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German Outbreak of *Escherichia coli* O104:H4 Associated with Sprouts

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ABSTRACT

BACKGROUND

A large outbreak of the hemolytic–uremic syndrome caused by Shiga-toxin–producing *Escherichia coli* O104:H4 occurred in Germany in May 2011. The source of infection was undetermined.

METHODS

We conducted a matched case–control study and a recipe-based restaurant cohort study, along with environmental, trace-back, and trace-forward investigations, to determine the source of infection.

RESULTS

The case–control study included 26 case subjects with the hemolytic–uremic syndrome and 81 control subjects. The outbreak of illness was associated with sprout consumption in univariable analysis (matched odds ratio, 5.8; 95% confidence interval [CI], 1.2 to 29) and with sprout and cucumber consumption in multivariable analysis. Among case subjects, 25% reported having eaten sprouts, and 88% reported having eaten cucumbers. The recipe-based study among 10 groups of visitors to restaurant K included 152 persons, among whom bloody diarrhea or diarrhea confirmed to be associated with Shiga-toxin–producing *E. coli* developed in 31 (20%). Visitors who were served sprouts were significantly more likely to become ill (relative risk, 14.2; 95% CI, 2.6 to ∞). Sprout consumption explained 100% of cases. Trace-back investigation of sprouts from the distributor that supplied restaurant K led to producer A. All 41 case clusters with known trading connections could be explained by producer A. The outbreak strain could not be identified on seeds from the implicated lot.

CONCLUSIONS

Our investigations identified sprouts as the most likely outbreak vehicle, underlining the need to take into account food items that may be overlooked during subjects' recall of consumption.

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Human infection with Shiga-toxin–producing *Escherichia coli* is a major cause of postdiarrheal hemolytic–uremic syndrome. This life-threatening disorder, which is characterized by acute renal failure, hemolytic anemia, and thrombocytopenia, typically affects children under the age of 5 years. Shiga-toxin–producing *E. coli* O157 is the serogroup that is most frequently isolated from patients with the hemolytic–uremic syndrome worldwide.[1]

In May 2011, a large outbreak of the hemolytic–uremic syndrome associated with the rare *E. coli* serotype O104:H4 occurred in Germany.[2-5] The main epidemiologic features were that the peak of the epidemic was reached on May 21 and May 22[4,5] and that the vast majority of case subjects either resided or had traveled in northern Germany. Almost all patients from other European countries or from North America had recently returned from northern Germany.[2,6,7] Of the affected case subjects, 90% were adults, and more than two thirds of case subjects with the hemolytic–uremic syndrome were female.[4]

Early studies in Hamburg suggested that infections were probably community-acquired and were not related to food consumption in a particular restaurant. A first case–control study that was conducted on May 23 and 24 suggested that raw food items, such as tomatoes, cucumbers, or leaf salad,[3] were the source of infection. The consumption of sprouts, which was previously implicated in outbreaks of Shiga-toxin–producing *E. coli* in the United States[8] and Japan,[9] was mentioned by only 25% of case subjects in exploratory interviews, so consumption of sprouts was not tested analytically.

This report describes the investigations that were conducted by the federal agencies under the auspices of the German Ministry of Health and the Ministry of Food, Agriculture, and Consumer Protection, as well as by the respective state agencies, to identify the vehicle of infection of this international outbreak.

METHODS

STUDY DESIGN

Three types of parallel studies were conducted: one case–control study, one recipe-based restaurant cohort study, and combined trace-back and trace-forward investigations. The main results of all three studies became available between June 2 and June 9, 2011. Results, even if preliminary, were communicated among the investigation groups and the Task Force EHEC (Enterohemorrhagic *Escherichia coli*) at the Federal Office of Consumer Protection and Food Safety in Berlin. If the results were judged to have appropriate validity, they were communicated as soon as possible to the public.

The case–control and cohort studies were conducted within the framework of the Communicable Diseases Law Reform Act of Germany. Mandatory regulations were observed, and review by an ethics committee was not required.

