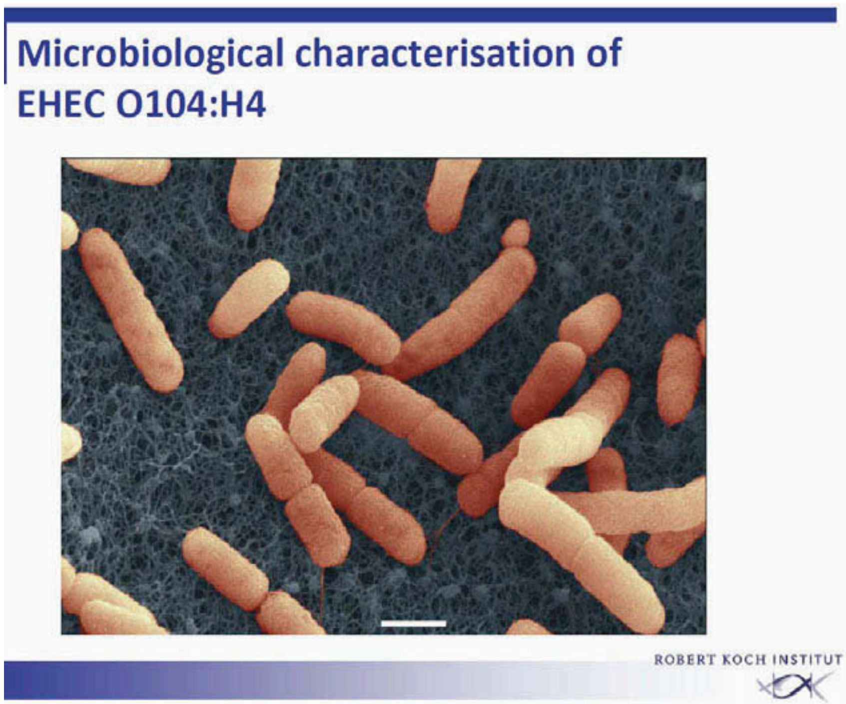

FIGURE A1-5 Electron micrograph of EHEC O104:H4.
SOURCE: Laue, Robert Koch Institute.

food products derived from animals (milk, meat). The usual EHEC strains (e.g., EHEC O157) are found in faeces of ruminants. EHEC O104:H4 has only rarely been identified previously in human beings (in a total of seven patients). A closely related EHEC strain, HUSEC041, was identified in 2001 by the laboratory of Karch at the University of Münster, Germany. Later, a few cases were identified in Korea in 2006, in Georgia in 2009, and in Finland in 2010.

A detailed microbiological characterization of EHEC O104:H4 was performed at the National Reference Centre for Gastrointestinal Bacteria at the RKI and the RKI-Consultant Laboratory of Karch in Münster (Bielaszewska et al., 2011; Brzuskiewicz et al., 2011). From the virulence markers, the outbreak strain was negative for Shiga toxin 1 and positive for Shiga toxin 2 (variant *vtx2a* of Shiga toxin 2). It was negative for Intimin (*eae*) and also negative for enterohaemolysin (*hly*). Macrorestriction analysis (pulsed-field gel electrophoresis) with a number of selected isolates obtained from various areas of Germany showed the same pattern, indicating early that the corresponding patients were all affected by one and the same outbreak event.

Surprisingly, the outbreak strain showed virulence characteristics of enteroaggregative *E. coli* (EAEC). It had the typical EAEC virulence plasmid with adhesion fimbriae type AAF/I. This virulence plasmid has not been described previously in EHEC isolates. All other previously identified EAEC or Shiga toxin–producing *E. coli* (STEC)/EAEC O104:H4 had AAF/III fimbriae. Subsequent sequencing revealed strong homology to an enteroaggregative *E. coli* (EAEC 55989). Obviously, the outbreak strain EHEC O104:H4 represents a virulence combination of two different pathogens. The origin of this outbreak strain with the characteristics of two different pathogens remains unclear for the time being. It is unclear whether the new EHEC O104:H4 pathotype had developed from two separate ancestors by horizontal gene transfer, leading to the observed acquisition of virulence factors (Figure A1-6) (Brzuskiewicz et al., 2011; Mellmann et al., 2011; Rasko et al., 2011). A number of mobile genetic elements can transfer traits in *E. coli* like the Stx-bacteriophage found in EHEC strains. Alternatively, an evolutionary model is discussed, postulating a common progenitor of EAEC

