REVIEW OF BOTULISM CASE REPORTS LOS ANGELES COUNTY, 2000-2007

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BACKGROUND

Botulism is a rare but serious paralytic illness caused by nerve toxins produced by the anaerobic bacterium *Clostridium botulinum* and rarely other species. These toxins block motor nerves, leading to paralysis. Death ensues if the respiratory muscles become paralyzed and mechanical ventilation is delayed. All suspected botulism reports are medical emergencies. Botulism is also a public health emergency because a food item contaminated with botulism toxin endangers others who may consume it. In recent years it has also been postulated that botulinum toxin could be used as a bio-weapon due to the extremely small dose required for clinical illness. Therefore, prompt and complete investigation of all reports of suspected botulism is a public health priority.

There are seven known botulinum toxins, four of which – types A, B, E, and F – affect humans. Clostridial spores germinate anaerobically and may produce toxin in a food item, a wound, or the intestine. Toxin may also be given therapeutically for medical or cosmetic reasons and cause paralysis if administered incorrectly or at too high a dose. Theoretically botulinum toxins could also be aerosolized as a bio-weapon and intoxicate victims by the respiratory route.

The patient's history, the progression of neurological findings, and specialized diagnostic procedures are integral to the diagnosis of botulism. The laboratory investigation is important to confirm the disease. An inadequate investigation has the potential to delay diagnosis or misclassify the type of botulism, for example calling a case wound botulism when it actually is foodborne botulism, endangering others at risk of consuming a contaminated food item.

The Los Angeles County (LAC) Department of Public Health has had a longstanding agreement with the California Department of Public Health permitting LAC to investigate all reports of suspected botulism in persons over the age of infancy. Infant botulism suspects in California are investigated and treated by the California Infant Botulism Program without assistance from local health departments.

The LAC Public Health Laboratory (PHL) conducts a complete range of botulism microbiological testing. Specimens of serum, stool, gastric contents, and food obtained can be tested for botulism toxin or clostridium culture. Clostridium isolates from patients' wounds are submitted by hospital laboratories for species confirmation and toxin production.

The objectives of this report were to summarize clinical and diagnostic results for investigations of suspected botulism cases reported to LAC from 2000-2007; describe confirmed botulism cases; evaluate completeness of laboratory investigations conducted; and identify investigatory aspects needing improvement.

METHODS

All available records of botulism cases and suspects over 1 year of age were reviewed; these included the botulism suspect worksheet, epidemiologic case history form, medical records on file, and laboratory records from the treating hospital and the PHL. Since 2005, the botulism suspect worksheet has been used to guide investigators and organize documentation of all botulism investigations. The epidemiologic case history form is completed only for confirmed cases meeting the following case definitions; these forms are then submitted to the California Department of Public Health in compliance with the California Code of Regulations, Title 17, Section 2502.

Standardized CDC case definitions for each form of botulism (excluding infant botulism) are as follows:

- A case of foodborne botulism is a clinically compatible case that is laboratory confirmed or that occurs among persons who ate the same food as persons who have laboratory-confirmed botulism.
- A probable foodborne botulism case is clinically compatible with an epidemiologic link to a suspicious food item.
- A case of confirmed wound botulism is a clinically compatible case that is laboratory confirmed in a patient who has no suspected exposure to contaminated food and who has a history of a fresh, contaminated wound during the two weeks before onset of symptoms.
- If a patient aged greater than one year of age has no history of ingestion of suspect food and has no wounds, but botulinum toxin or organisms are detected in a clinical specimen, the disorder is described as botulism, other.
- For purposes of this review, a case of clinical botulism was defined as a patient whose illness is clinically compatible with botulism but for whom the laboratory tests necessary for confirmation were either non-supportive or not done, and there was no alternative diagnosis made by the treating physician.

A laboratory specimen instruction sheet has been distributed annually since 2005 to all hospital emergency departments and laboratories, neurologists, and infectious disease physicians. Investigations were conducted by medical epidemiologists in ACDC who rotate telephone duty and after-hours call for LAC DPH. The initial investigator was responsible for all follow-up and completion of required documentation. All decisions and documentation were reviewed and approved by a senior physician.

RESULTS

- A total of 54 suspected botulism cases were reported to LAC DPH during the eight-year period (Table 1); one third (18) were confirmed. The male to female case ratio was 3.5 to 1 for all suspects and for all confirmed cases. The ages of all suspects ranged from 10 to 82 years; the mean age of confirmed cases and unconfirmed suspects did not differ. Confirmed botulism cases were more likely to be injection drug users (IDU) than were unconfirmed suspects, 72% versus 56%. Sixty-nine percent of suspects received botulinum antitoxin treatment, including all 18 of the eventually confirmed cases. More than half of the unconfirmed cases (53%) were also treated with antitoxin.

