Outbreak of Shiga Toxin-Producing *Escherichia coli* O157 Infection Associated with a Restaurant

San Francisco County, California – August 2013

SUMMARY OF INVESTIGATION AND OUTBREAK RESPONSE

Between Friday, August 23 and Monday, August 26, 2013, the San Francisco Department of Public Health Communicable Disease Control Unit (SFDPH CDCU) received eight reports of laboratory-confirmed *Escherichia coli* (*E. coli*) O157 infection in unrelated San Francisco residents. This number of reports represented a marked increase over the background incidence of *E. coli* 0157 in San Francisco of less than 1 case per month. The eight reports were received from three clinical laboratories. Case-patient residences were geographically dispersed throughout San Francisco but suggested moderate to high socioeconomic status. CDCU initiated standard follow-up interviews with all case-patients. While no common exposures or demographic characteristics were immediately apparent, cases tended to be younger, salad-eating, local-market shoppers.

On August 26, SFDPH requested assistance from the California Emerging Infections Program (CEIP), and an investigation was initiated to ascertain the source of infections and prevent further illnesses. The California Department of Public Health Microbial Diseases Laboratory (MDL) was asked to prioritize Pulse-Field Gel Electrophoresis (PFGE) testing of *E. coli* isolates from San Francisco and the surrounding counties. On August 28, 2013, a Health Alert was sent to local clinicians notifying them of the observed increase in cases, recommending increased testing for symptomatic patients, reminding them of the reporting requirement, and requesting forwarding of *E. coli* 0157 isolates to the SFDPH Public Health Laboratory.

Case-patients were re-interviewed with a detailed hypothesis-generating questionnaire. The hypothesis-generating questionnaire identified a common restaurant and dates of exposure: Burma Superstar restaurant on August 16 and 17. On August 30, a joint press release was issued by SFDPH and Burma Superstar in order to inform the public and assist in case finding. A total of 22 confirmed and probable case-patients were identified. A case-control study and a dining group level cohort study were initiated to identify suspect food items. A garlic noodle dish was strongly associated with illness, but the specific ingredient causing disease was not identified. An environmental investigation resulted in recommendations for the restaurant that included improved handwashing and food handling, as well as a requirement for Food Safety training. Although the outbreak was self-limited, lessons learned from this response may improve SFDPH's response to future similar events.

METHODS

Epidemiologic investigation

Case definitions Used for Analysis:
Case definitions were finalized subsequent to identification of the outbreak strain by PFGE and Multiple Locus Variable-number tandem repeat Analysis (MLVA).

Confirmed:
A confirmed case was defined as *E.coli* O157 infection with XbaI pattern EXHX01.0124/ EXHA26.0332 (referred to as MLVA pattern A) in a San Francisco resident or visitor to San Francisco with illness onset between August 16, 2013 and September 5, 2013.
Probable:
A probable case was defined as *E. coli* O157 infection or Shiga toxin-positive stool in a San Francisco resident or visitor to San Francisco with illness onset between August 16, 2013 and September 5, 2013; or a patient with diarrheal illness (defined as 3 or more loose stools in a 24 hour period) who was epidemiologically-linked to a confirmed case; or a patient with diarrheal illness or hemolytic-uremic syndrome (HUS) who ate food purchased from Burma Superstar on August 16 or 17, 2013.
Suspect:
During the outbreak investigation, a suspect case was defined as a San Francisco resident or visitor to San Francisco with acute diarrheal illness including bloody diarrhea with an onset between August 16, 2013 and September 5, 2013, with pending laboratory studies, or with *E. coli* 0157 disease but a non-outbreak MLVA or PFGE pattern.

Case finding:
Cases were identified via Confidential Morbidity Report (CMR) to SFDPH-CDCU, standard laboratory reporting to CEIP surveillance officers, and active search of the California Reportable Disease Information Exchange (CalREDIE). Additional cases were identified via self-report or physician-report to SFDPH-CDCU or SFDPH Environmental Health, or were identified via other known ill contacts.