CASE–CONTROL STUDY

From May 29 to June 4, we conducted a case–control study to further specify the type of raw vegetables associated with illness in this outbreak. A case was defined as clinically diagnosed hemolytic–uremic syndrome in an adult who was hospitalized in one of three hospitals in northern Germany, located in the cities of Bremen, Bremerhaven, and Lübeck. Control subjects were individually matched with case subjects on the basis of age group and neighborhood. Case and control subjects were predominantly asked about consumption of fruit and vegetable items, including sprouts, during the 14 days before the onset of illness (for case subjects) or before the interview date (for control subjects) (for details, see the Supplementary Appendix, available with the full text of this article at NEJM.org).

RECIPE-BASED RESTAURANT COHORT STUDY

Since the earlier studies had not identified a single source of infection, we conducted a cohort study at restaurant K in Lübeck, Schleswig–Holstein. Preliminary information revealed that several visitor groups with subsequent cases of gastroenteric disease had eaten in restaurant K between May 12 and May 16, 2011, which was defined as the outbreak period in this study. Using the booking notes, we identified cohorts that had eaten in the restaurant during this period and asked all members about the menu items they had consumed. We interviewed the chef of the restaurant about the ingredients and their quantities used to prepare the menu items offered in the restaurant.

A case was defined as an illness in a member of any of the cohorts that was associated with bloody diarrhea, self-reported laboratory-confirmed Shiga-toxin–producing *E. coli* O104 infection, or the hemolytic–uremic syndrome with an onset of diarrhea within 2 weeks after visiting restaurant K. Non–case subjects were those who remained healthy after visiting restaurant K. We excluded from the analysis all subjects who had diarrhea that was not bloody, who did not have laboratory-confirmed Shiga-toxin–producing *E. coli* O104 infection, or whose disease onset was later than 14 days after visiting restaurant K. For the analysis, we evaluated only data on ingredients that were used in the dishes that were served to the restaurant guests (i.e., data that were solely based on the information obtained from the chef) (for details, see the Supplementary Appendix).

To estimate the total number of cases accrued at restaurant K during the study period, we collected information on the total number of main dishes purchased in this period from billing data. Using the attack rate among persons who were served sprouts from the cohort study, we calculated the number of ill persons as the number of main dishes served containing sprouts times the attack rate among sprout eaters.

Table 1. Vegetables or Fruits Evaluated in a Case–Control Study in the German Outbreak.*

Food Item	Case Subjects Exposed	Control Subjects Exposed	Matched Odds Ratio (95% CI)	P Value
	no./total no. (%)			
Sprouts	6/24 (25)	7/80 (9)	4.35 (1.05–18.0)	0.04
Cucumbers	22/25 (88)	52/79 (66)	3.53 (0.96–12.9)	0.06
Apples	22/24 (92)	57/81 (70)	3.91 (0.86–17.7)	0.08
Peppers	16/24 (67)	35/80 (44)	2.66 (0.90–7.9)	0.08
Strawberries	19/26 (73)	43/81 (53)	2.33 (0.90–6.0)	0.08

* P>0.10 for raw onions, tomatoes, leaf salad, asparagus, carrots, and basil.

ENVIRONMENTAL, TRACE-BACK, AND TRACE-FORWARD INVESTIGATIONS

From physicians, patients, county and regional health departments, and foreign national public health institutes, we received information on clusters or apparently sporadic cases of illness that occurred in the context of the overall epidemic among persons who had probable exposure at only one location or venue (see the Supplementary Appendix). Information was continuously reported to national and local food-safety authorities and to the task force.

On the basis of findings in the early studies, food-safety authorities initially concentrated their investigations on tomatoes, cucumbers, and leaf salads, as well as on other vegetables eaten raw and salad ingredients, including toppings. Local and state food-safety authorities assessed distribution channels of raw food products connected with clusters or single case subjects with single exposures. In addition, both epidemiologically suspected and other raw food items were sampled and, after specific enrichment procedures, were tested by means of immunoassay for Shiga toxin and polymerase-chain-reaction assay for the Shiga-toxin stx2 prophage gene cluster and for genetic markers of the O104:HA strains. The task force initiated a trace-forward investigation for sprouts from suspect producer A to outbreak clusters, a study that was conducted by the food-safety authorities of the respective counties, compiled by the pertinent federal food-safety authorities, and analyzed by the task force. The task force also initiated a trace-back investigation from producer A.

