Clinical Infectious Diseases

SUPPLEMENT ARTICLE

The Epidemiology of Foodborne Botulism Outbreaks: A Systematic Review

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Background. We performed a systematic review of foodborne botulism outbreaks to describe their clinical aspects and descriptive epidemiology in order to inform public health response strategies.

Methods. We searched seven databases for reports of foodborne botulism outbreaks published in English from database inception to May 2015. We summarized descriptive characteristics and analyzed differences in exposure and toxin types by geographic region. We performed logistic regression to assess correlations between exposure source, implicated food, and outbreak size.

Results. There were 197 outbreaks reported between 1920 and 2014. The median number of cases per outbreak was 3 (range 2–97). The majority of reported outbreaks (109; 55%) occurred in the United States. Toxin types A, B, E, and F were identified as the causative agent in 34%, 16%, 17%, and 1% of outbreaks, respectively. The median duration between exposure and symptom onset was approximately 1 day. The mean percentage of cases requiring mechanical ventilation per outbreak was 34%. Seventy percent of all outbreaks and 77% of small outbreaks (≤11 cases) originated from point source exposures, while commercial foods were significantly (odds ratio, 6.9; 95% confidence interval, 2.2–21.1) associated with large outbreaks (≥12 cases).

Conclusions. Toxin type A accounted for half of outbreaks, and these outbreaks had a higher proportion of patient ventilatory failure. Most outbreaks were due to point source exposures, while outbreaks due to commercial food were larger. For effective responses to foodborne botulism outbreaks, these findings demonstrate the need for timely outbreak investigation and hospital surge capacity.

Keywords. botulism; foodborne outbreaks.

Foodborne botulism is a potentially fatal illness caused by consumption of food contaminated with neurotoxins produced by *Clostridium botulinum* and, rarely, by related species. Of the known types of botulinum toxin, types A, B, E, and F cause most human disease and deaths [1]. While outbreaks have been reported worldwide, characteristics of botulism outbreaks have never been systematically studied. A better understanding of the characteristics of outbreaks can assist with planning for future botulism events.

Current understanding of the epidemiology of a botulism outbreak relies on limited data from very few reports [2–4]. We performed a systematic review of worldwide foodborne botulism outbreaks published in the English literature. The purpose of the review was to describe the demographic characteristics; types of food sources and toxin types; clinical characteristics including adverse outcomes; time between exposure, symptom onset, and adverse outcomes; and outbreak duration. An improved understanding of the characteristics of botulism outbreaks can help inform clinicians and public health officials in their preparations for botulism events.

METHODS

Data Sources and Search Strategy

We searched Embase DIALOG, Embase OVID, Global Health OVID, Cochrane Library, CINAHL EBSCO, Scopus, and Medline OVID from database inception to May 2015 to identify indexed publications in the English literature using the following search terms: ["botulism," "botulinum toxin," or "*Clostridium botulinum*"]. The search strategy was developed with the assistance of an expert systematic review librarian (Centers for Disease Control and Prevention library). We also performed a hand-search of archived *Morbidity and Mortality Weekly Reports* articles and reviewed any additional articles identified by botulism subject matter experts and manuscript reviewers (Figure 1).

Study Selection

We defined an outbreak as at least 2 cases of author-reported foodborne botulism with an epidemiologic link to the same