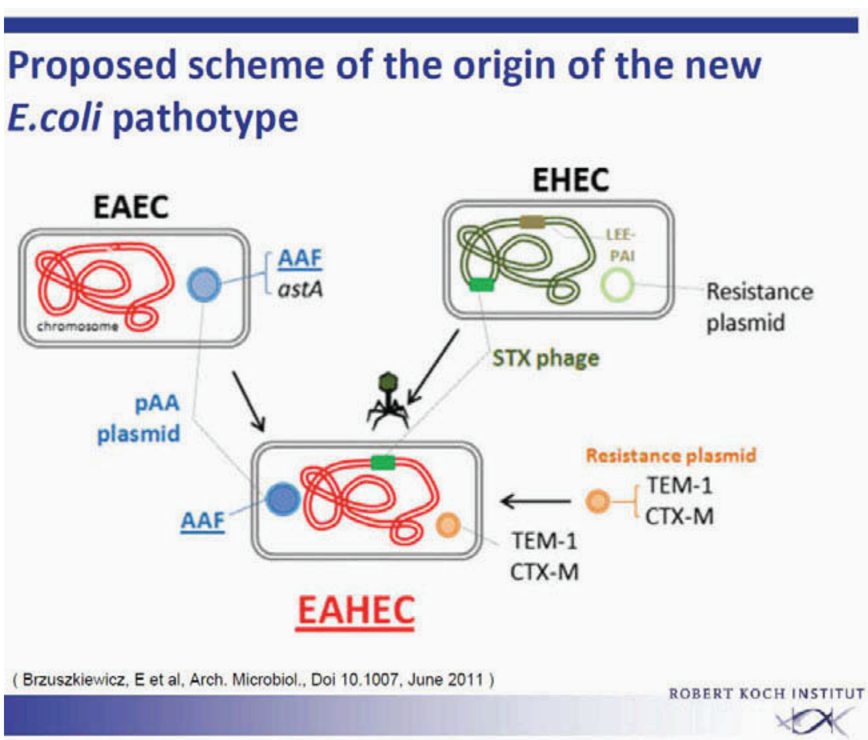

FIGURE A1-6 Putative origin of the EHEC outbreak strain as a combination of virulence traits derived from two different ancestors.
SOURCE: Brzuszkiewicz et al. (2011).

55989 and EHEC O104:H5 developing into two lines, each losing or acquiring virulence factors. The second explanation is favoured by the group from Karch, University of Münster.

The continuously updated EHEC datasheet on the RKI website summarized all known characteristics of the pathogen and suggested the proper microbiological diagnostic procedures.

ESBL Resistance Phenotype

The microbiological characterization revealed a resistance unusual for intestinal *E. coli*. The outbreak strain had an extended-spectrum β-lactamase (ESBL). This is an unusual property of intestinal *E. coli*. This resistance phenotype allowed efficient diagnostics of the outbreak strain. It permitted the use of the corresponding selective media for a targeted search in clinical samples, facilitating a rapid diagnosis. Colonies on an ESBL-agar plate were further characterized with multiplex polymerase chain reaction screening for genes of Shiga toxin 1 and 2 and Intimin.