RESULTS

CASE–CONTROL STUDY

We included 26 case subjects (9 male and 17 female) and 81 control subjects in the study. On univariable analysis, the only significant variable was sprouts (Table 1). Other food items, such as raw minced beef and milk and other dairy products, were not significantly associated with illness.

The sequential addition and removal of other variables resulted in a multivariable model containing only sprouts (matched odds ratio, 5.8; 95% confidence interval [CI], 1.2 to 29.0) and cucumbers (matched odds ratio, 6.0; 95% CI, 1.1 to 31.0). Before the date on which the public was advised not to consume sprouts (June 10, 2011), only 6 of 24 case subjects (25%) remembered having consumed them (Table 1, and the Supplementary Appendix). After that date, we wished to ascertain the possible degree of false recall among the case subjects. We tried to recontact all case and control subjects who had not reported sprout consumption previously. Of 8 case subjects who could be reached, 3 (38%) remembered having eaten sprouts in the 14 days before the onset of illness. By contrast, all 37 control subjects who had not reported sprout consumption in previous interviews continued to report that they had not eaten sprouts.

Table 2. Characteristics of 10 Cohorts of Subjects Who Visited Restaurant K between May 12 and May 16, 2011.*

Cohort No.	Size	Subjects with Data	Male Sex	Median Age (IQR)	Subjects with Diarrhea	Subjects with Bloody Diarrhea	Subjects with Laboratory-Confirmed STEC Infection	Subjects with HUS	Subjects Evaluated for Case Definition†	Subjects Fulfilling Case Definition	Attack Rate for Subjects Fulfilling Case Definition
		no.	*%*	*yr*		*no.*			*no. (%)*	*no.*	*%*
1	37	37	5	49 (45–57)	10	9	10	4	34 (92)	9	26
2	2	2	50	49 (46–52)	1	1	2	0	2 (100)	1	50
3	31	31	55	57 (45–68)	11	4	5	1	25 (81)	5	20
4	11	10	0	54 (53–55)	2	0	1	0	9 (90)	1	11
5	12	9	0	46 (43–48)	1	1	2	0	9 (100)	1	11
6	19	19	37	32 (15–49)	1	1	1	0	17 (89)	1	6
7	10	10	50	40 (40–42)	0	0	0	0	9 (90)	0	0
8	17	14	57	68 (65–73)	3	3	4	1	14 (100)	3	21
9	25	25	40	74 (69–75)	9	9	6	1	25 (100)	9	36
10	13	11	36	24 (21–48)	3	1	2	1	8 (73)	1	13
Total	177	168	32	53 (42–67)	41	29	33	8	152 (90)	31	20

* HUS denotes hemolytic–uremic syndrome, IQR interquartile range, and STEC Shiga-toxin–producing *Escherichia coli*.
† The case definition was the presence of bloody diarrhea, laboratory-confirmed infection with Shiga-toxin–producing *E. coli,* or the hemolytic–uremic syndrome with an onset of disease within 2 weeks after visiting restaurant K. According to the case definition, 16 subjects were excluded either because they had diarrhea that was not bloody or because the date of the onset of diarrhea was more than 14 days after visiting restaurant K or was unknown.

RECIPE-BASED RESTAURANT COHORT STUDY

We identified 10 cohorts with a total of 177 persons who had eaten at restaurant K (Table 2). Of these persons, we interviewed 168 (95%), including 161 who were interviewed directly and 7 for whom information was obtained from a proxy. Among the 152 persons who could be evaluated for the case definition, 31 (20%) had an illness that fulfilled the case definition. Among these subjects, the hemolytic–uremic syndrome developed in 8 (26%) (see the Supplementary Appendix).