Table 1. Botulism Case Reports by Gender, Mean Age, Injection Drug Use, Treatment, and Confirmation Status Los Angeles County, 2000-2007

	All Suspects n (%)	Confirmed Cases n (%)	Unconfirmed Suspects n (%)
Total	54 (100)	18 (33)	36 (67)
Male : Female	42 : 12	14 : 4	28 : 8
Mean age, years (range)	45.9 (10 – 82)	45.7 (17 – 82)	46.1 (10 – 55)
IDU	33 (61)	13 (72)	20 (56)
Got antitoxin	37 (69)	18 (100)	19 (53)

Figure 1 shows the confirmation status of the 54 suspected botulism cases by year of occurrence. The number of reports of suspected botulism ranged from 3 to 11 reports per year, while confirmed cases ranged from zero to eight cases annually. In 2000 and 2003, no botulism cases were confirmed.

Figure 1. Suspected Botulism Cases by Confirmation Status and year of Occurrence, Los Angeles County, 2000-2007

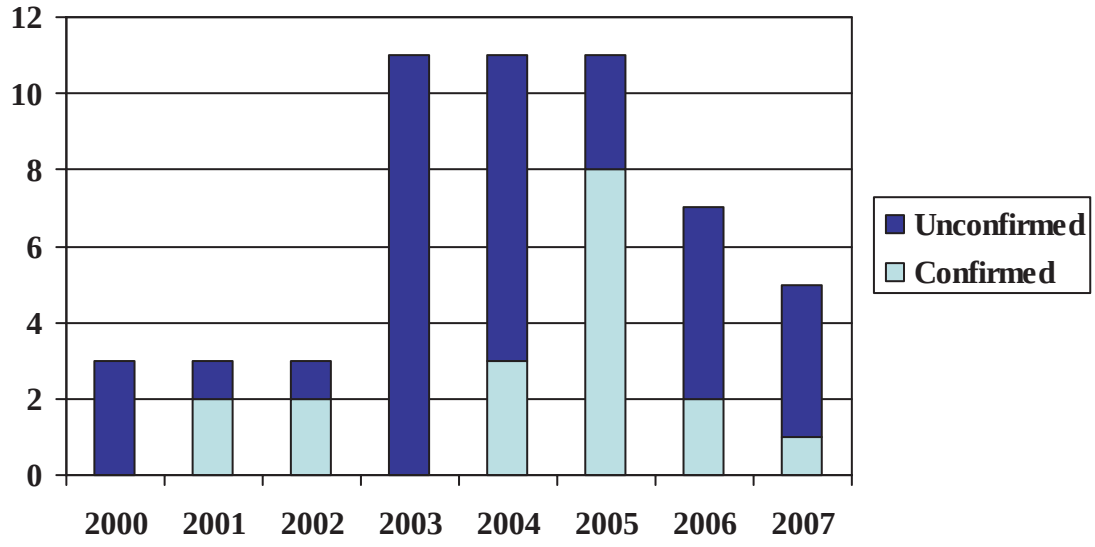

Table 2 breaks down the 18 confirmed botulism cases by year of occurrence, route of intoxication and toxin type. Fifteen of the 18 confirmed cases, 83%, were caused by botulinum toxin type A.

Table 2. Confirmed Botulism Cases by Year of Occurrence, Route of Intoxication, and Toxin Type* Los Angeles County, 2000-2007

Year	Foodborne Botulism Cases – Type*	Wound Botulism Cases - Type*
2000	-	-
2001	2 - AF	-
2002	-	2 - AA
2003	-	-
2004	-	3 - AA, not B
2005	2 - AA	6 - AAAABU
2006	-	2 - AA
2007	-	1 - A
Total	4	14

* A, type A toxin; B, type B toxin; F, toxin type F; U, unknown toxin type

There were three episodes of foodborne botulism with four confirmed cases: two isolated cases and one outbreak of two cases in a family. Sera and stool samples from all four cases were collected and tested. Food specimens were obtained in only two of the three episodes. One 2001 case was fatal and involved a mentally ill man. The case-patient's home had dozens of unrefrigerated containers of food; none of the food was tested for toxin since the patient's serum had already tested positive. The other 2001 case was caused by type F toxin produced by *Clostridium barratii*; toxin was detected in the case's serum, and the organism was isolated in two food items retrieved from the garbage. In 2005, a foodborne outbreak caused by type A occurred with a grandfather (fatal) and his grandson; the offending food item was not identified because a site visit to the home was delayed because other family members were unavailable for two days. By the time an investigator got into the home, no foods found in the home were a compatible medium for botulism, and the garbage had been tossed and collected by the sanitation department.