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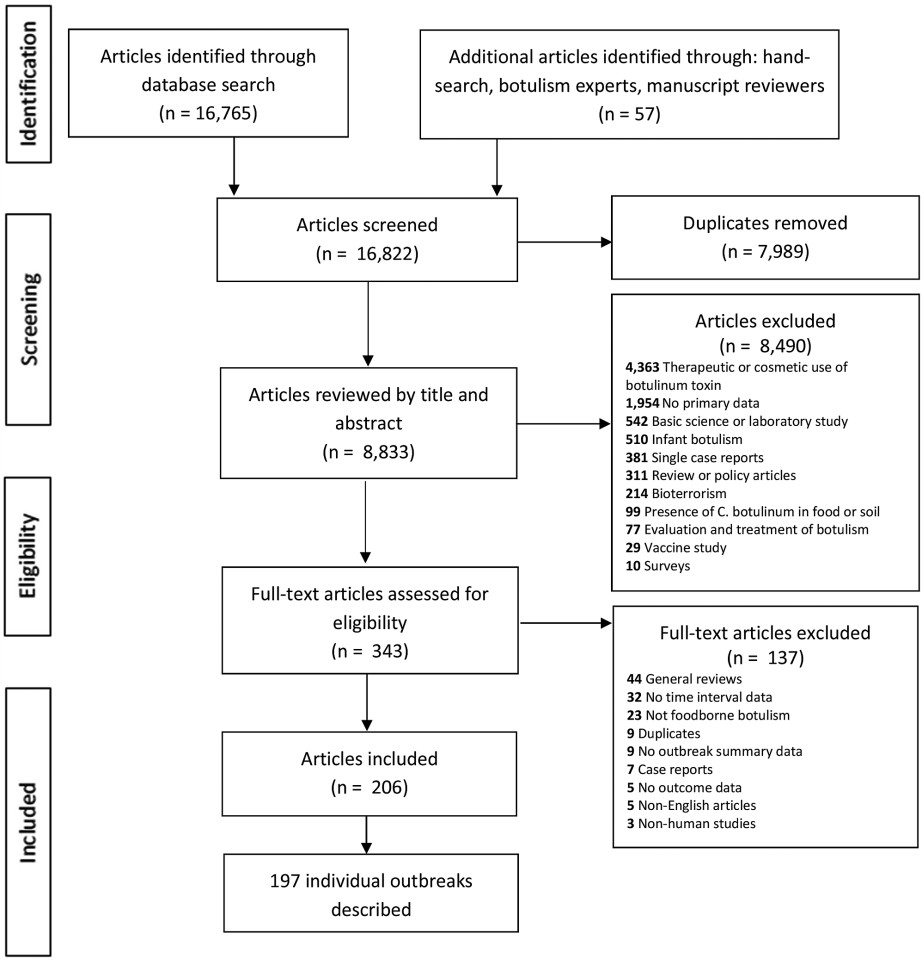

Figure 1. Flow diagram of article selection.

food. Three reviewers (D. M. D., K. C. S., and S. F. D.) screened all titles and abstracts and conducted full text reviews for those that reported data on human cases of botulism and contained clinical or epidemiologic data on botulism outbreaks or did not contain information in the abstract to assess article content. Inclusion was limited to published reports in the English language. We excluded duplicate reports, reports related to nonfoodborne botulism outbreaks, and general reviews of foodborne outbreaks. Outbreaks deemed eligible must also have been based on articles that provided at least 1 outbreak time interval and case outcome. Data abstraction was conducted in duplicate and recorded in Excel and Access databases (Microsoft, Richmond, Washington).

Data Abstracted

For outbreaks in the review, we included author-reported total number of case-patients, irrespective of whether classic botulism symptoms or signs (cranial nerve palsy with or without descending weakness or paralysis) [5] were reported. When information was available, we identified cases with classic botulism symptoms who met criteria for laboratory-confirmed foodborne botulism (defined as patient's clinical specimens yielding *C. botulinum* or its toxin or if toxin was detected in the food consumed) [5]. Because case definitions varied among these author-reported outbreaks, we performed a subgroup analysis limited to laboratory-confirmed outbreaks that involved case-patients who had symptoms clinically compatible (ie, those consistent with cranial nerve palsy with or without descending weakness or paralysis) with botulism to assess the validity of our overall findings.

The number of cases per outbreak was dichotomized, using the 90th percentile as the cutoff to define outbreak size, as small (≤11 cases) or large (≥12 cases). For outbreaks that spanned multiple countries, the country from which the exposure originated was used for tabulation purposes. When a study reported a range of hours or days for a certain time interval (eg, "16–20 hours," or "1–2 days"), the maximum value was used. "Time to symptom onset" referred to the onset of any symptom or sign following exposure. Point source outbreaks were defined as outbreaks caused by a single food consumed

by all outbreak case-patients at a single time point. In contrast, intermittent common source outbreaks involved consumption of the implicated food by outbreak case-patients over a period of time. Where applicable, we classified suspected foods as "commercial products" or "noncommercial products." Commercial products were defined as those prepared for sale or distribution by a business or restaurant. "Home-canned foods" were defined as noncommercial foods preserved at home using cans or jars. Noncanned, noncommercial foods prepared for individual or personal consumption in a noncommercial setting were grouped as "other noncommercial products." Food sources were considered confirmed sources of an outbreak only when botulinum toxin was detected in the food [5]. Outbreaks were considered laboratory confirmed when at least 1 case-patient or the food source was laboratory confirmed. Toxin type was extracted from reports when available.

Data elements extracted included case demographics; clinical features; botulinum testing results; type of exposure; number of case-patients hospitalized, administered antitoxin, mechanically ventilated, or who died; clinical time intervals, including exposure to symptom onset, exposure to admission, and exposure to death; type of antitoxin administered; and dates of first and last exposure, symptom onset, and hospitalization. Data elements were extracted as available. Due to the limited amount of data reported by authors, we were unable to abstract information about comorbid conditions in a systematic manner. Data abstracted were independently reviewed by multiple reviewers. Discrepancies between reviewers were adjudicated through group discussion.