Absence of Direct Microbiological Evidence for Contamination of Seeds with EHEC O104:H4

The identification of seeds as the source and sprouts as the vehicle of infection relied on sophisticated and elegant epidemiological analysis (i.e., indirect evidence). Direct microbiological evidence has not been obtained so far (Aurass et al., 2011). Intensive bacteriological screening of the fenugreek sprouts and seeds was performed. A large number of samples were also taken at the production site of the sprouts, including the water supply or waste water. All attempts to identify the outbreak strain on seeds or sprouts or in the samples obtained at the production site failed. Sampling sprouts in households with EHEC cases was successful in one or two cases. However, these results were more than questionable. One positive result was obtained from a single box of sprouts originating from the incriminated producer. However, it had already been opened in a household with EHEC cases and might simply have been contaminated by the handling. In another example the outbreak strain was identified in salad samples found in a trashcan days after disposal. Also here, the causal connection is unclear.

One reason for the failure to identify the outbreak strain through bacteriological screening may be the enormous size of the incriminated fenugreek seed lot. The lot size was around 15,000 kg. If only a minor part of this lot had indeed been contaminated, searching for contaminated seeds would resemble the search for a needle in a haystack. In addition, on the same day, the sprout-producing enterprise received another lot of seeds from the same seed distributor. The incriminated lot had been distributed to 70 different companies, 54 of them in Germany and 16 of them in 11 European countries (Appel et al., 2011). However, despite the two additional independent clusters (home-grown sprouts and the cluster in France; see above), no obvious other outbreaks were recognized. Despite all efforts to remove the incriminated lot from the supply chain, it is difficult to estimate how effective and complete this removal has been. Especially in private households, growing sprouts from small aliquots of seeds could lead to new infections. It is known that *E. coli* can survive on dried seeds for longer periods of time, potentially for years.

Incubation Time and Shedding Time

Detailed analysis revealed a median incubation time of 8 days. The maximum was 18 days. Seventy-five percent of the patients developed clinical symptoms after 10 days. Some of the patients showed a shedding of the pathogen for an extensive period. A few patients shed the pathogens for up to 8 months. It remains to be determined whether shedding might even be longer and whether a carrier status may develop. For enteroaggregative *E. coli* this extensive shedding period is not unexpected. It is known that aggregative bacteria adhere more strongly and remain in the gastrointestinal tract for longer periods of time. A close collaboration with the local health authorities proved to be important in the analysis of this outbreak (e.g., for these shedding studies) (Robert Koch Institute, 2011).

Secondary Infections

Even after the end of the outbreak had been announced, recommendations were made to enforce the standard hygiene rules, regarding both personal and hand hygiene and in particular kitchen and food hygiene. This included the recommendation to always clean kitchen utensils carefully when preparing food intended for raw consumption. A small number of secondary infections were observed, predominantly consisting of household members of patients. Therefore, stringent adherence to hygienic practices was strongly suggested in those households where EHEC patients or persons with diarrhea were present.

Single nosocomial infections occurred in hospitals (coloscopy). Transmission also occurred through the preparation or distribution of food. Also several laboratory infections were found. Therefore, raised awareness of the risk of infection was also emphasized in public announcements during the months after the official end of the outbreak.

Communication

The RKI made great efforts to inform the medical experts and the public health service and the professional societies (clinical and microbiological) about details of the outbreak in a very timely fashion. During the outbreak, at least daily updates were distributed by e-mail. The Internet proved to be the most important tool for distribution of information. Usually visits to the RKI homepage result in 4 to 6 million page uses per month. During the outbreak months, May and June 2011, the numbers increased to 16.5 and 17.9 million, respectively. The information provided also included outbreak case definition, forms concerned with sample reporting, diagnostic procedures, information on hygienic measures, etc.

When a whole country is concerned about the safety of its food, the risk communication is important. It proved be helpful to clearly and reliably state the current knowledge and the known risks and their prevention. Also lack of knowledge or uncertainty should be stated clearly, as well as the point in time when new information might be expected. This is important in order to maintain public confidence in recommendations. Farmers requested information because a substantial number of farms suffered economically and were in danger of going out of business.

