

OREGON PUBLIC HEALTH DIVISION • DEPARTMENT OF HUMAN SERVICES

INSIGHTS FROM CHOCOLATE CHIP COOKIES

OUTBREAK INVESTIGATIONS have been a core activity for public health agencies for more than 150 years. As with fire and police departments, we expect that government will be able to respond to health problems that threaten the common weal. Most outbreaks investigated by public health agencies are of enteric illness—90% in Oregon. A small but high-profile fraction of those are multi-state outbreaks caused by commercially distributed foodstuffs.

Outbreaks of salmonellosis and similar illnesses are more subtle than a burning building or an assailant with a gun. The fireman is rarely the first to determine that your house is on fire, but public health workers are often the first to notice that outbreaks have occurred. As individuals get sick, seek medical attention, and are diagnosed, they rarely suspect that they are the victims of a common-source outbreak. The attack rate in commercial product outbreaks is often so low—only a single case for every 1,000 or 100,000 consumers—that cases may be scattered across states with no more than one or two identified in any given jurisdiction. Of course many more persons are ill—dozens more for every confirmed case, usually—but they literally don't count. Depending on the shelf life of the product and the persistence of the production problem, cases can be scattered in time as well as space. These and other factors can conspire to delay the recognition of outbreaks and at the same time decrease that sense of urgency underpinning most successful investigations.

A multi-state outbreak of hemorrhagic escherichiosis was recently traced to consumption of commercially packaged

chocolate chip cookie dough: to be specific, Nestlé Toll House brand



WARNING
Eat at your own risk

refrigerated cookie dough products. The outbreak highlights recurrent issues in complex outbreak investigations.

Escherichia coli O157:H7 has a long history in Oregon and elsewhere, leaving a signature trail of abdominal cramps, bloody diarrhea, and kidney damage in its wake. Typical food vehicles include fresh produce (e.g., lettuce, spinach), beef, raw milk, venison, and other products laced with ruminant (especially bovine) feces. Commercial cookie dough, while an “obvious” suspect for salmonellosis—particularly if made with raw eggs*—would not be on anyone's short list for O157 suspects.

RECOGNIZING THE OUTBREAK

Beginning in March, the outbreak transpired in the usual way: cases popping up like little mushrooms around the country—one here, one there—with nothing to suggest a cluster until pulsed-field gel electrophoresis subtyping reports from public health labs began trickling in. PFGE is the national standard for molecular subtyping of enteric bacteria. Although often referred to as molecular “fingerprinting,” molecular “tissue typing” captures better the subtlety of the situation: some patterns are very rare, and some patterns are common. What we can now call the cookie dough pattern is one of the common ones, having shown up in both outbreak and sporadic cases for years.

Recognizing an anomaly is harder when the background rate is high, and fingering the source is harder when some of your cases aren't really part of the cluster. The technical term for this is “misclassification,” and it can happen when cases aren't classified correctly. In the instant outbreak, it took a newer DNA sequence-based method, MLVA,† to sort the wheat from the chaff. That

* not the case with the Nestlé products, by the way

† It is admittedly bad form to use an acronym without first spelling it out, but due to the space limitations inherent in this format, we are cutting this corner with apologies to our readers. Those interested in a fuller explanation are invited to explore details online.

method is not widely available, causing delays as isolates were forwarded to CDC for sub-subtyping.

INVESTIGATION CONTROVERSY

Following the typical pattern, early cases were interviewed (or not) with a hodge-podge of questionnaires depending on the whim of the state or county where they happened to reside. A fraction of these questionnaires were collected and sifted for common exposure.

There is an ongoing national discussion about how best to approach this phase of an investigation, generally referred to as hypothesis generation. It's a little like the old parable of the blind men feeling up an elephant: everybody wants to get their hand in, but the experience just isn't the same for everyone. The obvious question “Why doesn't everyone just use the same questionnaire?” turns out to have many answers, not least of which is that no one has a questionnaire that everyone likes, and no one has data about what kind of questionnaire works best. Using a single questionnaire does make it easy to pool data and should reduce interviewer bias. That's swell, but it isn't the whole story. Interviews are best done by people with experience and access to all the other interviews done to date. Ideally, one person does them all, making it possible to pursue hints that may stretch the call-and-response rhythm of a long questionnaire. That may be feasible when there are only a handful of cases, all in the same jurisdiction, but as outbreaks expand reality intrudes.

