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Julia Brennan Date

A Descriptive Analysis of Wound Botulism — United States, 1999–2014

By

Julia Brennan APN
Master of Public Health

Global Environmental Health

William Caudle PhD
Committee Chair

Kevin Chatham-Stephens MD MPH
Committee Member

Paige Tolbert PhD
Committee Member

A Descriptive Analysis of Wound Botulism — United States, 1999–2014

By

Julia Brennan APN

BSN
Villanova University
2000

MS
University of California, San Francisco
2007

Thesis Committee Chair: William Caudle PhD.
Thesis Committee Chair: Kevin Chatham-Stephens MD MPH

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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2017

Abstract

A Descriptive Analysis of Wound Botulism — United States, 1999–2014
By Julia Brennan APN

Abstract

Purpose The primary objective of this paper is to describe the clinical features and geographic distribution of laboratory-confirmed wound botulism cases in the United States from 1999–2014. The secondary objective is to evaluate predictors of mechanical ventilation in confirmed cases of wound botulism.
Methods Using all laboratory-confirmed wound botulism cases from 1999–2014 from CDC's National Botulism Surveillance database I characterized clinical features and geographic distribution of wound botulism cases. Using a Firth logistic regression model, I evaluated predictors of mechanical ventilation.
Results From 1999–2014, 366 cases of laboratory-confirmed wound botulism occurred in the United States. Of those, 350 reported injecting illicit drugs. All cases occurred within 12 states, the majority of which were on the West Coast; California had 309 (84.4%) cases. The covariates associated with mechanical ventilation were facial paralysis and shortness of breath.
Conclusions Wound botulism cases in the United States are increasing alongside heroin use. The majority of patients have symmetric and normal strength and symmetric deep tendon reflexes. Facial paralysis and shortness of breath are predictors for mechanical ventilation and can help identify patients who need intensive respiratory monitoring and rapid treatment with botulinum antitoxin.

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CDC disclaimer: The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Intro/Background and Significance

Botulism is a rare and potentially fatal illness caused by one of seven types of botulinum toxins (A, B, C, D, E, F and G) [1, 2]. These neurotoxins, which are some of the most potent known toxins, impair the release of the neurotransmitter acetylcholine at the neuromuscular junction. Botulinum toxin works by cleaving select vesicular and membrane bound proteins thereby inhibiting the nerve's ability to release acetylcholine into the synaptic gap [3]. Acetylcholine is the neurotransmitter responsible for muscle contraction; inhibiting it results in a rapidly progressive constellation of signs and symptoms, such as drooping eyelids, facial paralysis, slurred speech, and muscle weakness. In severe cases, paralysis can progress and impair the muscles required for respiration, resulting in respiratory failure requiring intubation or a tracheostomy and rarely death.

Botulism is most frequently caused by toxin from *Clostridium botulinum,* an anaerobic, gram-positive, spore-forming bacillus [1, 2, 4]. *Clostridium* spores, found naturally in soil, are heat-resistant and produce botulinum toxin when the spores are in an anaerobic, low acid (pH >4.6), and low salt environment [1]. Exposures to toxin leading to botulism occur through one of several known routes: ingestion of contaminated food, *in situ* colonization of a wound or intestinal tract with *C. botulinum*, or the therapeutic or cosmetic use of botulinum toxin. These exposures result in foodborne botulism, infant botulism, wound botulism, adult intestinal colonization, and iatrogenic botulism [1, 5, 6]. In 2014 the majority of botulism cases in the United States were infant (n=128, 80%) followed by wound (n=27, 10%), foodborne (n=20, 9%), and finally cases in which the exposure was unknown (n=2, 1%) [6, 7].

Wound botulism occurs when a wound is contaminated with *C. botulinum* and the conditions of the wound (anaerobic, low acid and low salt) allow for germination then production of botulinum toxin in the wound. Historically, injuries or traumatic wounds contaminated with soil were the most common cause of wound botulism. In the mid-1980s the main cause of wound botulism shifted from traumatic injuries to injection drugs [8]. Although injecting any type of illicit drug can be associated with wound botulism, heroin in general, and black tar heroin (BTH) specifically, has an association with wound botulism [9, 10].

Concurrent to the increase in drug-associated wound botulism cases, U.S. surveillance data indicated more people were using injection (intravenous and subcutaneous) heroin. In 2014 an estimated 914,000 people reported having used heroin in the previous year [11]. Additionally, between 2000 and 2010, the overall number of hospitalizations for skin and soft tissue infections doubled — more so in cities that have predominantly BTH, which had twice as many infections as other cities [12]. BTH and wound botulism have broadly similar geographic distributions. The majority of BTH sales and use occur west of the Mississippi River and the majority of wound botulism cases occur on the West Coast. Between 1951 and 1998, California reported 127 cases of wound botulism, and the rest of the United States combined reported less than a dozen cases [8, 10, 13]. Although the exact mechanism of contamination is unknown, personal habits like skin cleaning before injecting, needle exchange, and sharing paraphernalia are not associated with wound botulism [9, 10]. There is, however, a dose-response relationship between an increasing monthly dose of subcutaneous or intramuscular, but not intravenous, BTH and risk of wound botulism [10]. Additionally, BTH, thick and tarry in substance, is commonly associated with sclerosed veins and often leads to intramuscular and subcutaneous injecting rather than intravenous injection [9, 10]. Both intramuscular and subcutaneous injection are more likely to create anaerobic environments conducive to botulism germination.

