

OREGON PUBLIC HEALTH DIVISION • OREGON HEALTH AUTHORITY

SPROßEN MACHEN KRANK: E. COLI O104 STRIKES EUROPE

One of the most devastating outbreaks of foodborne disease in world history is finally sputtering to an end. As of 21 July, more than 3,900 cases have been linked to the *Escherichia coli* O104:H4 outbreak, including 770 with hemolytic uremic syndrome (HUS).^{*} Forty-three persons have died.¹ The vast majority live in Germany, but cases have been reported in at least 13 other countries, including six in the United States. With the exception of a small satellite cluster in France (about which more later) and an isolated case in Sweden, all cases live in or recently visited Germany and were presumably exposed there. The outbreak was caused by an unusual bug with a much higher rate of HUS and death than is typically seen with Shiga-toxigenic *E. coli* (STEC) infections. The vehicle for this outbreak, however, was a variation on a familiar theme.

In early May, German public health authorities sounded an alarm about an epidemic of HUS and hemorrhagic colitis centered in Hamburg. Antecedent bloody diarrhea was common, and stool assays found STEC.

HUS is a hallmark of severe STEC infections, notably *E. coli* O157:H7.² For many years O157 was the only commonly identified STEC, as microbiologists took advantage of a biochemical quirk[†] to pick out O157 from fecal samples that are always awash in non-toxicogenic *E. coli*. More recently, many clinical labs have switched to screening for Shiga toxin or its gene, and the proportion of reported STEC infections due to O157 has fallen to ~50%.

THE PATHOGEN

The outbreak's etiologic agent was quickly identified as O104:H4 — an antigenic pairing reported rarely

(and never in the United States). This pathogen is anything but another garden variety STEC.³ It lacks intimin, previously thought to be an essential virulence factor. It possesses characteristics typical of both STEC and enteroaggregative *E. coli* (EAEC), resulting in an "augmented virulence potential," perhaps facilitating absorption of Shiga toxin through enhanced adherence. While STEC have ruminant animal reservoirs (cattle, sheep, goats, deer), EAEC are thought to have only human reservoirs, and the authors suggest that the vehicle may have been contaminated with human excrement.

THE ILLNESS

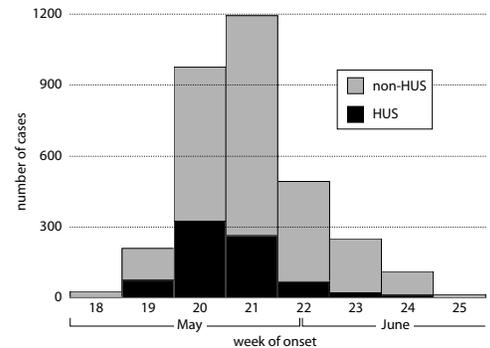
The clinical illness, according to a recently published summary, was fundamentally similar to O157 infection: a typically afebrile diarrheal illness that often progressed to bloody diarrhea and sometimes HUS.⁴ The main differences were the extraordinarily high proportion (20%) of reported cases that developed HUS, the high number of fatalities even among patients without HUS (16), and a relatively high rate of neurologic symptoms. Surveillance artifacts and case definitions could account for some of these differences, and more time is needed to analyze the unhappy wealth of data now available. But there seems to be little doubt that this bug was much worse than usual; hundreds of patients are looking at lifelong medical problems.

Limited data also suggest a median incubation period of 8 days (range, 2–18) — much longer than for O157 (~4 days; range, 1–10).^{4,5}

IDENTIFYING THE SOURCE

The source was not identified quickly, and official warnings about a series of red herrings devastated produce sales across Europe. On 26 May, consumers were warned to avoid all fresh cucumbers, tomatoes, and salad greens (e.g., lettuce). Spanish cucumbers were then fingered specifically — the result of a misunderstood lab test. Economic costs were estimated to be

Figure. Epidemic Curve, O104:H4 outbreak (data as of 28 June (N=3,230))



well north of \$500M, and it looked as if the European Union might dissolve in a food fight. Next, sprouts — most likely bean sprouts — were identified as the culprit. Confusion reigned for another week, with bulletins and press accounts referring to "sprouts" generically, seemingly indifferent to the definition of sprouts as "baby plants."