Conclusion

This outbreak of EHEC infections was the largest recorded outbreak of a bacterial infection observed in Germany in many decades. The enormous rate of HUS cases makes it the largest outbreak of HUS worldwide. It revealed how rapidly a food-borne pathogen can spread and cause serious illness and death. It demonstrates the importance of proper surveillance systems in order to detect an outbreak early and of a rapid reporting system in notifying the corresponding health authorities, in this case the RKI in Germany. According to the specifications of the German Infection Protection Act, a rapid report by the physician or the diagnostic laboratory to the local health authorities is required. In retrospect, between the onset of the disease, the visit to the doctor or hospital, diagnosis, and the report to the local health authority and subsequently to the state authorities and finally to the RKI, a substantial period of time passed, varying from a few days up to several weeks. Measures were taken to improve reporting and to prevent the notification delay. In the analysis of outbreak clusters a close cooperation of health authorities and food safety authorities and a rapid exchange of information is necessary.

The origin of the outbreak strain and how the seeds were contaminated remain unclear. It also remains to be determined whether EHEC O104:H4 will have a reservoir, in human beings, in animals, or in the environment. There is no evidence today that EHEC O104:H4 has become endemic anywhere in humans, animals, or in the environment in Germany. After the sprouts had been identified as the vehicle of this outbreak and after the sprout distribution ended, no further outbreak clusters were identified to be associated with the consumption of sprouts. It is unclear how frequently EHEC is present on sprouts, which are often consumed raw and represent a particularly vulnerable food for bacterial contamination. A rapid and sensitive EHEC diagnostic should also be available in routine diagnostic laboratories in order to identify outbreak events early and reliably. Detailed subtyping should predominantly be performed in specialized laboratories, also in such an outbreak situation. It seems appropriate to observe these aspects or questions also in the future.

The outbreak had enormous consequences, not only for the patients affected but also economically because of strongly reduced trade in salads and salad ingredients. Spanish cucumbers had been discussed by a local health authority as a potential source of the pathogen. This assumption was not confirmed by laboratory analysis, and attempts to show a connection to the outbreak strain failed; however, it affected the sale and led to a major drop in the consumption and export of Spanish vegetables. Farmers in a number of vegetable-exporting countries were in turn compensated by the European Union in the amount of 220 million Euros for this loss in income.

In summary, the events in Germany during the summer of 2011 revealed the importance of functioning public health institutions, both at the county and state level and at the federal level.

A final detailed report of the EHEC O104:H4 outbreak in Germany is available through the RKI website (http://edoc.rki.de/documents/rki_ab/reQHS31jDrGxc/PDF/23NXL3JomOyAA. pdf) in an English version.

Declaration of Interest

The author declares no conflict of interest and has received no payment in preparation of this manuscript.

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A2

ONE HEALTH AND HOTSPOTS OF FOOD-BORNE EIDS

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Summary

In this section, we focus on a One Health approach to food-borne emerging infectious diseases (EIDs), their causes, global patterns, and the drivers of their emergence. First, we review two case studies that show the complexity of food-borne pathogen emergence across the One Health domain. Second, we examine the composition of food-borne diseases with respect to their causal agents (pathogen type), their association with pathogens of zoonotic origin, and their apparent disassociation with pathogens that show drug resistance. Third, we analyze the socioeconomic, environmental, and ecological drivers of food-borne EID events. Finally, we use published, spatially explicit information on the drivers of disease emergence to produce a preliminary "hotspot" map that reveals the epicentres, or hotspots, of food-borne EID events globally.

Introduction

One Health's focus on the intersection of human, domestic animal, and environmental health is ideally suited to managing emerging zoonoses. However, the patterns of emergence are complex and poorly understood and for food-borne infections may involve multiple pathways. Food-borne infections can include directly transmitted or vector-borne diseases, for example, Rift Valley fever (Arzt et al., 2010). Single strains of drug-resistant microbes can infect livestock, wildlife, and humans (e.g., *E. coli* O157:H7) (Hughes et al., 2009; Nielsen et al., 2004; Rahn et al., 1997). Finally, viral pathogens that originate in wildlife may be driven to emerge by the intensification of livestock production (Pulliam et al., 2011) or by contamination of bush meat (Wolfe et al., 2005) or other food sources

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