In univariable analysis of all raw food items, only visitors who had been served sprouts were significantly more likely to become ill (Table 3). The P value for the risk ratio for all other items was greater than 0.15. Of 115 persons who had been served sprouts, 31 (27%; 95% CI, 19 to 36) became case subjects, whereas none of 37 persons who had not been served sprouts reported having gastrointestinal symptoms that fulfilled the case definition. Thus, all 31 case subjects had been served menu items containing sprouts. Nearly half the menu items served in the restaurant contained raw sprouts as a garnish or were served with a side salad containing raw sprouts. Side salads contained radicchio, Chinese cabbage, lettuce, cucumber, tomato, and sprouts. No menu item contained cooked sprouts. During this period, the restaurant used only one type of sprout assortment, which was received from a distributor in Schleswig-Holstein and contained four types of sprouts: lentil sprouts, alfalfa sprouts, fenugreek sprouts, and adzuki bean sprouts.

During the outbreak period, 884 main dishes containing sprouts were served to the guests of the restaurant. Applying the attack rate of 27% among sprout eaters, we extrapolated that a total of 239 cases of bloody diarrhea (95% CI, 168 to 318) occurred among customers of this restaurant.

ENVIRONMENTAL, TRACE-BACK, AND TRACE-FORWARD INVESTIGATIONS

The task force identified 41 clusters or cases with single exposures. One of the clusters was a hotel in lower Saxony in which Swedish citizens were affected (cluster 1) (Fig. 1). A “spicy sprout mixture” that was sampled from the distributor (distributor 1) of the hotel’s restaurant on June 2, 2011,

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

tested positive for Shiga toxin on a commercial immunoassay. Although confirmatory testing later proved to be negative, immediate trace back led to producer A in Lower Saxony, at which a total of 452 water, seed, sprout, and surface samples tested negative for Shiga-toxin–producing *E. coli* O104:HA. Producer A was licensed as a horticultural farm and produced 18 different sorts of sprouts at the time. Protective measures consisted of regularly instructing employees on the application of proper hygiene necessary for the production of sprouts and the frequent testing of sprouts for salmonella, according to European Union regulations, as well as for coliforms.

All employees of producer A were interviewed, and 5 of 15 had become ill in May 2011 or tested positive for O104:H4. Employees frequently ate sprouts produced at their company. Preferred types were fenugreek, broccoli, and garlic sprouts.

Tracing forward from producer A led to four distributors (Fig. 1). Distributor 1 was connected not only to the restaurant in which cluster 1 had occurred but also to restaurant K. Distributor 4 delivered food to a caterer in Frankfurt that was linked to a cafeteria outbreak that occurred early in the epidemic.[3]

Subsequently, 22 more distributors (for a total of 26) that obtained sprouts from producer A were identified. Distributors were located in 7 of the 16 federal states. Each of the 41 case clusters could be linked with at least one of the identified sprout distributors (Fig. 2).[10] Fenugreek or lentil sprouts were suspected as the outbreak vehicle because these types of sprouts were the common ingredients in two different sprout mixtures that were packaged for distribution by producer A and had been supplied to most of the 41 clusters.

In mid-June, investigations on the origin of sprouts that were consumed by additional case subjects revealed that two case subjects from Lüneburg, Lower Saxony, had eaten a homegrown sprout mix that included fenugreek sprouts. The seeds for these sprouts had been purchased at a retail store that had the same supplier of seeds (supplier X) as producer A (Fig. 1).

DISCUSSION

We report evidence from epidemiologic, microbiologic, and food trace-back and trace-forward investigations that incriminates sprouts as the vehicle of infection in this large outbreak of the hemolytic–uremic syndrome associated with Shiga-toxin–producing *E. coli*. Although definitive molecular evidence is lacking, the argument that sprouts were responsible for this outbreak is strong on the basis of the following five factors: both epidemiologic studies implicated sprouts, the restaurant study showed that 100% of cases of illness could be explained by the consumption of sprouts, no other food ingredient consumed at restaurant K was associated with the risk of illness, all 41 clusters or cases of single exposure could be linked to sprout producer A and its distribution channels, and several employees of sprout producer A who frequently consumed sprouts at the company became symptomatically ill early in the outbreak period or tested positive for Shiga-toxin–producing *E. coli* O104:H4.