Quality Appraisal

Quality of the literature used was determined using a modified Newcastle-Ottawa scale adapted for this topic [6] and involved assigning a score from 0–9 (see Supplementary Materials 2).

Analytical Methods

Exposure source, implicated foods, and toxin type were compared across geographic locations, as were differences in exposure source and implicated food by outbreak size. Mortality was compared between outbreaks in which all case-patients received antitoxin matching the outbreak-associated toxin type vs outbreaks in which no case-patients received matching antitoxin. Bivariate analyses were restricted to outbreaks with complete data on the variables assessed.

The median time intervals for case-patients and mean proportions (hospitalizations, mechanical ventilations, deaths, and administrations of matching antitoxin) from each outbreak were abstracted or derived by reviewers from available data. For outcomes listed above, proportions are reported as means. As the data regarding time were skewed, time intervals are reported as medians of medians, with interquartile range of medians, similar to reported outbreak time intervals for other infectious diseases [7]. Primary analyses included all case-patients, regardless of clinical presentation or laboratory confirmation. Our subanalysis was restricted to laboratory-confirmed outbreaks that involved only case-patients whose clinical presentation was compatible with botulism. Comparisons between categorical variables were performed using χ^2 or Fisher exact tests. Differences between continuous variables were assessed using either Mann-Whitney *U* test or Kruskal-Wallis with Dunn's test. We built 3 logistic regression models to estimate the probability of a large outbreak as a function of exposure source, food type, or both. We combined home-canned and other noncommercial foods into a single category for comparison to commercial foods for our regression analysis. The reference groups used in the logistic models were noncommercial foods and point source exposures. All analyses were done using SAS 9.4 (SAS Institute Inc., Cary, North Carolina) or Stata 12 (College Park, Texas).

RESULTS

Search Results

Database and hand searches identified 16 822 publications of which 343 were selected for full text review (Figure 1). A total of 206 publications met the inclusion criteria and described 197 outbreaks of foodborne botulism (Supplementary Materials 1).

General Outbreak Characteristics

The 197 eligible outbreaks included 1367 individual case-patients. The median number of case-patients per outbreak was 3, with a range of 2–97 (Figure 2). Among outbreaks with date available, 183 were reported between 1920 and 2014. For the 114 outbreaks where the age of case-patients was reported, the median age per outbreak ranged from 6.5 to 78.5 years, with 74 (38%) outbreaks involving at least 1 pediatric patient (age <18 years) and 3 (1.5%) outbreaks reporting a case during pregnancy. Alternative diagnoses were considered and reported for 54 outbreaks. The most common alternative diagnoses reported in these outbreaks, for at least 1 case-patient, were viral infections (26%), myasthenia gravis (23%), and cerebrovascular events (19%). Eighty-six (44%) outbreaks were laboratory confirmed and involved only cases (n = 523) with clinically compatible botulism. A total of 13 asymptomatic case-patients were reported; 4 of these individuals were laboratory confirmed by detection of *C. botulinum* (n = 3) or toxin (n = 1) in stool.

Seventy percent of outbreaks were due to a point source exposure (n = 138); the most common food (n = 83, 42%) was a home-canned product (Table 1). In 6% of outbreaks, the contaminated food was unknown. Toxin type A was reported in 34% of outbreaks, followed by type E (17%) and type B (16%; Table 1). Two outbreaks caused by toxin type F from *Clostridium baratii* were reported, 1 in France and 1 in Spain. In 64 (32%) outbreaks, the toxin type was not determined or not reported (Table 1). Among the subgroup of 86 laboratory-confirmed outbreaks describing

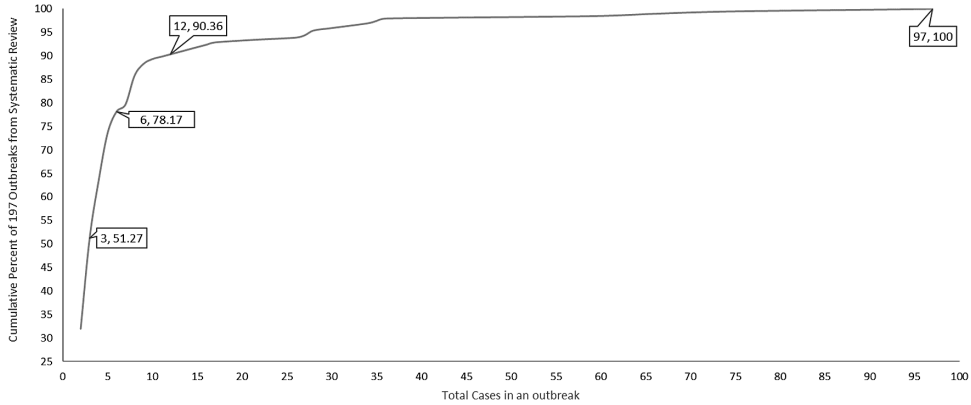

Figure 2. Total cases per outbreak by cumulative percentage of outbreaks.

only clinically compatible case-patients, 74% were due to a point source exposure and 40% involved a home-canned food. Toxin type was known for 94% of these outbreaks, with type A the reported cause of 54% followed by type B (23%) and type E (21%; data not shown).