Surveillance may underrepresent cases of injection drug-related wound botulism because presenting signs and symptoms for opioid overdose and botulism can look similar. Additionally, providers may not notify public health officials or request botulinum antitoxin for treatment [8, 10]. Given the large number of people using injection heroin and the increase in injection drug use (IDU)-related wound botulism, identifying and treating botulism quickly could reduce progression to mechanical ventilation and associated morbidity and mortality.

The primary objective of this paper is to describe the clinical features and geographic distribution of laboratory-confirmed wound botulism cases in the United States between 1999 and 2014. The secondary objective is to evaluate predictors of mechanical ventilation in laboratory-confirmed wound botulism cases.

Research methods

I analyzed all of the laboratory-confirmed wound botulism cases from 1999–2014 from CDC's National Botulism Surveillance database. Botulism is a nationally notifiable disease and passive surveillance is done by CDC's National Botulism Surveillance System. Data collection begins when a medical provider requests botulinum antitoxin from the CDC, California Department of Public Health (CDPH), or Alaska Department of Health and Social Services (ADHSS). CDC, CDPH, and ADHSS are the only three sources of botulinum antitoxin in the United States. Surveillance case report forms are completed by CDC staff when botulinum antitoxin is released to a medical provider. Information for the case report form, including demographics, clinical characteristics, and exposures (including IDU), is voluntarily reported to CDC by medical providers. All of the cases in this analysis were laboratory-confirmed by detecting botulinum toxin in serum or culturing *C. botulinum* from the wound [6].

I analyzed continuous data (age and time from symptom onset to hospital admission) using means and standard deviations and categorical data using frequencies and percentages (Table 1). Case report forms were used to collect dates for the onset of signs and symptoms, onset of neurologic symptoms, first visit to a provider, and admission to a hospital. I used the collected dates to calculate the median time from onset of symptoms to onset of neurologic symptoms, to seeing a provider, and to being admitted to the hospital. CDC staff categorize wound botulism cases into four wound botulism categories: injury-related, operative, drug-related and other. Wounds without an obvious cause or with more than one potential cause are categorized as other. I used descriptive data associated with the cases to re-categorize them into more specific categories when appropriate. I assessed geographic location of cases by state then analyzed cases following the distribution of BTH, which occurs west of the Mississippi River [8, 10]. Because cases have historically been concentrated in California, I evaluated case locations by California compared to not-California. Wound botulism rates by state were compared using 2010 U.S. census populations [14].

To assess annual number of cases and account for outbreaks, I calculated the median, Q1, Q3 and IQR. Proximal and distal upper and lower extremity strength measurements, reported by medical providers, were analyzed for symmetry. Strength was reported as 0–5 according to the Medical Research Council Scale: 0 (no evidence of contractility), 1 (slight contractility, no movement), 2 (full range of motion, gravity eliminated), 3 (full range of motion with gravity), 4 (full range of motion against gravity with some resistance) or 5 (full range of motion against gravity and full resistance). Symmetry was assessed by evaluating the right and left side measurements as a pair. Each patient potentially had four pairs: proximal upper extremity, distal upper extremity, proximal lower extremity, and distal lower extremity. Deep tendon reflex (DTR) measurements were assessed for symmetry and reflex strength. Symmetry was assessed by evaluating left side and right side measurements as pairs.

To address the hypothesis that covariates, such as ptosis, sex, and difficulty swallowing, were associated with mechanical ventilation, I used a Firth logistic regression model. Firth logistic regression allows for small response numbers. The variable mechanical ventilation was created as a measure of respiratory failure and severe disease by including any case that was intubated or had a tracheostomy. I assessed covariates for implausible values and missing data. Next, I assessed bivariate relationships with the covariates and the dependent variable mechanical ventilation, using chi square, Fisher's exact, or Firth logistic regression. I started with a saturated logistic model fit with sex, race, toxin type, and wound category (drug, operative, injury) and all significant covariates. I used backwards elimination to identify the best fitting model. Covariates with the highest *p* value were eliminated one at time until all covariates had significant *p* values ($p<0.05$).

All statistical analysis was done using SAS, version 9.3; an alpha level of 0.05 was used. All tests were two-sided test with 95% confidence intervals.

Results

There were 366 cases of laboratory-confirmed wound botulism in the United States between 1999 and 2014. Of the 366 laboratory-confirmed cases, 26 (7.1%) were not associated with the release of botulinum antitoxin from the CDC or CDPH to the provider and are limited to demographic information. The median age was 44.2 years (range 5–67 years). Of 366 cases, 280 (76.5%) were men, 130 (35.6%) were white, and 107 (29.2%) reported Hispanic ethnicity. Of the 366 cases, 348 (95.1%) were categorized as drug associated, 10 (2.7%) were due to injury, 1 (0.03%) was operative, and 7 (1.9%) were unknown (Figure 1). Of the 355 cases with a reported toxin type, type A was the predominate type (n=335, 91.5%) followed by type B (n=18, 4.9%), unknown type (n=9, 2.5%), and four (1.1%) cases that did not have enough serum submitted in their laboratory specimen to differentiate between type A, B or E (Table 1).