Case interviews:
Cases were interviewed using a standardized hypothesis-generating questionnaire (Appendix 1) which collected basic demographic and clinical information and a 72-hour food history. For specific food items of interest (lettuce, other leafy greens, fresh tomatoes, strawberries, cantaloupe, beef) identified through standard follow-up interviews, purchase location, date, and brand/type was collected. Case-patients were also questioned regarding farmer's market, grocery store, and restaurant exposures, including restaurants named by other case-patients. The questionnaire concluded with a "shot-gun" list of 164 common food items.

Statistical methods and analytic approach:
A common restaurant and dates of exposure (Burma Superstar restaurant on August 16 and 17) were identified among three case-patients during hypothesis-generating interviews. A case-control study to identify suspect food items was promptly initiated. Anyone who ate at Burma Superstar and met the definition of a confirmed, probable or suspect case was eligible for inclusion in the study as a case. Controls consisted of non-ill meal companions identified by cases; five individuals who were initially identified as controls reported symptoms and were reclassified as cases. Cases and controls were interviewed using a standardized questionnaire (Appendix 2) which collected information on clinical characteristics, date and time of the purchase of the suspect meal, whether patrons ate in the restaurant or picked up the food for take-out, and specific food items consumed. Descriptive statistics

were performed using Microsoft Excel 2007. Case-control and dining group study data were entered into a Microsoft Access 2007 database and analyzed using SAS 9.3.

Binomial probabilities were used to assess the likelihood that a particular food item was associated with illness. All case-patient dining groups were included in this analysis and a background consumption rate was estimated from restaurant records of the number of menu items sold on August 16 and 17. Binomial p-values were calculated comparing the proportion of case-patient dining groups who consumed a menu item to the background consumption rate. Saturday-specific and takeout-specific p-values were also calculated.

Restaurant management provided register receipts for all food purchases on Saturday, August 17. A dining group-level cohort study was conducted among Saturday case-patients. A dining group was defined as a group of persons who consumed a meal and shared a single check at Burma Superstar (either take-out or dine-in) on August 16 or 17. Case-patient dining groups contained at least one case (confirmed or probable). Unaffected dining groups consisted of all remaining dining groups among whom no illnesses were reported. Attack rates, relative risk, and chi-square p-values were calculated.

Environmental Investigation

Once Burma Superstar was identified as a potential exposure site for the outbreak, Environmental Health Inspectors from the San Francisco Environmental Health Food Safety Program began an on-site investigation on August 29.   The environmental investigation included interviews with the restaurant's owner, manager and staff, an onsite inspection with issuance of an inspection report enumerating violations and required corrections, observation of preparation of key menu items such as garlic noodles, and review of pertinent documentation. Documentation reviewed included food safety certification, employee work schedules from August 16-18, the employee sick leave log, and a list of menu items sold on the dates of potential exposure. The restaurant closed voluntarily from August 31-September 1, 2013.

All 31 Burma Superstar employees who worked August 16, 17, or 18 were interviewed (in English, Mandarin, Cantones, Spanish, or Burmese). One stool sample was obtained from each employee. Invoices were obtained for produce items sold to the restaurant during the dates of potential exposure, in order to facilitate trace back of suspect raw garnish items. Once interviews were conducted with individuals who tested positive for the *E. coli* outbreak strain but who did not eat at Burma Superstar, additional restaurants and retail vendors were identified as potential sources of exposure. CEIP staff investigated whether a wholesale produce vendor that supplied Burma Superstar may also have supplied these facilities with common produce items.

Laboratory Investigation

SFDPH-CDCU, CDPH, and CEIP staff followed-up with laboratories and medical providers to ensure specimens from potential cases were forwarded to the appropriate local Public Health Laboratory for confirmation; confirmed isolates were sent to the Microbial Diseases Laboratory (MDL) for PFGE and

MLVA. In addition, SFDPH Public Health Laboratory performed cultures of 31 stool specimens provided by employees of the suspect restaurant to determine if any of them were potentially infectious.

RESULTS

Epidemiologic Investigation

Twenty-six case-patients were identified, with 13 meeting the confirmed case definition, 9 meeting the probable case definition and 4 meeting the suspect case definition. Of the nine probable cases, five were dining partners of confirmed cases who reported diarrhea when interviewed for the case-control study; two had antibiotic exposure prior to stool collection, were culture negative and later developed HUS; two had bloody diarrhea after eating at the suspect restaurant but no stool was collected. The four suspect cases were determined to have PFGE and MLVA patterns that were different from the outbreak strain and were excluded from the final analysis. Of the 22 confirmed and probable cases, 20 (91%) reported eating at Burma Superstar on August 16 or 17, 2013. Thirteen were San Francisco County residents, six were residents of neighboring health jurisdictions, and three were out-of-state residents.