Outbreak Comparisons by Geographic Location

Outbreaks were reported from 27 countries, with 109 (55%) occurring in the United States and 29 (15%) in Canada; the remainder were in Europe (n = 25, 13%), Asia (n = 22, 11%), Africa (n = 6, 3%), Australia (n = 3, 2%), and 1 each in New

Table 1. Characteristics of Foodborne Botulism Outbreaks Reported Worldwide

	All Outbreaks and All Case-Patients (N = 197)		Laboratory-Confirmed Outbreaks With Clinically Compatible Case-Patients (N = 86)	
Characteristic	Outbreaks, n (%)	Cases, n (%)	Outbreaks, n (%)	Cases, n (%)
Total	197 (100)	1367 (100)	86 (100)	523 (100)
Number of cases	NA	3 (2–97)[a]	NA	3 (2–97)[a]
Median age (y)	NA	33 (6.5–78.5)[a]	NA	38 (6.5–78.5)[a]
% Male	NA	50 (0–100)[a]	NA	50 (0–100)[a]
Location				
United States	109 (55)	578 (42)	50 (58)	238 (46)
Canada	29 (15)	135 (10)	10 (12)	27 (5)
Europe	25 (13)	155 (11)	11 (13)	43 (8)
Asia	22 (11)	326 (24)	10 (12)	94 (18)
Africa	6 (3)	124 (9)	5 (6)	121 (23)
Other	6 (3)	49 (4)	0 (0)	0 (0)
Exposure source				
Point	138 (70)	722 (53)	64 (74)	347 (66)
Intermittent common	47 (24)	595 (44)	21 (24)	171 (33)
Unclear	12 (6)	50 (4)	1 (1)	5 (1)
Food vehicle type				
Commercial	52 (26)	698 (51)	21 (24)	211 (40)
Noncommercial: home canned	83 (42)	354 (26)	34 (40)	159 (30)
Noncommercial: other	50 (25)	248 (18)	25 (29)	135 (26)
Unclear	12 (6)	67 (5)	6 (7)	18 (3)
Laboratory evidence				
Suspected food vehicle	92 (47)	563 (41)	7 (8)	20 (4)
Confirmed food vehicle	105 (53)	804 (59)	79 (92)	503 (96)
Toxin type				
A	66 (34)	475 (35)	44 (51)	193 (37)
B	31 (16)	273 (20)	19 (22)	113 (22)
E	34 (17)	344 (25)	17 (20)	198 (38)
F	2 (1)	7 (0)	1 (1)	2 (0)
Unclear	64 (32)	268 (20)	5 (6)	17 (3)

Abbreviation: NA, not applicable.
[a]Median and range are reported.

Zealand, Argentina, and Greenland. Three outbreaks involved more than 1 country; all involved commercially distributed products. There was a significant difference ($P < .001$) in the type of food associated with outbreaks geographically (Table 2). Compared with the United States, in which other noncommercial foods accounted for only 18 (17%) of 109 outbreaks, these foods were more commonly implicated in Canadian outbreaks (16/29, 55%) and African outbreaks (4/6, 67%). Commercial products were more commonly implicated in Europe (16/25, 64%) and Asia (7/22, 32%) than in the United States (21/109, 19%). Toxin type, when identified, significantly varied by region (overall $P < .001$). Toxin type A was the most frequent cause of outbreaks in the United States (46/109, 42%) and Asia (6/22, 27%), type E in Canada (13/29, 45%), and type B in Europe (6/25, 24%; Table 2).

Similar trends were observed for the subset of laboratory-confirmed outbreaks with clinically compatible case-patients. Fifty (58%) occurred in the United States, 10 (12%) in Canada, 11 (13%) in Europe, 10 (12%) in Asia, and 5 (6%) in Africa. Of the 50 US outbreaks, 58% were associated with home-canned foods. In Europe, commercial products were most frequently implicated when compared to the United States (64% vs 15%, $P < .001$). Toxin type A was responsible for 58% of outbreaks in the United States, 45% in Europe, and 50% in Asia, while 50% of Canadian outbreaks were caused by toxin type E (data not shown).