Of the 366 wound botulism cases, 348 (95.1%) were categorized as drug-related but 350 (95.6%) reported IDU. The median age for cases reporting IDU was 45 (range 21–67 years), six years older than the median age for non-IDU cases which was 39 (range 5–59). Data on type of substance injected and route of injection were reported for 78 cases. Of those, 57 (73.1%) used one drug, 16 (20.5%) used two types of drugs, 4 (5.1%) used three types of drugs, and 1 (1.3%) did not report which drug they used. Injecting BTH was reported by 60 (76.9%) patients, injecting other or unspecified heroin was reported by 30 (38.5%), injecting methamphetamine by 10 (12.8%), and injecting methadone by 1 (1.3%) patient. Selecting heroin was not mutually exclusive from BTH, so providers were able to report the use of both. Of the 60 cases who injected BTH, 27 people reported 1 route of injection, 13 patients reported 2 routes of injection, 3 patients reported using 3 routes, and 17 did not report how they injected. Of the 43 patients who reported how they injected BTH (some with multiple routes of injection) — over half (n=37, 86.0%) injected subcutaneously, 14 (32.6%) injected intramuscularly, and 11 (25.6%) injected intravenously. For drugs other than BTH, the route of injection was reported for 7 cases, 2 of whom reported injecting via two routes. Of the 7 non-BTH cases who reported how they injected (some with multiple routes of injection) — 5 (71.4%) injected subcutaneously, 2 (28.6%) injected intramuscularly, and 2 (28.6%) injected intravenously. Additionally, sniffing or snorting drugs was reported for 6 cases. The drugs snorted were methamphetamine (n=4), heroin (n=3), and cocaine (n=2); some cases did not indicate which drug they sniffed, and several indicated sniffing more than one type of drug. Two cases were re-categorized as injection drug-related cases based on information in memos to the CDC indicating both of these cases had evidence of injection drug use, track marks, and recent subcutaneous heroin use.

Wound location and characteristics were collected for 171 (46.7%) of the 366 cases. Wounds were identified in 142 (83.0%) of the 171 cases with wound data, and 134 (94.4%) of those were patients who reported IDU. Data on the condition of the wound was collected for 38 cases, 25 (65.8%) of those were described as infected. Of the 25 infected wounds, 23 (92%) also reported IDU. When wounds were identified (n=142), most were location unknown (n=72, 50.7%), on the upper and lower extremities (n=23, 16.2% and n=22, 15.5%, respectively), or in multiple areas (n=11, 7.8%). Other wound locations included buttocks (n=9, 6.3%), head and neck (n=2, 1.4%), mouth (n=2, 1.4%), and abdomen (n=1, 0.7%).

Median time from any symptom onset to the onset of neurologic symptoms was 0 days (n=55; range 0–3 days). Median time from symptom onset to seeing a provider was 1 day (n=137; range -12–7 days). When the cases who saw a provider prior to the onset of their symptoms were removed from the analysis (n=7), this interval remained 1 day (n=130; range 0–7 days). Data to assess the time from symptom onset to hospitalization was available for 139 cases. The median time was 1 day (range -12–7 days). Five patients were hospitalized prior to onset of symptoms for other conditions like fractures or injuries. When those five patients were removed the median time from symptom onset to hospital admission increased to 1.5 days (n=134).

Wound botulism cases were distributed among 12 states, with the majority of cases located in California (n=309, 84.4%) (Table 2). Drug-related cases remain the primary category regardless of the state the case occurred in (Figures 2 and 3). Of the 366 cases, 362 (98.9%) occurred west of the Mississippi River. West of the Mississippi River toxin type A was predominant (n=334, 92.3%) followed by toxin type B (n=15, 4.14%) and undetermined or unknown toxin type (n=13, 3.6%). East of the Mississippi River there were only 4 cases (1.1%) and those cases were predominantly toxin type B (n=3, 75%) followed by type A (n=1, 25%).

For all states, the median number of cases was 23 cases a year with an interquartile range of 11.5 cases (Q1=15.5, Q3=27). California alone had a median of 19.5 cases a year with an interquartile range of 6.5 cases a year (Q1=14, Q3=20.5). Figure 4 shows monthly cases by type of wound botulism. An increase in cases, only associated with drug-related wound botulism, is visible in July/August and November. Outbreaks occurred in August 2003, January 2003, December 2004, November 2008, and August 2011. Figure 4 shows the monthly variation without outbreaks.

Measurement pairs were available to assess proximal upper extremity strength and symmetry for 43 cases, 39 (90.7%) of which were symmetric. The majority of the 43 cases (right n=36, 83.7% and left n=35, 81.3%) with proximal upper extremity strength measurements were rated as 3, 4, or 5 (Table 3). Measurement pairs for distal upper extremity symmetry were available for 41 cases, 40 (97.56%) of which were symmetric. The majority of distal upper extremity measurements (right n=32, 75.6% and left n=34, 82.9%) were 4 or 5 (Table 3). Measurement pairs for proximal lower strength were available for 42 cases, 40 (95.2%) of which were symmetric. The majority of proximal lower extremity measures were 4 or 5 (right n= 31, 73.8% and left n=31, 73.8%) (Table 3). Measurement pairs for 34 cases were available for distal lower extremity strength, 33 (97.1%) of which were symmetric. Over 50% of distal lower extremity strength measures were strength 5 (right n=18, 51.4% and left n=18, 52.9%). There were 8 asymmetric measurement pairs: 4 proximal upper measures, 1 distal upper measurement, 2 proximal lower measures, and 1 distal lower measurement. Two patients accounted for 6 of those asymmetric measurements. The greatest side-to-side difference was from 3 to 5 for one patient’s proximal upper extremity measure. All other asymmetric measurements were one level different (from 3 to 4 or from 4 to 5).