The epidemic curve is depicted in Figure 1. Diarrhea onset dates ranged from August 18 to August 24. The peak of illness onset (August 19) corresponds with the expected incubation period for *E. coli* following an exposure on August 16 or 17. Among those eating food purchased from Burma Superstar, median incubation period was 3 days (range, 1 to 6 days); median duration of illness was 5 days (range 2 to 12 days). Two confirmed cases with an illness onset of August 23 and 24 may have been secondary to a household contact; however, both ate the suspect meal as well.

Basic demographic and clinical information was available for all 22 confirmed and probable case-patients. Median age of case-patients was 29 years (range 1-66); 55% were female.   Clinical characteristics are summarized in Table 1. Overall, seven (32%) were hospitalized and four (18%) developed HUS (Table 1). No deaths occurred. Common symptoms included diarrhea (100%), bloody diarrhea (77%), abdominal cramps (82%), and fever (32%). Six case-patients received antibiotics, two of whom developed HUS. Additionally, one household contact of a confirmed case developed diarrhea on September 12, 2013 and was hospitalized with HUS. The patient's stool specimen grew *E. coli* O157 matching the outbreak PFGE pattern. This individual likely was a secondary case, but did not meet the formal case definition because of a late date of illness onset and is not included in this analysis.

Case-control study results:
The initial 13 case-patients identified 27 well meal companions for Burma Superstar meals on August 16 and 17; 22 were reachable for control interview. Of these, 55% (12/22) reported gastrointestinal symptoms following the suspect meal and were ineligible as controls. One ultimately met the confirmed case definition; five met the probable case definition; six were excluded from the case control study because they had mild symptoms or were symptomatic prior to the suspect meal.

Nineteen of 20 case-patients who ate at Burma Superstar and 10 controls completed the interview. Results of the case-control study are summarized in Table 2. Sixty-eight percent (13/19) of cases ordered take-out. Seventy-four percent (14/19) of cases consumed garlic noodles, a dish that involves raw

garnishes of scallions and cucumbers, but 70% of controls also ate the dish. Because meals were shared family-style with most persons tasting some of every dish, cases and controls reported very similar food item intake. No single menu item was found to be statistically significantly associated with illness by the case-control study.

Dining-group level analysis:

The dining group binomial analysis is presented in Table 3. The 19 interviewed cases (confirmed and probable) represented 12 case-patient dining groups, 8 of which dined on August 17. Fifty-eight percent (7/12) ordered takeout. The background prevalence of ordering takeout among all dining groups was 25% (54/217) (binomial P value=0.013; Table 3). Sixty-seven percent (8/12) of case-patient dining groups ordered garlic noodles compared to 10% (21/217) of all dining groups (binomial P value p<0.000).

Among those who dined on Saturday, August 17, 63% (5/8) of case-patient dining groups ordered take-out compared to 23% (49/209) of unaffected dining groups (P= 0.021). Sixty-three percent (5/8) of case-patient dining groups ordered garlic noodles compared to 8% (14/209) of unaffected dining groups (p<0.0001). Other items commonly consumed by cases were not significantly associated with illness. For example, the Tea Leaf Salad was ordered by 58% (5/8) of case-patient dining groups and 64% (134/209) of control dining groups (p=0.687). Nearly all case-patient dining groups ordered a dish containing raw scallions.

Food specific attack rates for the August 17 are summarized in Table 4. The attack rate among dining groups eating garlic noodles on August 17 was 24% compared to 2% among those not ordering garlic noodles (RR=15.6, p<0.000). The attack rate was also high among groups ordering sesame chicken (25%), however all these groups also ordered garlic noodles. Groups ordering takeout were five times more likely to develop illness (p=0.036) and groups ordering garlic eggplant, a dish containing raw scallions, were six times more likely to develop illness (p=0.072).