Outbreak Comparisons by Outbreak Size and Exposure Type

A total of 177 (90%) outbreaks were small (≤11 cases) and 20 (10%) were large (≥12 cases); exposure information was available for 155 small and 19 large outbreaks (Table 3). Most of the small outbreaks originated from point source exposures. Among small outbreaks, 81% of point source exposures were associated with home-canned or other noncommercially processed foods; for large outbreaks, 50% of point source exposures were associated with home-canned or other noncommercially processed foods. In univariate analyses, intermittent common source exposure and commercial foods were both significantly associated with large outbreaks. In the multiple logistic regression model, only commercial food vehicles remained significantly associated with large outbreaks (odds ratio, 6.87; 95% confidence interval, 2.23–21.11; Table 3).

The median number of days for symptom onset between the first and last case-patient was <1 (range, <1–6 days) for point source outbreaks (Figure 3) and 5 (range, 1–62 days) for intermittent common source outbreaks ($P < .0001$). Similar findings were observed in our subset of laboratory-confirmed outbreaks with clinically compatible case-patients (data not shown).

Hospital Admission, Mechanical Ventilation, and Death by Toxin Type and Outbreak Size

Fatalities were reported in 115 (58%) outbreaks. The mean percentage of deaths per outbreak was 31.4% (standard deviation [SD], 34.7%).

Table 2. Characteristics of Foodborne Botulism Outbreaks by Geographic Region

Characteristic	United States (N = 109)	Canada (N = 29)	Europe (N = 25)	Asia (N = 22)	Africa (N = 6)	Across All Regions *P* Value (Test)
Range of years	1920–2012	1934–2012	1922–2014	1937–2013	1959–2008	
Median number of cases (range)	3 (2–59)	3 (2–36)	5 (2–28)	5 (2–75)	5 (3–97)	.012 (KW)
P value[a]	Reference	0.882	0.331	0.003	0.065	
Exposure source, n (%)						.847 (exact)
Point	76 (70)	22 (76)	18 (72)	16 (73)	4 (67)	
Intermittent Common	27 (25)	6 (21)	6 (24)	3 (14)	2 (33)	
Unclear	6 (6)	1 (4)	1 (4)	3 (14)	0 (0)	
Food vehicle type, n (%)						<.001 (exact)
Commercial	21 (19)	4 (14)	16 (64)	7 (32)	1 (17)	
Noncommercial: home canned	66 (61)	8 (28)	3 (12)	6 (27)	0 (0)	
Noncommercial: other	18 (17)	16 (55)	4 (16)	5 (23)	4 (67)	
Unclear	4 (4)	1 (4)	2 (8)	4 (18)	1 (17)	
P value[b]	Reference	<0.001	<0.001	0.008	0.003	
Toxin type, n (%)						<.001 (exact)
A	46 (42)	4 (14)	6 (24)	6 (27)	2 (33)	
B	15 (14)	3 (10)	6 (24)	4 (18)	2 (33)	
E	12 (11)	13 (45)	4 (16)	3 (14)	1 (17)	
F	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	
Unclear	36 (33)	9 (31)	7 (28)	9 (41)	1 (17)	
P value[c]	Reference	<0.001	0.015	0.480	0.431	

Abbreviation: KW, Kruskal-Wallis test.

[a]Mann-Whitney *U* test using the United States as the reference.

[b]Fisher exact test using the United States as the reference.

[c]Fisher exact text using the United States as the reference and unknown toxin types excluded.

Table 3. Characteristics of Foodborne Botulism Outbreaks by Size

	Smaller (n = 155)		Larger (n = 19)	
Characteristic	Point Source	Intermittent Common Source	Point Source	Intermittent Common Source
Food vehicle type				
Commercial	23 (19)	14 (39)	4 (50)	10 (91)
Noncommercial: home canned	62 (52)	11 (31)	2 (25)	1 (9)
Noncommercial: other	34 (29)	11 (31)	2 (25)	0 (0)
Total	119 (100)	36 (100)	8 (100)	11 (100)
	Odds ratio (95% confidence interval)			
Logistic model (ref = smaller outbreaks)	**Model 1**[a]		**Model 2**[b]	**Model 3**[c]
Commercial vs noncommercial[d]	**9.43 (3.19–27.87)**		N/A	**6.87 (2.23–21.11)**
Intermittent common vs point source	N/A		**4.38 (1.69–11.39)**	2.77 (0.96–8.00)

Abbreviation: N/A, not applicable.

Outbreak size was categorized as smaller, 2–11 cases and larger, ≥12 cases. Figures in bold are statistically significant.

[a]Food type (ref group noncommercial): probability of larger outbreak = $1/1+e^{-\alpha+\beta1(\text{food type})}$.