Data were available to assess biceps/triceps reflexes for 23 pairs. Of those, 22 (95.7%) were symmetric. One case accounted for all of the asymmetric measures. Normal biceps/triceps reflexes were reported for 9 patients (37.5%) on the right side and 8 (34.8%) patients on the left side (Table 4). Brachial DTR symmetry was assessed for 23 cases. Of those cases, 22 (95.7%) were symmetric. Normal brachial reflexes were reported for 9 (39.1%) patients on the right side and 10 (43.5%) on the left side (Table 4). Patellar DTR symmetry was assessed for 25 cases, 24 (96%) of which were symmetric. Normal patellar reflexes were reported for 12 (48%) on the right side and 13 (53%) on the left side. Ankle DTR symmetry was assessed for 22 cases, and 21 (95.5%) were symmetric. Normal ankle DTRs were reported for 8 (36.4%) on the right side and 9 (40.9%) on the left side.

Intubation was required for 95 (26%) cases and tracheostomy was reported for 35 (9.6%) cases. In total, any type of mechanical ventilation was used for 105 (28.7%) cases. Of the 105 cases requiring mechanical ventilation, 102 (97.1%) were people who reported IDU. The average age for patients requiring mechanical ventilation was 44.3 years and 80 (76.2%) had identifiable wounds. Bivariate analysis showed that the following covariates had statistically significant relationships with mechanical ventilation: location in California (OR 0.35, CI 0.19-0.62, p= 0.0003), heroin injection (OR 3.4, CI 1.5-7.7, p=0.0037), methamphetamine injection (OR 4.7, CI 1.0-20.9, p=0.0451), facial paralysis (OR 2.2, CI 2.5-12.9, p=<0.0001), extraocular palsy (OR 2.5, CI 1.3–5.1, p=0.0095), shortness of breath (OR 5.2, CI 2.4–11.0, p<0.0001), impaired gag reflex (OR 2.2, CI 1.0–4.7, p=0.0434) and palatal weakness (OR 3.5, CI 1.5–8.4, p=0.0044) (Tables 5, 6 and 7). All significant covariates were included in the model with toxin type, sex, wound botulism category, and race. The final model showed facial paralysis (*p*=0.0042) and shortness of breath (*p*=0.0006) were predictive for mechanical intubation when holding race, sex, toxin type and wound category type constant.

Discussion

In this analysis, I described clinical features and geographic distribution for 366 laboratory-confirmed wound botulism cases from 1999–2014 from CDC's National Botulism Surveillance database. I found the number of wound botulism cases has increased; that facial paralysis and shortness of breath were predictive for mechanical ventilation; and that most confirmed wound botulism cases had symmetrically normal or near normal strength. The presence of these signs and symptoms in a patient who injects drugs can trigger early contact with the local or state public health department to request botulinum antitoxin. Furthermore, these signs and symptoms can help identify patients who need more intensive respiratory monitoring due to their risk for mechanical ventilation. Finally, these findings support the need to continue heroin prevention and harm reduction work and to identify the causal link between BTH and wound botulism.

Wound botulism cases continue to increase, which likely reflects an actual increase in cases, not surveillance artifact. The cases included in this analysis were all laboratory confirmed. The only change to the wound botulism case definition during the study timeframe was the addition of a probable case definition in 2011; however, I did not include probable cases in this analysis [15]. Additionally, botulism surveillance or reporting systems did not change during this timeframe. I considered education and increased awareness as a cause for the increased number of cases. However, California implemented a botulism campaign in 1995 targeted at people injecting drugs, methadone clinic staff, and Emergency Department providers but the number of cases in California increased at a similar rate to other states without education campaigns [10]. In the mid-

1980s, drug-associated wound botulism became, and continues to be, the leading cause of wound botulism [8]. In the mid-1990s the source regions for heroin in the United States shifted from Mexico and Asia to Mexico and Columbia resulting in widespread access to cheaper and more pure heroin [16]. This change has likely contributed to the steady increase in overall heroin use in the United States [8, 11, 12, 17]. Therefore, it is reasonable to conclude the increase in wound botulism cases continues to be driven by heroin, and we will continue to see the number of wound botulism cases increase as long as heroin use continues to rise.

Measuring upper and lower extremity strength and checking deep tendon reflexes are quick assessments which can be done in triage or emergency settings. With few exceptions, I found strength and DTR measurements were symmetric. Additionally, approximately half of the upper extremity strength measures and almost all of the lower extremity strength measures were normal or near normal (reported as 4 or 5 on the 5 point scale). Previous studies have reported extremity strength can be retained despite respiratory failure [18]. Therefore, assessing strength measurements and symmetry when a person presents with cranial nerve palsy can assist in identifying possible botulism cases. However, strength alone should not be used to gauge disease progression or severity.

Despite the increasing number of annual cases, wound botulism continues to be a rare illness which may suffer from under-reporting due to the rapid progression to respiratory failure, association with injection drug use, and the overlap the presenting signs and symptoms have with opioid overdose. Botulinum antitoxin, wound debridement, supportive care, and mechanical ventilation are the mainstays of treatment for wound botulism [2, 4]. Antibiotics, common in wound botulism treatment, are primarily aimed at treating the infected wound [4, 18]. Mechanical ventilation is initiated in wound botulism patients for a variety of reasons, including diaphragmatic and accessory muscle paralysis, pharyngeal muscle paralysis, and inability to manage secretions [2]. Wound botulism patients who require mechanical ventilation have longer hospital stays and longer recovery courses [19]. Botulinum antitoxin, available from the CDC by consultation with local or state public health departments, binds up circulating toxin and stops the progression of symptoms. Antitoxin also reduces the duration of mechanical ventilation and time to sustained recovery if received within 24 hours of symptom onset [20]. Botulism patients experience rapidly descending flaccid paralysis, masking the traditional signs and symptoms associated with respiratory failure like gasping, restlessness, or the use of accessory muscles [2]. Subsequently, traditional techniques for monitoring respiratory deterioration like pulse oximetry or monitoring signs and symptoms, are not effective. Instead, more intensive respiratory monitoring, like vital capacity, is indicated [2]. Therefore, it is important to differentiate wound botulism cases from opioid overdose patients so patients who need botulinum antitoxin are identified and receive appropriate respiratory and supportive care as quickly as possible.