Although the demographic profile of cases was classic for sproutbreaks,⁵ German investigators apparently blew off sprouts when "only" 3 of 12 persons interviewed volunteered sprout consumption. Subsequent questionnaires did not even ask about sprouts, much less the kind of exploratory questions (deli sandwiches? salad bars?) which, we have learned, can coax this history from victims. The investigation finally circled back to sprouts with analyses of subgroups of cases, wherein the range of likely exposures could be confined to one or two meals. Eventually, sprouts from the Gärtnerhof company were publicly named as the suspect.

Nothing happened publicly to narrow this range of possibilities or to embargo specific seed lots[‡] until a satellite outbreak of indistinguishable O104:H4 infections popped up in Bordeaux, France. It was quickly determined that at a village fair on 8 June the victims had consumed a blend of mustard, fenugreek, and arugula sprouts "home grown" from seeds purchased at a local garden center. The little 50-g packets of those seeds had, in turn, been imported

[‡] Almost all sproutbreaks stem from cultivation of contaminated seeds.

* The triad of microangiopathic hemolytic anemia, thrombocytopenia and renal insufficiency

† Most *E. coli* ferment sorbitol, whereas most O157 do not.



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from a British garden supplier. It transpired that fenugreek sprouts had been common to the sprout mixes produced by Gärtnerhof in Germany.

More recently, the noose has tightened around fenugreek sprouts grown from seeds exported from Egypt in 2009.⁶ Seeds from the same exporter went to both the German sprouter and the British garden supplier. Fenugreek is a common spice used in Indian and Middle Eastern cuisine, and it is commonly sold as whole or ground seeds. The seeds can also be sprouted or grown as an herb. The EU has now halted the import of all Egyptian fenugreek, and efforts are underway to find and embargo any other seed from the same source, which was apparently distributed to many countries in Europe and perhaps elsewhere.⁶

COULD IT HAPPEN HERE?

Could O104:H4 infections occur in Oregon? Definitely. New pathogens will continue to pop up as surely as microbes multiply. Be it from imported spices, domestic produce, factory-farmed poultry, or the kid next door, we are constantly under microbiological siege.

Could sprouts cause an outbreak here? Yes: we've had many sproutbreaks already and will continue to see them as long as people eat sprouts without a kill step. Soaking seeds in bleach and testing the irrigation water reduce but do not eliminate the risk associated with raw sprout consumption.

Could we have an outbreak this big? Probably not — at least from sprouts. We first recognized sprouts as the cause of an outbreak in Oregon in 1996.⁷ It took us more than 5 weeks

of investigation to convince ourselves that a food confessed by only 40% of the cases could be the source. At that time we didn't know how to ask the right questions to ferret out sprout consumption.

But that was 1996. Over the last 15 years we've gotten much better at figuring out commercial product outbreaks in general and sproutbreaks in particular. Sprouts are mentioned in every modern textbook as one of the "usual suspects" for foodborne outbreaks, and they are the classic vehicle for clusters of illness in which adult women predominate. Given a background consumption rate of ~5%, we now consider reported sprout consumption in excess of 15% to be highly suspicious, because the background rate is so low. Indeed, we now rarely need more than 3 or 4 cases to pinpoint sprouts as a source. We can't do much about the initial bolus of infections, but once case reports appear we are well positioned to stop sproutbreaks quickly, limiting both the clinical and economic damage.[§]

WHAT CAN PHYSICIANS DO?

What starts most of these investigations is lab or physician reporting. That usually means a specific diagnosis, although we are eager to hear about suggestive anecdotes.[¶] Ordering appropriate diagnostic tests on your patients is always helpful. Find out what your lab tests for when you submit a stool specimen. A routine request for "enteric pathogens," for example, may not find STEC, so you may need to ask for it specifically. In any case, know that

§ but see Proverbs 16:18.

¶ e.g., "A heckuva lot of people coming in with bloody diarrhea lately."

your suspicions, testing and reporting may help stop a nasty outbreak.

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