[b]Exposure source (ref group point source: probability of larger outbreak = $1/1+e^{-\alpha+\beta1(\text{exposure source})}$.

[c]Both food type and exposure source: probability of larger outbreak = $1/1+e^{-\alpha+\beta1(\text{food type})+\beta2(\text{exposure source})}$.

[d]Home-canned and other noncommercial foods were grouped together into a single noncommercial category.

The incubation period was statistically significantly shorter in toxin type E outbreaks (median, 0.8 days; interquartile range [IQR], 0.4–1.0) compared to toxin type A outbreaks (median, 1.0 days; IQR, 1.0–2.0) and toxin type B outbreaks (median, 1.0 days; IQR, 1.0–2.0; $P < .001$; Table 4). There were no significant differences in terms of mean percentage of hospital admissions between toxin types A, B, and E outbreaks (Table 4). The mean percentage of cases supported with mechanical ventilation was significantly higher in toxin type A outbreaks (43.6%; SD, 34.6%) compared to toxin type B outbreaks (24.5%; SD, 27.8%; $P = .034$), but no significant differences were noted for mean percentage of mechanically ventilated cases comparing either toxin type A or B outbreaks to toxin type E outbreaks. Compared to toxin type B outbreaks, toxin type E outbreaks had a shorter exposure to death interval (median, 1.7 days vs 6 days; $P = .006$), as well as a higher mean number of deaths per outbreak (2.4 vs 0.6; $P = .014$; Table 4). The interval from exposure to death and the mean percentage of deaths were not significantly different between toxin type A and toxin type E outbreaks. The absolute numbers compared were small in the subanalysis of laboratory-confirmed outbreaks with only clinically compatible case-patients and, in most instances, did not reach statistically significant differences. The only significant difference was a shorter incubation period for type E outbreaks (median, 0.8 days; IQR, 0.5–1 days) compared to type A outbreaks (median, 1 day; IQR, 1–2 days; $P = .011$; Table 4).

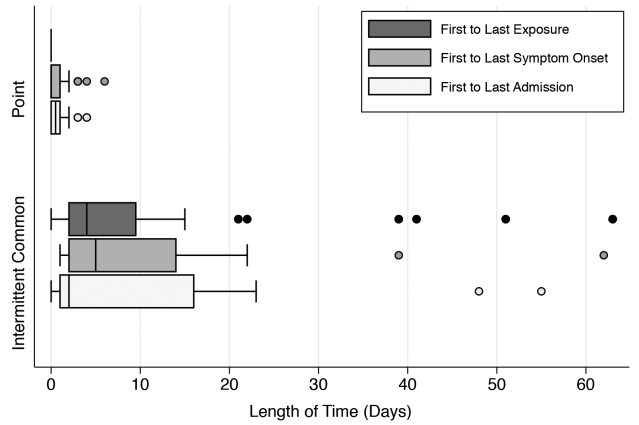

Figure 3. Outbreak duration by source type.

Similar proportions of case-patients were admitted regardless of outbreak size. The mean percentage of cases mechanically ventilated was 34.9% (SD, 34.9) for small outbreaks compared to 20.1% (SD, 14.7) for large outbreaks. The mean percentage of deaths was 33.5% (SD, 35.5) for small outbreaks and 12.8% (SD: 19.2) for large outbreaks. The mean number of deaths was 1.2 (SD, 1.5) for small outbreaks and 4.1 (SD, 5.8) for large outbreaks. These findings failed to reach statistical significance at the $P < .05$ level (Table 5). Similar trends were noted in the subanalysis (Table 5).

A lower percentage of deaths was observed overall for outbreaks in which all case-patients received matching antitoxin compared to those outbreaks where no matching antitoxin was administered (7.8% vs 53.9%; $P < .001$; Table 6). This overall difference was due, in part, to significantly lower percentages of death in outbreaks due to toxin type A and toxin type E, in which all cases received matching antitoxin. Subanalysis of laboratory-confirmed outbreaks with only clinically compatible case-patients also revealed a lower percentage of deaths for toxin type A outbreaks in which all cases received matching antitoxin (Table 6).