Two previous studies examined predictors for mechanical ventilation. A study of 115 Thai patients with foodborne botulism found vomiting and any cranial nerve palsy and urinary retention or difficulty swallowing were predictive for mechanical ventilation [21]. While vomiting is a common presenting symptom in foodborne botulism, it is infrequently associated with wound botulism [1]. Because these findings are linked to a foodborne botulism outbreak their generalizability to wound botulism patients may be limited. Another study evaluated predictors for respiratory failure in 20 patients with drug-related wound botulism [19]. They found detectable toxin in the serum was associated with respiratory failure but did not find a significant relationship between signs or symptoms and respiratory failure [19]. In this analysis, I found facial paralysis and shortness of breath predicted mechanical ventilation in laboratory-confirmed wound botulism cases. This may differ from previous findings because of the sample size. These presenting signs and symptoms in a person who injects drugs can help identify them as a person who will benefit from the implementation of botulism appropriate respiratory monitoring and receiving botulinum antitoxin as quickly as possible.

There are a number of limitations with this study. First, surveillance captures a limited range of cases. Case report forms are only completed when botulinum antitoxin is sent to the patient, potentially missing cases for which antitoxin is not warranted, as in the case of improving signs or symptoms. Additionally, botulism rapidly progresses and can present similar signs and symptoms as opioid overdose. Therefore, it is possible a person may die from respiratory failure and the cause may be an assumed overdose without consideration of botulism. Surveillance also misses people with less severe symptoms who do not present for treatment, or when they do, do not prompt a call to the CDC for antitoxin. Another limitation of the study is missing data. For example, although the majority of cases were categorized as drug related, few case reports provided detailed data on the specific drugs used, the route of use, wound location, or wound characteristics, limiting the generalizability of the findings. Missing data may occur for several reasons — the sign or symptom was not present when the case report form was completed, the patient did not report the sign or symptom, or the sign or symptom was present but not reported on the case report form.

Conclusion

As the number of people injecting heroin has increased throughout the United States so has the number of wound botulism cases. Until we are able to identify how black tar heroin use can cause botulism, patients and providers will continue to rely on the rapid consideration and treatment of botulism to prevent illness progression and morbidity and mortality. The presence of cranial nerve palsies in a person who injects drugs should prompt the consideration of wound botulism.

Facial paralysis and shortness of breath should prompt the implementation of appropriate respiratory monitoring. Additionally, we may continue to see an increase in injection drug-related wound botulism moving forward, highlighting the need to 1) continue heroin use prevention and harm reduction efforts and 2) identify the link between BTH and wound botulism to prevent wound botulism cases.

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Tables and Figures

Table 1. Wound Botulism Cases — United States, 1999–2014 (N=366[a])

	n (%)
Sex	
Male	280 (76.5)
Female	86 (23.5)
Race	
Unknown	203 (55.5)
White (reference)	130 (35.5)
Black	21 (5.7)
American Indian/Alaska Native	10 (2.7)
Asian/ Pacific Islander	1 (0.3)
Other	1 (0.3)
Ethnicity	
Hispanic	107 (29.2)
Non-Hispanic (reference)	95 (26.0)
Unknown	164 (44.8)
Botulism toxin type	
A	335 (91.5)
B (reference)	18 (4.9)
Unknown	9 (2.5)
AB/ABE Undetermined	4 (1.1)
Wound Category	
Drug associated	348 (95.1)
Injury (reference)	10 (2.7)
Unknown	7 (1.9)
Operative	1 (0.3)
Injection drug use (IDU) n=365	350 (95.9)
Type of drug	
Heroin n=235	30 (12.8)
Black tar heroin n=72	60 (83.3)
Methamphetamine n=235	10 (4.3)
Location	
Case in California	309 (84.4)
Cases not in California	57 (15.6)
Respiratory Interventions	
Intubated	95 (26.0)
Tracheostomy	35 (9.6)
Mechanically ventilated	105 (28.7)

[a] Unless otherwise noted

Table 2. Distribution of Wound Botulism Cases by State — United States, 1999–2014 (N=366)

State	n (%)	2010 U.S. Census Population	Rate per 100,000
California	309 (84.4)	37,253,956	0.83
Washington	34 (9.3)	6,724,540	0.51
Texas	8 (2.2)	25,145,561	0.03
Oregon	4 (1.1)	3,831,074	0.10
Colorado	3 (0.8)	5,029,196	0.06
New Mexico	2 (0.6)	2,059,179	0.10
Arizona	1 (0.3)	6,392,017	0.02
Kansas	1 (0.3)	2,853,118	0.04
Maryland	1 (0.3)	5,773,552	0.02
Michigan	1 (0.3)	9,883,640	0.01
New York	1 (0.3)	19,378,102	0.01
Pennsylvania	1 (0.3)	12,702,379	0.01

Table 3. Extremity Strength Measurements in Wound Botulism Patients — United States, 1999–2014