Environmental Investigation

The environmental investigation of Burma Superstar revealed the need for formal Food Safety training, as well as several violations that could have resulted in contamination or cross-contamination of food items. These violations included inadequate handwashing practices and inadequate sink facilities. Employees generally worked in all areas of the restaurant and prepared dine-in and take-out meals. A single food handler prepared the garlic noodle dish, however additional employees added the raw garnishes prior to serving. All food handlers denied illness or knowledge of illness among coworkers and residents in their personal household(s). Invoices obtained by Environmental Health did not reveal any common produce items between Burma Superstar and the markets/restaurants frequented by the two confirmed cases who did not eat at Burma Superstar. Trace-back of produce items did not reveal a source of infection/contamination.

Laboratory Investigation

E. coli O157 (presumed H7) was isolated from 17 of 26 case-patients. Thirteen isolates had the PFGE pattern combination EXHX01.0124/EXHA26.0332, the outbreak strain. All 13 isolates also had MVLA

pattern A. Four suspect cases had different PFGE patterns and were determined to not be associated with the outbreak. Stool specimens from three probable cases were culture negative for *E. coli*, presumably due to antibiotic exposure prior to specimen collection.

Each of the 31 food workers submitted one valid stool specimen for testing. All 31 food worker stool specimens were culture negative for *E. coli* 0157.

DISCUSSION

E. coli 0157 is present in the feces of cattle, and is spread to other food items such as meat and produce by direct contamination of food or water, irrigation, and cross-contamination of food items.[1] Person-to-person spread by the fecal-oral route is also common, due to the low infectious dose. The most common transmission route for *E. coli* 0157 outbreaks in the United States is foodborne, with beef and various raw produce items being the most commonly associated foods. An epidemiologic study of *E. coli* 0157 outbreaks in the United States from 1982-2002 revealed that produce-related outbreaks occurring in restaurants were associated with cross-contamination approximately half the time. The remainder involved produce that was contaminated before its arrival at the restaurant.[2]

The etiologic agent of the current outbreak was *E. coli* 0157 with PFGE pattern EXHX01.0124/EXHA26.0332 (MLVA pattern A). The outbreak involved 13 confirmed cases and 9 probable cases with illness onset between August 18 and August 23, 2013. Epidemiologic investigation revealed the point source of the outbreak to be Burma Superstar restaurant, with 20 out of 22 case-patients dining in the restaurant on either August 16 or 17. The risk of illness among dining groups ordering garlic noodles on August 17 was 15 times the risk among groups who did not order garlic noodles, strongly implicating the dish as the cause of illness. The specific ingredient of the noodle dish that may have contained *E. coli* was not definitively identified, though raw garnishes were suspected. Environmental investigation revealed hand washing violations and potential cross-contamination but no ill food handlers. The increased risk of illness among those ordering takeout could not be definitively explained.

Potential routes of transmission for this outbreak included cross-contamination of food on the restaurant premises, or at a wholesale food facility that supplied the restaurant. However, trace back of produce items did not conclusively lead to a source of infection/contamination, a common outcome in this sort of outbreak investigation. Testing of employees also did not reveal a food worker infected with *E. coli* 0157; however, testing occurred approximately two weeks after the exposure date, and a potentially ill or shedding employee may have already recovered by the time the stool sample was collected.

Strengths of the epidemiologic investigation include the relatively prompt identification of Burma Superstar as the source of the outbreak based on a hypothesis-generating questionnaire, and detailed subsequent interviews that allowed for case-control analyses of specific menu items. The principal limitation of the epidemiologic investigation was its relatively small sample size, which made findings of statistical significance less likely. In addition, a case-control study using well meal companions is less well-suited to an investigation of a "family-style" restaurant, where all dining companions are likely to

sample the same dishes. This limitation was overcome by the addition of a dining group-level analysis and a cohort study using register receipts

Strengths of the environmental investigation include the detailed inspection and thorough observation of food handling practices at the restaurant during repeated visits over a period of several weeks. The environmental investigation was limited by the relatively short exposure period (two days) and the lag time before case-patient stool culture results became available and the outbreak was identified. Because of this lag time, a potential source of cross-contamination or a potentially ill food handler may no longer have been present at the time the restaurant was inspected.