Table 4. Comparison of Events and Outcomes per Outbreak by Toxin Type

	All Outbreaks (N = 131)						*P* Value[b]			
	Type A	*N/n*[a]	Type B	*N/n*[a]	Type E	*N/n*[a]	Overall	A vs B	A vs E	B vs E
Median (IQR) exposure to symptom onset in days	1.0 (1.0–2.0)	38/256	1.0 (1.0–2.0)	22/220	0.8 (0.4–1.0)	29/160	<.001	NS	<0.001	<0.001
Mean (SD) % admitted	84.5 (27.0)	62/448	80.0 (30.4)	30/252	82.5 (25.5)	30/227	.577	N/A	N/A	N/A
Mean (SD) % mechanically ventilated	43.6 (34.6)	56/417	24.5 (27.8)	25/235	29.4 (31.7)	28/222	.036	0.034	NS	NS
Median (IQR) exposure to death in days	2.1 (1–6)	19/78	6.0 (6–8)	7/35	1.7 (1–2.4)	16/70	.015	NS	NS	0.006
Mean (SD) number of deaths	1.3 (2.1)	66/475	0.6 (1.1)	31/273	2.4 (4.3)	34/344	.026	NS	NS	0.014
Mean (SD) % died	28.9 (34.5)	66/475	16.7 (27.2)	31/273	32.1 (34.0)	34/344	.084	N/A	N/A	N/A
	Laboratory-Confirmed Outbreaks With Clinically Compatible Cases (N = 80)						*P* Value[b]			
	Type A	*N/n*[a]	Type B	*N/n*[a]	Type E	*N/n*[a]	Overall	A vs B	A vs E	B vs E
Median (IQR) exposure to symptom onset in days	1.0 (1.0–2.0)	25/115	1.0 (1.0–1.5)	15/101	0.8 (0.5–1.0)	16/101	.025	NS	0.011	NS
Mean (SD) % admitted	84.1 (28.0)	42/184	83.3 (29.7)	19/113	88.4 (18.0)	15/159	.994	N/A	N/A	N/A
Mean (SD) % mechanically ventilated	43.0 (34.9)	39/177	27.1 (30.0)	16/104	46.1 (32.5)	14/157	.233	N/A	N/A	N/A
Median (IQR) exposure to death in days	2.1 (1.5–6.5)	15/57	6.5 (3–8)	6/14	2.3 (1–5)	7/35	.291	N/A	N/A	N/A
Mean (SD) number of deaths	1.4 (1.7)	44/193	0.5 (0.7)	19/113	2.5 (4.6)	17/198	.062	N/A	N/A	N/A
Mean (SD) % died	33.6 (36.2)	44/193	21.1 (30.9)	19/113	26.6 (27.6)	17/198	.302	N/A	N/A	N/A

Abbreviations: IQR, interquartile range; N/A, not applicable; NS, not significant; SD, standard deviation.

[a] *N/n*: number of outbreaks for which data were available over the total number of cases reported in those outbreaks.

[b] Kruskal-Wallis with Dunn's test used to compare means and medians across toxin types.

Quality Appraisal Results

Outbreak reports were scored between 1 and 7, with a mean score of 5 (Supplementary Materials 2).

DISCUSSION

Our study highlights key characteristics of foodborne botulism outbreaks that can inform clinicians and public health officials in

Table 5. Comparison of Events and Outcomes per Outbreak by Outbreak Size

	Outbreak Size: All Outbreaks				
Events and outcomes	Smaller	*N/n*[a]	Larger	*N/n*[a]	*P* Value[b]
Median (IQR) exposure to admission in days	2.0 (1.1–3.8)	92/295	1.8 (1–4.8)	4/99	.719
Mean (SD) % admitted	82.5 (29.3)	162/624	84.1 (16.9)	16/537	.112
Mean (SD) % mechanically ventilated	34.9 (34.9)	139/544	20.1 (14.7)	15/511	.304
Median (IQR) exposure to death in days	3.0 (1.5–6.5)	69/242	6 (2–6)	3/64	.602
Mean (SD) number of deaths	1.2 (1.5)	177/683	4.1 (5.8)	20/684	.110
Mean (SD) % died	33.5 (35.5)	177/683	12.8 (19.2)	20/684	.070
	Laboratory-Confirmed Outbreaks With Clinically Compatible Cases				
	Smaller	*N/n*[a]	Larger	*N/n*[a]	*P* Value[b]
Median (IQR) exposure to admission in days	2.0 (1.5–3)	45/134	1.0 (1-1)	2/29	.078
Mean (SD) % admitted	84.2 (27.4)	77/277	88.6 (11.8)	5/198	.271
Mean (SD) % mechanically ventilated	40.9 (34.4)	70/259	21.2 (14.6)	5/198	.249
Median (IQR) exposure to death in days	2.5 (1.5–7)	30/99	N/A	1/17	N/A
Mean (SD) number of deaths	1.1 (1.5)	80/290	5.7 (6.9)	6/233	.074
Mean (SD) % died	30.3 (34.1)	80/290	14.8 (12.5)	6/233	.510

Abbreviations: IQR, interquartile range; SD, standard deviation.