	Proximal Upper Extremity n (%)		Distal Upper Extremity n (%)		Proximal Lower Extremity n (%)		Distal Lower Extremity n (%)	
	Right N=43	Left N=43	Right N=41	Left N=41	Right N=43	Left N=42	Right N=35	Left N=34
0:No contractility	2 (4.6)	2 (4.6)	-	-	3 (7.0)	3 (7.1)	1 (2.9)	1 (2.9)
1:Slight contractility	2 (4.6)	2 (4.6)	2 (4.9)	2 (4.9)	-	-	-	-
2:Full range of motion without gravity	4 (9.3)	4 (9.3)	1 (2.4)	1 (2.4)	2 (4.7)	2 (4.8)	2 (5.7)	2 (5.9)
3:Full range of motion with gravity	12 (27.9)	11 (25.6)	6 (14.6)	5 (12.2)	7 (16.3)	6 (14.3)	5 (14.3)	4 (11.8)
4:Full range of motion with gravity and some resistance	12 (27.9)	13 (30.2)	16 (39.0)	17 (41.5)	14 (32.6)	15 (35.7)	9 (25.7)	9 (26.5)
5:Full range of motion with gravity and full resistance	11 (25.6)	11 (25.6)	16 (39.0)	16 (39.0)	17 (39.5)	16 (38.1)	18 (51.4)	18 (52.9)

Table 4. Deep Tendon Reflex Measurements in Wound Botulism Patients — United States, 1999–2014.

	Biceps/Triceps n (%)		Brachial n (%)		Patellar n (%)		Ankle n (%)	
	Right N=24	Left N=23	Right N=23	Left N=23	Right N=25	Left N=25	Right N=22	Left N=22
0:No response	4 (16.7)	3 (13.0)	5 (21.7)	4 (17.4)	4 (16)	3 (12)	4 (18.2)	4 (19.2)
1:Sluggish or diminished	8 (33.3)	8 (34.8)	6 (26.1)	6 (26.1)	5 (20)	5 (20)	5 (22.7)	5 (22.7)
2:Expected response	9 (37.5)	8 (34.8)	9 (39.1)	10 (43.5)	12 (48)	13 (52)	8 (36.4)	9 (40.9)
3:More brisk, slightly hyperactive	-	1 (4.4)	-	-	1 (4)	1 (4)	2 (9.1)	1 (4.6)
4: Brisk, hyperactive	3 (12.5)	3 (13.0)	3 (13.0)	3 (13.0)	3 (12)	3 (12)	3 (13.6)	3 (13.6)

Table 5. Signs and Symptoms in Wound Botulism Patients — United States, 1999–2014 (N=366)

	n (%)
Neck weakness	133 (36.3)
Difficulty swallowing	130 (35.5)
Drooping eye lids	122 (33.3)
Slurring speech	117 (32.0)
Diplopia	109 (29.8)
Shortness of breath	87 (23.8)
Extra ocular palsy	80 (21.9)
Thick tongue sensation	74 (20.2)
Change in voice	74 (20.2)
Impaired gag reflex	62 (16.9)
Palatal weakness	55 (15.0)
Facial paralysis	53 (14.5)
Hoarse voice	45 (12.3)
Vomiting	25 (6.8)

Table 6. Wound Botulism Cases by Mechanical Ventilation — United States, 1999–2014

	Mechanically Ventilated n (%)	Not Ventilated n (%)	P value
Sex			
Male	78 (74.3)	202 (77.4)	
Female	27 (25.7)	59 (22.6)	0.5110(NS)
Race			
Unknown	51 (48.6)	152 (58.2)	
White	47 (44.8)	83 (31.8)	
Black	5 (4.8)	16 (6.1)	
American Indian/Alaska Native	2 (1.9)	8 (3.1)	
Asian/ Pacific Islander	0 (0)	1 (0.4)	
Other	0 (0)	1 (0.4)	
Ethnicity			
Hispanic	32 (30.5)	75 (28.7)	0.7968(NS)
Non-Hispanic (reference)	30 (28.6)	65 (24.9)	
Unknown	43 (41.0)	121 (46.4)	
Botulism toxin type			
A	99 (94.3)	236 (90.4)	
B	1 (1.0)	17 (6.5)	
Unknown	2 (1.9)	7 (2.7)	
AB/ABE Undetermined	3 (2.9)	1 (0.4)	
Wound Category			
Drug associated	101 (96.2)	247 (94.6)	
Injury	2 (1.9)	8 (3.1)	
Unknown	1 (1.0)	6 (2.3)	
Operative	1 (1.0)	0 (0)	
Injection drug use (IDU) n=365	102 (97.1)	248 (95.0)	0.7062(NS)
Type of drug			
Heroin n=235	21 (20.0)	9 (3.5)	0.0037
Black tar heroin n=72	37 (35.2)	23 (8.8)	0.8927(NS)
Methamphetamine n=235	8 (7.7)	2 (0.8)	0.0451
Location			
Case in California	77 (73.3)	232 (88.9)	0.0003
Cases not in California	28 (26.7)	29 (11.1)	

Table 7. Signs and Symptoms by Mechanical Ventilation in Wound Botulism Patients — United States, 1999–2014

	Mechanically Ventilated n (%)	Not Ventilated n (%)	P value
Neck weakness	72 (68.6)	61 (23.4)	0.9183 (NS)
Difficulty swallowing	69 (65.7)	61 (23.4)	1.0 (NS)
Drooping eye lids	72 (68.6)	50 (19.2)	0.3765 (NS)
Slurring speech	66 (62.9)	51 (19.5)	0.2720 (NS)
Diplopia	59 (56.2)	50 (19.2)	0.6836 (NS)
Shortness of breath	60 (57.1)	27 (10.3)	<0.0001
Extra ocular palsy	52 (49.5)	28 (10.7)	0.0095
Thick tongue sensation	42 (40.0)	32 (12.3)	0.1777 (NS)
Change in voice	41 (39.1)	33 (12.6)	0.0880 (NS)
Impaired gag reflex	40 (38.1)	22 (8.4)	0.0434
Palatal weakness	36 (34.3)	19 (7.3)	0.0044
Facial paralysis	44 (41.9)	9 (3.5)	<0.0001
Hoarse voice	26 (24.8)	19 (7.3)	0.0607 (NS)
Vomiting	12 (11.4)	13 (5.0)	0.5366 (NS)