RECOMMENDATIONS

This *E. coli* 0157 outbreak was self-limited, with exposures and subsequent illness onsets occurring during an approximately one-week period in August 2013. Although the outbreak came to public health attention rapidly, and epidemiologic and environmental investigations were initiated promptly, the resulting control measures are not likely to have influenced the course of the outbreak. Nonetheless, the Environmental Health investigation of Burma Superstar revealed several violations that may have contributed to the outbreak, and their correction may lead to prevention of future food-borne illnesses due to cross-contamination and other factors. Resulting requirements for the restaurant include installation of separate handwashing and food preparation sinks, improved routine handwashing and sanitizing by staff, and managers' participation in formal Food Safety training. The association of HUS with receiving antibiotics that was observed in this outbreak has been well-documented elsewhere;[3] if a clinician Health Alert is produced for a future *E. coli* 0157 outbreak, the recommendation to refrain from prescribing antibiotics if *E. coli* 0157 is suspected should be included.

Several actions taken by SFDPH and the CEIP during this outbreak may have contributed to the success of the investigation, and may be useful strategies in future outbreaks. The prompt issuing of a Health Alert for community providers may have enhanced case finding, allowing for a more robust epidemiologic investigation and the exclusion of affected individuals from sensitive occupations or settings. The active engagement of the Health Officer in the outbreak response, including making a site visit to the Burma Superstar restaurant, promoted a collaborative relationship between the restaurant and SFDPH. This cooperation facilitated voluntary closure of the restaurant for several days, as well as facilitating interviewing of employees and the availability of register receipts and invoices for epidemiologic and environmental investigations. Finally, the surge capacity and expertise provided by CEIP to CDCU was invaluable at all stages of the outbreak response.

REFERENCES

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2 Rangel JM, Sparling PH, Crowe C, Griffin PM, Swerdlow DL. Epidemiology of *Escherichia coli* O157:H7 outbreaks, United States, 1982–2002. *Emerging Infectious Diseases* 2005; 11: 603-609.

3 Wong CS, Mooney JC, Brandt JR, Staples AO, Jelacic S, Boster DR, Watkins SL, Tarr PI. Risk factors for the Hemolytic Uremic Syndrome in children infected with Escherichia coli O157:H7: a multivariable analysis. *Clinical Infectious Diseases* 2012; 55: 33-41.

FIGURES

Figure 1: Epidemiological Curve

Epidemiological Curve: Foodborne Outbreak of *E. coli* O157 associated with Burma Superstar Restaurant, August 2013, San Francisco
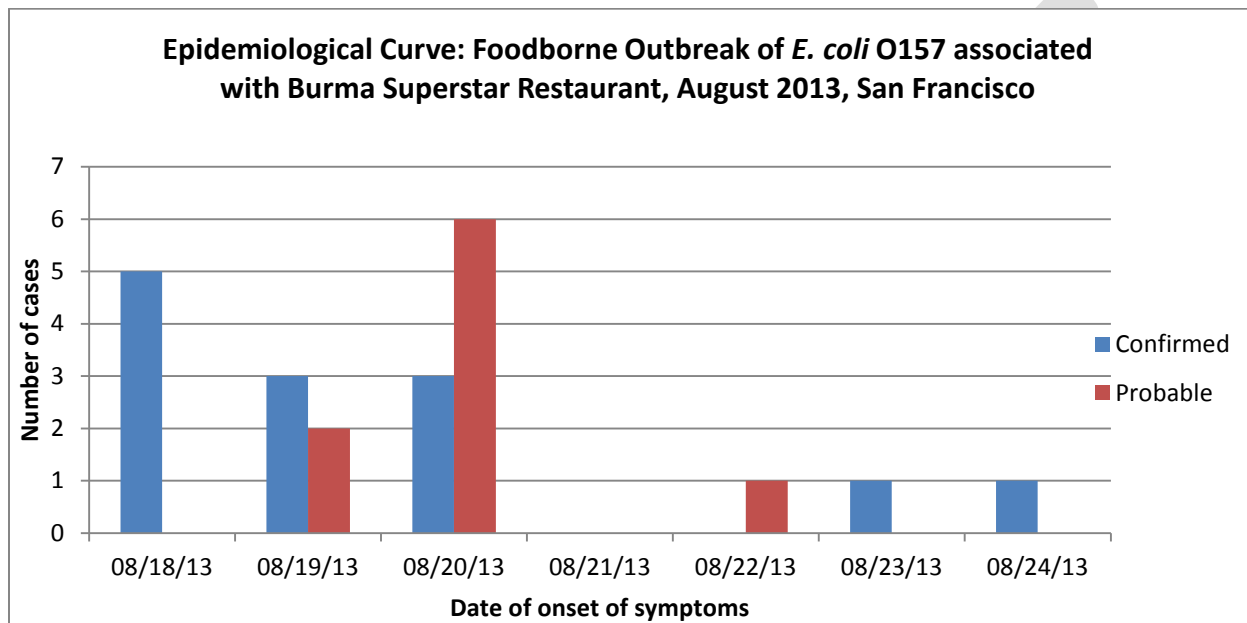
Table 1: Clinical characteristics of confirmed and probable cases (n=22)