Information obtained during the outbreak investigation in Germany already hinted at an outbreak source before producer A in the seed and sprout distribution chain. Seeds that were used by producer A and by the two case subjects from

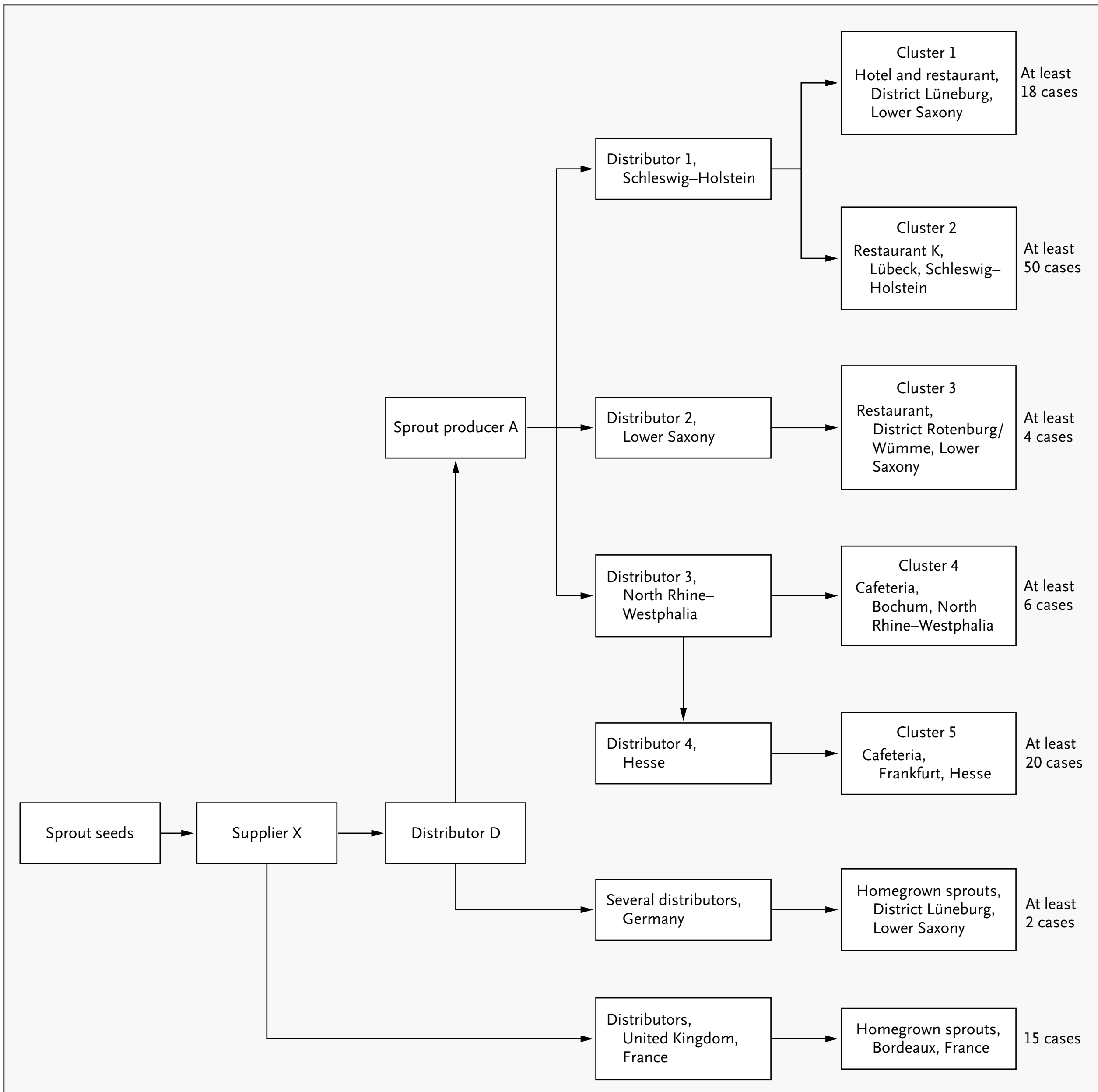

Figure 1. Anatomy of the German Outbreak.