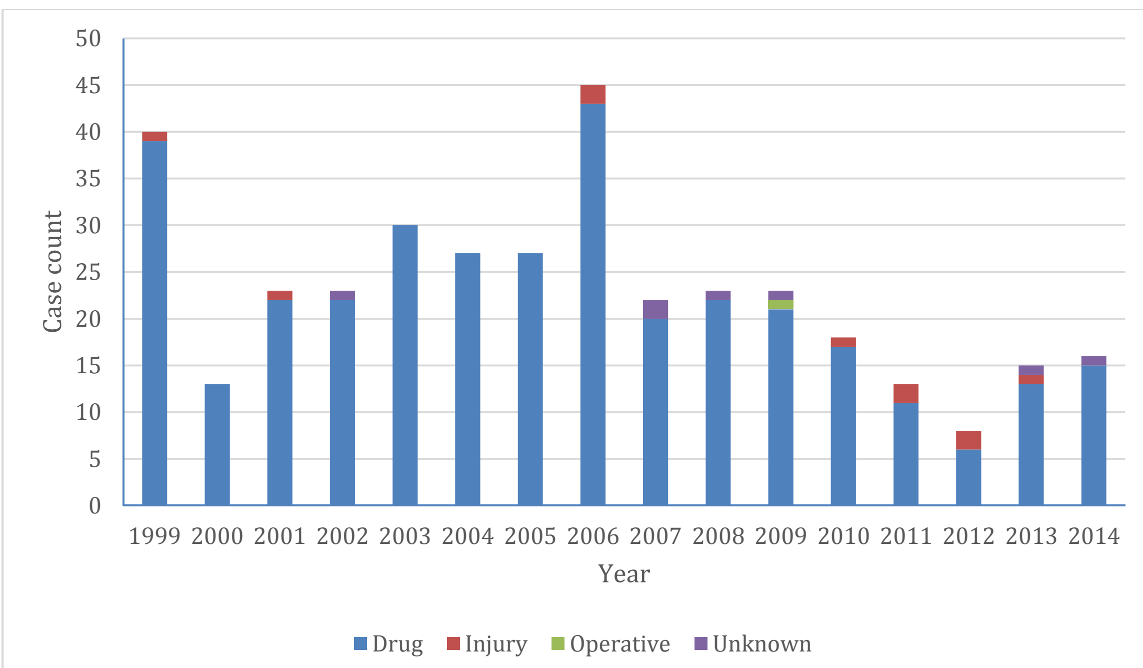

Figure 1. Wound Botulism Cases by Year and Wound Category — United States, 1999–2014

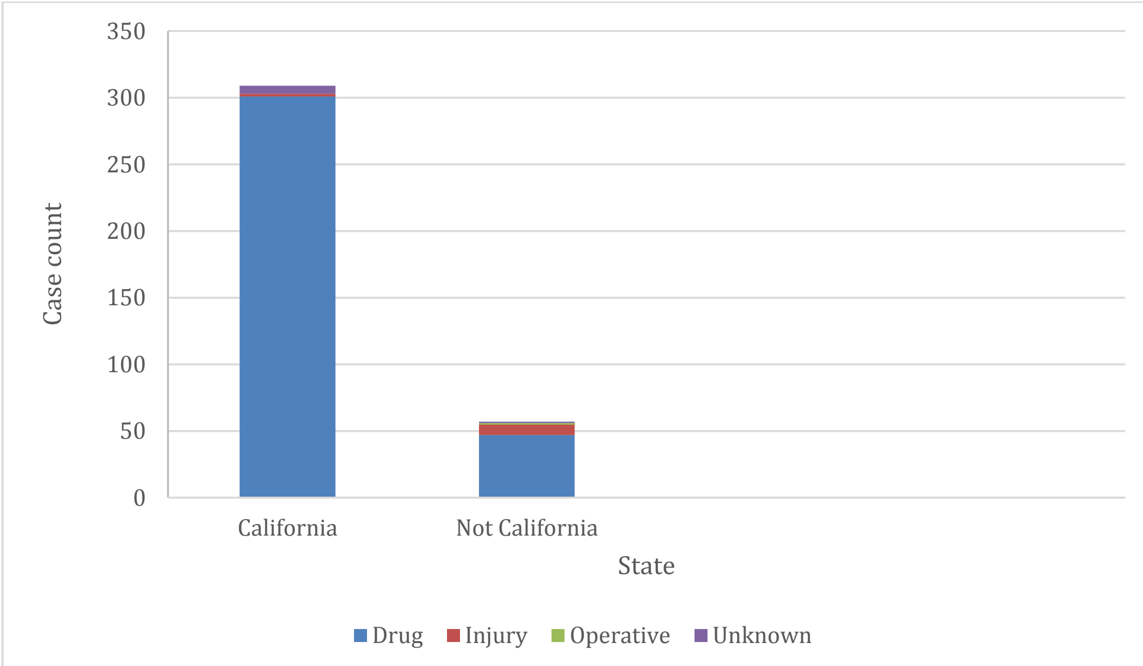

Figure 2. Wound Botulism Cases by Wound Category and Location — United States, 1999–2014