Clinical characteristics	N	%
Diarrhea	22	100.0
Abdominal Cramps	18	81.8
Bloody Diarrhea	17	77.3
Fever	7	31.8
Hospitalization	7	31.8
Antibiotics	5	22.7
Hemolytic-uremic syndrome (HUS)	4	18.1
HUS and received antibiotics	2	9.1

Table 2: Meal companion case-control study: menu items consumed (Case/control definitions are final definitions after reclassification.)

Menu Item	Cases (N=19)		Controls (N=10)		OR (95% CI)	Chi-square P value
	N	%	N	%		
Any noodle	17	89	7	70	3.64 (0.50 - 26.76)	0.187
Garlic noodle	14	74	7	70	1.20 (0.22 – 6.53)	0.832
Any salad	15	79	7	70	1.61 (0.28 – 9.20)	0.593
Tea leaf salad	13	68	6	60	1.44 (0.29 – 7.10)	0.650
Any rice	10	56	8	80	0.31 (0.05 – 1.94)	0.196
Coconut rice	8	42	6	60	0.49 (0.10 – 2.31)	0.359

Table 3: Dining group binomial analysis: food items ordered

	Case-patient Dining Groups			All restaurant dining groups				Binomial P value		
	All (n=12)	Saturday Only (n=8)	Take-out only (n=7)	Saturday (n=217)	Friday (n=226)	Dine-in (Saturday) (n=163)	Takeout (Saturday) (n=54)	All[a]	Saturday Groups only	Takeout groups only
Take-out	58.3%	62.5%	100.0%	24.9%	N/A	0.0%	100.0%	0.034	0.021	N/A
Garlic Noodles	66.7%	62.5%	57.0%	9.7%	6.2%	9.8%	9.3%	0.000	0.000	0.002
Tea Leaf Salad[b]	58.3%	62.5%	50.0%	64.1%	55.8%	65.6%	59.3%	0.951	0.687	0.810
Sesame Chicken	25.0%	25.0%	43.0%	3.7%	8.0%	1.8%	9.3%	0.075	0.033[c]	0.021[c]
Coconut rice	50.0%	50.0%	43.0%	61.3%	N/A	63.2%	55.6%	0.935	0.846	0.854
Garlic Eggplant	16.7%	25.0%	29.0%	5.1%	3.5%	3.7%	9.3%	0.658	0.059	0.133
Samusa Soup	8.3%	0.0%	13.0%	18.4%	14.6%	21.5%	9.3%	0.930	1.000	0.540

[a] P values in this column calculated using the most conservative prevalence estimate

[b] Tea Leaf Salad "maybe" responses (n=2) are not included as "Yes"

[c] All case-patient dining groups ordering sesame chicken also ordered garlic noodles

Table 4: Saturday, August 17th dining group-level cohort study: attack rates of suspect foods

	Number of dining groups that ordered food item			Number of dining groups that did not order food item				
	Ill	Total	Attack rate (%)	Ill	Total	Attack rate (%)	RR	p-value
Take-out	5	54	9.26	3	163	1.84	5.03	0.036
Garlic Noodles	5	21	23.81	3	196	1.53	15.56	0.000
Garlic Eggplant	2	11	18.18	6	206	2.91	6.24	0.072
Tea Leaf Salad	5	139	3.60	3	78	3.85	0.94	1.000
Sesame Chicken	2	8	25.00	6	209	2.87	8.71	0.021
Coconut rice	4	132	3.03	4	85	4.71	0.64	0.073