Shown are the trading connections from supplier X to sprout producer A and through four distributors to five outbreak clusters, as well as to two other distributor groups leading to a cluster of illnesses caused by Shiga-toxin–producing *E. coli* in Lüneburg and an outbreak in France unrelated to producer A. Known case subjects at restaurant K included those who were part of the cohort study and others who were not.

Lower Saxony who grew their own sprouts originated from supplier X. In June 2011, an outbreak of the hemolytic–uremic syndrome associated with Shiga-toxin–producing *E. coli* O104:HA occurred in Bordeaux, France.[11] The *E. coli* responsible for the outbreak was genetically related to that in the German outbreak, and there was an epidemiologic association with consumption of homegrown fenugreek sprouts. These findings spurred trace-back investigations by a task force (set up by the European Food Safety Authority (EFSA), which consisted of experts from the European Commission, relevant European Union member states, the European Center for Disease Prevention and Control, the World Health Organization, the Food and Agriculture Organization of the United Nations, and EFSA staff members. It concluded that a certain lot of fenugreek seeds that was imported in late 2009 from Egypt was the most likely common link for the outbreaks in Germany and France.[12] With respect to the point of contamination, it is possible that it occurred at the site where seeds were produced, during transportation, or at the importer. By August 2011, this question had not been resolved.

The account of the outbreak was dramatic: 4321 outbreak cases, including 3469 cases of Shiga-toxin–producing *E. coli* and 852 cases of the hemolytic–uremic syndrome, had been reported by July 26, 2011, when the outbreak was declared to be over.[13] By that time, 50 patients had died. After epidemiologic and food-safety investigations had concurred in identifying sprouts as the outbreak vehicle, the public had been advised on June 10 to abstain from the consumption of raw sprouts, to eliminate raw sprouts in possession at that time, and to remove any sprouts stemming from producer A.[14] In addition, producer A was temporarily closed. Cases of illness still occurred until the end of July 2011, partially as a consequence of secondary transmission,[15] but the number of cases dropped substantially.

Early in the outbreak investigation, raw food products other than sprouts had been suspected as the vehicle. The three studies that we present here built on these findings and complement one another. The early epidemiologic findings helped food-safety authorities to streamline their investigations, which led them to turn their attention to producer A. Since the case–control study was conducted before sprouts came into focus, the significant association between sprouts and illness is therefore revealing and important. Nevertheless, the findings received strong support only through the restaurant study and the food trace-back and trace-forward investigations. The restaurant study provided an idea of why tomatoes, cucumbers, and leaf salad had been suspected early on. The one dish that frequently exposed guests to sprouts was the side salad, which contained tomatoes, cucumbers, three sorts of leaf salads, and sprouts. Sprouts may have been the ingredient that visitors recalled least in such a mixed salad. This hypothesis is also suggested by the results of the repeated interviews in the case–control study. Because the earlier studies had attempted to find a vehicle that explained the majority of cases, sprouts were missed. Although international guidelines[16] generally recommend otherwise, this experience suggests that food items or ingredients that are deemed to be hard to remember should be included in analytical studies, even if such items are mentioned by less than 50% of those surveyed.