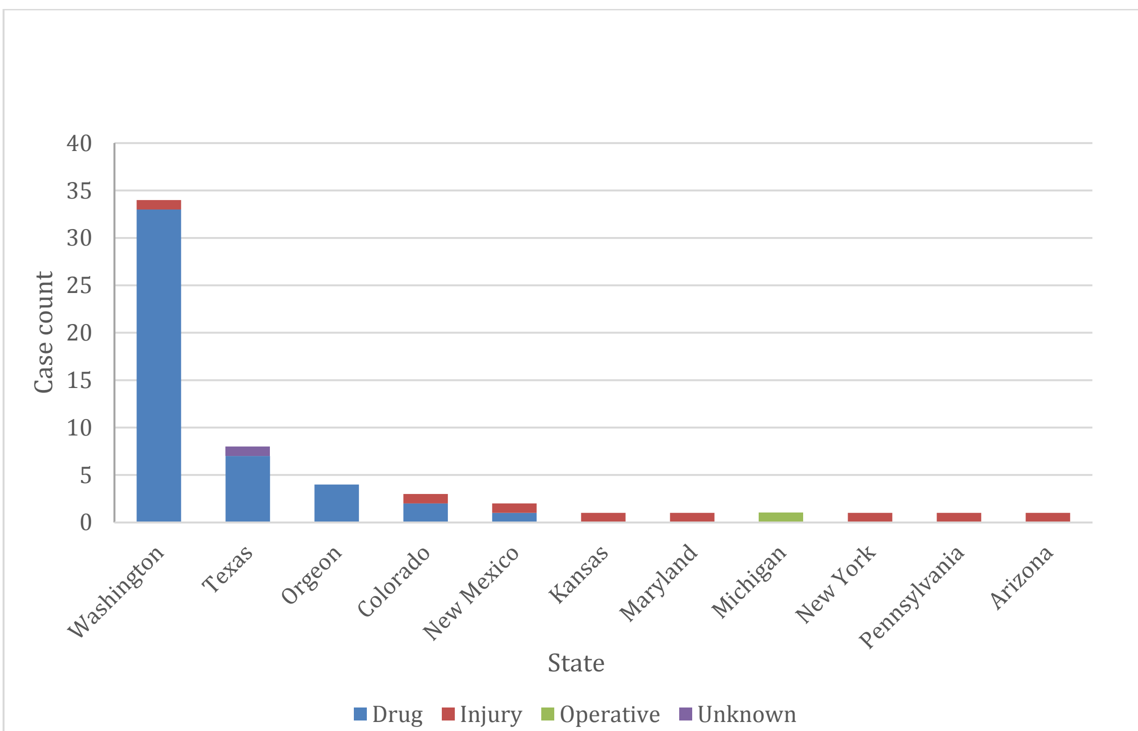

Figure 3. Wound Botulism Cases by Wound Category in Non-California States — United States, 1999–2014

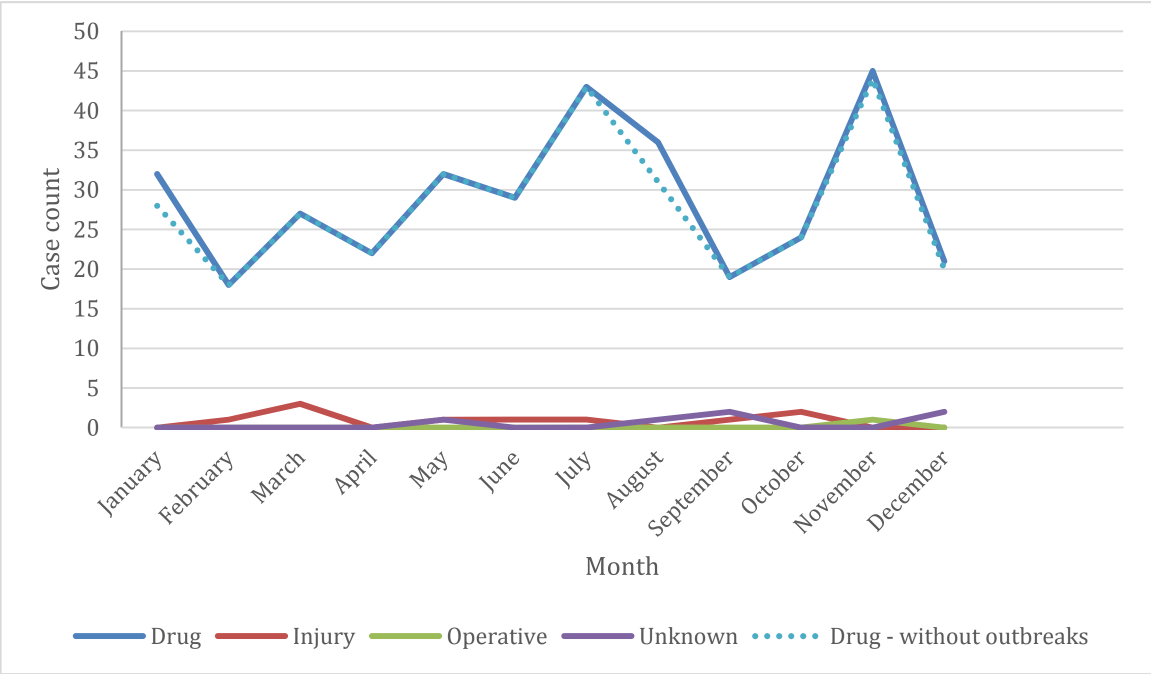

Figure 4. Wound Botulism by Wound Category Type and Month — United States, 1999–2014