Debate often centers on the form of the questionnaire(s): whether to use “open-ended” questions (“What did you eat for breakfast on May 3rd?”, “What kind of snack foods do you eat?”) or more structured “closed” questions (“Did you eat any blueberries, any strawberries, any blackberries? Did you handle a Chia Pet®?”). Overall we favor more closed designs. Experience suggests that the ability to recog-



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nize is better than the ability to recall, yielding a more complete history, and closed questionnaires are certainly much easier to merge into a common data set. That said, the dichotomy is often overblown: no decent questionnaire is all open or all closed, and different styles work better or worse depending on circumstances. Regardless of the style, any questionnaire involves compromises. Time and patience are limited, and the potential universe of questions is not. You can't ask about everything.

COOKIE DOUGH FINGERED

Oregon's Shotgun™ questionnaire* did include a question about consumption of raw cookie dough,[†] but this questionnaire was used for only one interview nationwide.[‡] It would be self-serving to speculate how much faster the source could have been identified had everyone been using that questionnaire nationally. What *did* solve the mystery was a series of free-form interrogations of four patients in one state. These four had cookie baking (and dough tasting) in common, and this "coincidence" was quickly corroborated by re-interviews of cases around the country—virtually none of whom had previously been asked the question. The single documented Oregon case in the cluster, with onset on May 5, confessed to dough consumption during a public health visit to her home.

Regardless of the questionnaire(s) used, interview data must be merged to find common exposures (e.g., food items) among cases. At the end of the day, it boils down to how many ate the bagged spinach and how many didn't. Epidemiologists need a shared lexicon in order

to pool results. A common questionnaire is one way to achieve that, but common questions on different questionnaires can also be merged, sidestepping the issue of whose questionnaire is best for whom and under which circumstances. We in Oregon have been working to develop a "data dictionary" for food exposures that offers at least a partial solution to the Babel of existing approaches. A shared dictionary would make it feasible to quickly compare apples and oranges (and hundreds of other items) with comparison data from control interviews or known or estimated background rates. Thus, even if the Oregon questionnaire asks about 400 foods and state X asks about 125, we should at least be able to pool data for the 115 items common to both. More data means more statistical power, which can translate to a more rapid identification of the source.

By the next morning, many cases had been re-contacted, and something like 20/24 cases reported eating raw commercial cookie dough in the week before onset. Coincidence? Not likely. Even assuming some ridiculously high background rate—for example, 25% of people eating raw dough each week—the likelihood of getting 20/24 by chance is < 0.00000001 . A quickie case-control study was done to satisfy armchair epidemiologist critics, but the result was a foregone conclusion. The real question was whether the astronomical statistical association could be attributed to anything other than causation. In brief, no.

RESPONSE

Apprised of the situation, Nestlé promptly pulled the plug on America's leading brand of prepackaged cookie dough. As of this writing, 74 outbreak cases have been identified from 32 states.

Ten days later, Nestlé announced that O157:H7 had been cultured from a leftover package of cookie dough manufactured in February. In an odd twist, the dough isolate is *not* a PFGE match to the case isolates. To date, it has not been determined *how* the cookie dough became contaminated: not just once but on multiple occasions or even continuously over a period of at least 7 weeks.[§] An orgy of product and ingredient testing and record review continues at the Virginia plant and its suppliers'.

PUBLIC HEALTH INADEQUACIES

The biggest impediment to effective outbreak investigation is rarely questionnaire design, communication breakdown, reporting delay, or misclassification. Rather, the rate-limiting step is finding people with the time and energy to investigate at all. Making good questionnaires, tracking people down, interviewing them (often multiple times), collecting records, analyzing data: these all take training, experience, and time. In many jurisdictions, resources are scant. Outbreak investigation is but one of many health department activities, and budgets are always finite.

The urgency of investigations can dissipate as requests for interviews are relayed from agency to agency and person to person until what could take minutes or hours takes days or weeks. In many multistate investigations, interview data may be available for fewer than half of the cases. No, the real scandal of outbreak investigation is not the erroneous implication of an innocent product—which is extremely rare—but the outbreaks that drag on for weeks or months due to feckless efforts, and the clusters that are never investigated at all.

[§] based on production dates for containers recovered from case's homes.

* www.oregon.gov/DHS/ph/acd/keene.shtml

[†] although the context was concern about raw eggs

[‡] and that case said "yes" to cookie dough