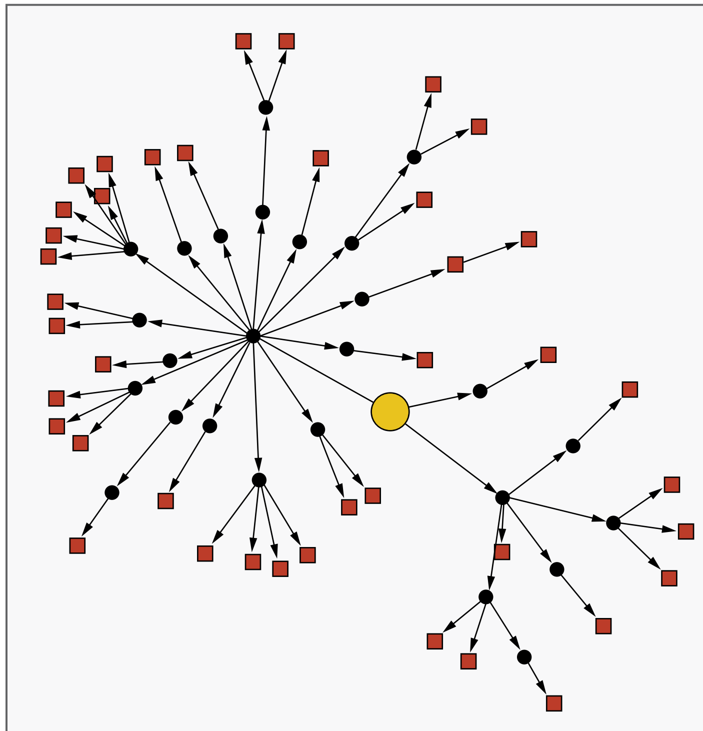

Figure 2. Trading Network Leading to the German Outbreak.
The trading network for the contaminated sprouts led from producer A in Lower Saxony (yellow circle) to 26 sprout distributors (black dots) and 41 identified outbreak clusters (red squares), established by combined back and forward tracing.

Producer A was licensed as a horticultural company. Although hygienic measures were satisfactory and local food-safety authorities had inspected the company routinely under the same conditions as a food-processing company, it became apparent that European legislation has important deficits regarding Shiga-toxin–producing *E. coli*. Production of food that is vulnerable to contamination with this pathogen, such as sprouts or sprout seeds, should be monitored for this organism so that hygienic measures prevent amplification. In addition, both incoming seeds and outgoing food products should be tested for Shiga-toxin–producing *E. coli*.

In general, focused restaurant studies provide a favorable situation to identify the vehicle, even in large, geographically dispersed outbreaks, because place and time of exposure are known and menu cards can be used to spur visitors' memories. If one or few specific menu items are identified, ingredients can be further analyzed.[17] If not, the reason may be that a common ingredient is contained in many menu items, resulting in the necessity to collect detailed ingredient information of the whole or a large part of the menu,[18,19] information that needs to be obtained from those preparing the food.

In conclusion, we have presented investigative results regarding an outbreak of the hemolytic–uremic syndrome associated with Shiga-toxin–producing *E. coli*. Under favorable circumstances, the recipe-based restaurant cohort study proved to be a quick method for detecting suspected food ingredients with high reliability in a complicated setting of exposures. Recommendations regarding sprout use and consumption may need to be strengthened or adjusted as a consequence of this outbreak.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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REFERENCES