[a] *N/n:* number of outbreaks for which data were available over the total number of cases reported in those outbreaks.

[b] Mann-Whitney *U* test used.

Table 6. Associations Between Mortality, Antitoxin Administration, and Toxin Type

	All Outbreaks				
Mean (SD) % Died	No Cases Confirmed Receiving Matching Antitoxin	*N/n*[a]	All Cases Confirmed Receiving Matching Antitoxin	*N/n*[a]	*P* Value[b]
All outbreaks	53.9 (38.9)	44/175	7.8 (16.9)	33/200	<.001
Toxin type A	74.4 (32.3)	9/49	7.5 (15.8)	21/153	<.001
Toxin type B	33.3 (40.8)	6/23	8.3 (20.4)	6/27	.211
Toxin type E	58.3 (42.0)	10/33	10.0 (22.4)	5/18	.035
	Laboratory-Confirmed Outbreaks With Clinically Compatible Cases				
Mean (SD) % died	No Cases Confirmed Receiving Matching Antitoxin	*N/n*[a]	All Cases Confirmed Receiving Matching Antitoxin	*N/n*[a]	*P* Value[b]
All outbreaks	54.3 (41.2)	20/85	10.3 (19.5)	23/85	<.001
Toxin type A	74.4 (32.3)	9/49	9.2 (18.0)	15/59	<.001
Toxin type B	37.5 (47.9)	4/12	12.5 (25.0)	4/14	.405
Toxin type E	45.8 (41.7)	4/11	16.7 (28.9)	3/10	.354

Abbreviation: SD, standard deviation.

[a] *N/n*: number of outbreaks over the number of cases for which data were available.

[b] Mann-Whitney *U* test used to compare outbreaks where antitoxin matching the implicated toxin type was administered and outbreaks where no matching antitoxin was administered.

the development of preparedness and response plans. We found that point source outbreaks were the most common type of exposure source, although intermittent common sources still caused nearly a quarter of outbreaks. As expected, outbreak duration was significantly longer for intermittent common source outbreaks and longer still for those due to a commercial food. However, it is worth noting that for some point source outbreaks, the time from exposure to symptom onset or admission spanned several days. This is an important observation because when there is an outbreak with an unknown exposure, clinicians and public health officials should anticipate that cases may continue presenting for several days after the index case presents. Diverse food types were noted, suggesting that multiple food sources can serve as a conduit for botulism. This is consistent with an extensive report of 65 years of human botulism by Meyer and Eddie [8]. Better understanding of the epidemiology of botulism outbreaks can help tailor local prevention and public health response strategies.

As previously reported [9–10], toxin type varied among geographic regions, likely reflecting different food preferences and availability. Outbreaks that involved toxin type E had the shortest median incubation period, and those that involved type A had the highest mean percentage of case-patients mechanically ventilated, consistent with previous reports [11]. Among all outbreaks, the lowest mean number of deaths was observed in toxin type B outbreaks, consistent with the usually milder clinical disease associated with this toxin type [11]. A significantly lower percentage of deaths was reported in outbreaks where all cases received appropriate antitoxin, which is similar to findings reported by others [12–14]. Recognizing the toxin types involved in regional outbreaks may be important for countries as they consider antitoxin sources and supplies.

This review is subject to certain limitations that may influence the generalizability of the findings. Most notably, this review is based on observational data. Our search strategy was restricted to only indexed English articles and therefore excluded outbreak reports that may have been published in other languages or were not indexed in referenced electronic databases. Further, because these outbreaks spanned nearly a century and occurred worldwide, substantial heterogeneity between outbreaks is to be expected, particularly with regard to differences in food preferences, methods of food preparation, the existence of food safety regulations, and access to the modern, intensive care often required for the clinical management of botulism. Data elements were incomplete in many reports, which limits the amount of data upon which to draw conclusions, such as whether medical comorbidities influenced outcomes. Additionally, the implicated toxin type was unknown in roughly a third of outbreaks; therefore, several of our analyses were restricted to only outbreaks where a specific toxin type had been identified.

Foodborne botulism outbreaks continue to be reported worldwide, and there is the potential for botulinum toxin to be used in an intentional bioterrorism event. The size and duration of outbreaks may vary depending on the type and sources of exposure, as well as whether an exposure is restricted to a focal geographic location or widely distributed. Clinicians and public health officials should consider these issues to proactively anticipate clinical resource management decisions, improve prevention strategies such as community outreach and messaging to reduce community-specific risk, and preparedness strategies such as antitoxin stockpiling and delivery. Ongoing surveillance and timely investigation of botulism outbreaks are critical to mitigate the public health impact of future botulism outbreaks.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of

the authors, so questions or comments should be addressed to the corresponding author.

Notes

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