1. Tarr PI, Gordon CA, Chandler WL. Shiga-toxin-producing Escherichia coli and haemolytic uraemic syndrome. Lancet 2005; 365:1073-86.
2. Askar M, Faber MS, Frank C, et al. Update on the ongoing outbreak of haemolytic uraemic syndrome due to Shiga toxin-producing Escherichia coli (STEC) serotype O104, Germany, May 2011. Euro Surveill 2011;16:19883.
3. Frank C, Faber MS, Askar M, et al. Large and ongoing outbreak of haemolytic uraemic syndrome, Germany, May 2011. Euro Surveill 2011;16:19878.
4. Frank C, Werber D, Cramer JP, et al. Epidemic profile of Shiga-toxin–producing *Escherichia coli* O104:H4 outbreak in Germany. N Engl J Med 2011. DOI: 10.1056/NEJMoa1106483.
5. Wadl M, Rieck T, Nachtnebel M, et al. Enhanced surveillance during a large outbreak of bloody diarrhoea and haemolytic uraemic syndrome caused by Shiga toxin/verotoxin-producing Escherichia coli in Germany, May to June 2011. Euro Surveill 2011;16:19893.
6. European Centre for Disease Prevention and Control. ECDC rapid risk assessment: outbreak of Shiga toxin-producing E. coli (STEC) in Germany. June 14, 2011 (http://www.ecdc.europa.eu/en/publications/Publications/1106_TER_Risk_Assessment_EColi_revised.pdf).
7. World Health Organization. International Health Regulations: EHEC outbreak in Germany (http://www.euro.who.int/en/what-we-do/health-topics/emergencies/international-health-regulations/ehec-outbreak-in-germany).
8. Taormina PJ, Beuchat LR, Slutsker L. Infections associated with eating seed sprouts: an international concern. Emerg Infect Dis 1999;5:626-34.
9. Michino H, Araki K, Minami S, et al. Massive outbreak of Escherichia coli O157:H7 infection in schoolchildren in Sakai City, Japan, associated with consumption of white radish sprouts. Am J Epidemiol 1999;150:787-96.
10. Bundesinstitut für Risikobewertung (BfR). Bedeutung von Sprossen und Keimlingen sowie Samen zur Sprossenherstellung im EHEC O104:H4 Ausbruchsgeschehen im Mai und Juni 2011 (Stellungnahme Nr. 023/2011 des BfR. July 5, 2011) (http://www.bfr.bund.de/cm/343/bedeutung_von_sprossen_und_keimlingen_sowie_samen_zur_sprossenherstellung_im_ehec_o104_h4_ausbruchsgeschehen_im_mai_und_juni_2011.pdf).
11. Gault G, Weill FX, Mariani-Kurkdjian P, et al. Outbreak of haemolytic uraemic syndrome and bloody diarrhoea due to Escherichia coli O104:H4, south-west France, June 2011. Euro Surveill 2011;16:19905.
12. European Food Safety Authority. Tracing seeds, in particular fenugreek (Trigonella foenum-graecum) seeds, in relation to the Shiga toxin-producing E. coli (STEC) O104:H4 2011 outbreaks in Germany and France. July 5, 2011 (http://www.efsa.europa.eu/en/supporting/doc/176e.pdf).
13. Robert Koch-Institute. Informationen zum EHEC-/HUS-Ausbruchsgeschehen von Mai bis Juli 2011 in Deutschland — Ende des Ausbruchs. Epidemiol Bull 2011;31:295-6 (http://www.rki.de/cln_160/nn_2030884/DE/Content/Infekt/EpidBull/Archiv/2011/31__11,templateId=raw,property=publicationFile.pdf/31_11.pdf).
14. *Idem*. Neue Erkenntnisse zum EHEC-Ausbruch: Gemeinsame Pressemitteilung von BfR, BVL und RKI. June 10, 2011 (http://www.rki.de/cln_169/nn_467482/DE/Content/Service/Presse/Pressemitteilungen/2011/08__2011.html).
15. Hauri A, Gotsch U, Strotmann I, et al. Secondary transmissions during the outbreak of Shiga toxin-producing Escherichia coli O104 in Hesse, Germany, 2011. Euro Surveill 2011;16:19937.
16. Foodborne disease outbreaks: guidelines for investigation and control. Geneva: World Health Organization, 2008.
17. Mody RK, Greene SA, Gaul L, et al. National outbreak of Salmonella serotype saintpaul infections: importance of Texas restaurant investigations in implicating jalapeño peppers. PLoS One 2011;6(2): e16579.
18. Buchholz U, Mermin J, Rios R, et al. An outbreak of food-borne illness associated with methomyl-contaminated salt. JAMA 2002;288:604-10.
19. Wheeler C, Vogt TM, Armstrong GL, et al. An outbreak of hepatitis A associated with green onions. N Engl J Med 2005; 353:890-7.