There were 14 confirmed wound botulism cases, 11 (79%) were due to type A toxin. Sera were collected from all wound botulism cases, and 13 were positive. The only type B case was diagnosed in 2005 in a patient whose serum tested negative for toxin but whose wound culture grew *C. botulinum* type B. A wound specimen for cultured was obtained from eight of the fourteen suspects (57%), of which two were positive, including one case whose serum was toxin negative. For two cases there was insufficient serum to permit definitive toxin typing; these were reported as "not B" and "toxin present, type unknown." Collection of other specimens that would assist with ruling out foodborne botulism was rarely done; only three gastric specimens and one stool specimen were submitted; LAC DPH did not obtain any food items from these eventually confirmed wound botulism cases.

Disposition of Remaining Suspects

Of the remaining 36 suspects, 17 (47%) were considered to have clinical botulism that was not confirmed, including 14 cases of possible wound botulism, two cases of possible foodborne botulism, and one possible iatrogenic case. Because these cases failed to meet the formal case definitions, they were not reported to the California Department of Public Health.

For the 14 suspected botulism cases believed to have unconfirmed wound botulism, serum samples were obtained and tested for twelve (86%); the other two were a married couple, both IDU, who presented together with compatible signs and symptoms but left the emergency department against medical advice before specimens were obtained. Wound cultures were obtained from 6 of the 14 clinical wound botulism suspects (43%), none of which grew *C. botulinum*. Stool specimens were available from only 3 of the 14 suspects (21%), and no gastric aspirates or food samples were obtained.

Two unconfirmed clinical botulism cases were investigated in persons who were not injection drug users and who had no other recent wounds. Specimens of serum, stool and food were obtained in both investigations, but tests did not identify botulinum toxin or toxigenic organisms. These suspects were felt to have possible foodborne botulism based on the clinical presentation and lack of an alternative diagnosis.

A case of possible iatrogenic botulism was reported in a child with cerebral palsy who received quarterly injections of botulinum toxin to relieve muscle spasms. Because of development of antibodies against BoTox® (type A toxin) his treatment was changed to Myobloc® (type B toxin). Because these products are not bioequivalent, there is the potential for overdosing the patient if the Myobloc dosage is not adjusted downward. Serum obtained one month after the change to Myobloc did not contain measurable botulinum toxin, but the clinical presentation and its timing after treatment were consistent with iatrogenic botulism.

Eighteen patients originally reported as possible botulism cases eventually received another diagnosis. The most common diagnosis was Guillain-Barré syndrome in nine patients; interestingly two of these were stool culture positive for campylobacter, and another had a history of recent diarrheal illness. In addition, there were four patients with nonspecific inflammatory conditions of the central nervous system, two patients with strokes, two with a neoplasm, and one case of myasthenia gravis. The remaining case had no alternative diagnosis but was not compatible with botulism.

Variations in Investigation by IDU Status

This analysis showed that botulism suspects who are injection drug users are investigated differently from other suspects. There were 33 IDU suspects and 20 suspects without a history of IDU (one omitted for missing data). Among IDU botulism suspects, 85% had serum tested, but only 65% of non-IDU suspects had serum tested. Wound specimens were obtained from just 45% of the IDU suspects; only one non-IDU had a wound that was screened as a potential toxin source. Samples of stool, food and gastric contents were more likely to be collected from non-IDU suspects; but in only 50% of those investigations was a stool sample collected.

CONCLUSION

From 2000 to 2007, LAC evaluated 54 reports of possible botulism, of which 18 were confirmed. A near equal number (17) were felt to be botulism based on clinical criteria and absence of an alternative diagnosis, but these cases were not laboratory-confirmed and thus not officially reported in state and national statistics. There were 19 patients with other diagnoses. Sixty-two percent of reported suspects were IDU, including 14 confirmed botulism cases, 14 unconfirmed cases of clinical botulism, and four patients with other or unknown diagnoses.

It is the responsibility of treating physicians to obtain clinical specimens from the patients; despite use of a detailed collection guide, specimen collection was often incomplete. Among suspects who were IDU, serum collection was high, but a wound specimen was obtained from fewer than half of the suspects; understandably, not every patient has an obvious wound to be drained.

In a number of investigations, the report to LAC DPH was made prior to obtaining diagnostic tests that pointed to an alternative diagnosis. For example, tests such as the edrophonium (Tensilon®) challenge, EMG, lumbar puncture, or visualization studies of the head often are pending when the case is first reported. A positive finding from one of these tests may cancel the need for further botulism work-up. Nonetheless Public Health must improve compliance with published specimen submission guidelines. Once specimens are in the hands of Public Health, tests can be cancelled in the event another diagnosis is reached.

Public Health depends on the treating physicians to get the patient's history of risk factors, especially exposure to suspicious foods. For suspected foodborne botulism, Public Health is responsible for collecting potentially contaminated food items. Unfortunately, many patients are already placed on a ventilator and sedated by the time Public Health is notified, so historical information is limited. Many of these individuals have no next of kin or are homeless, further limiting our ability to conduct a full investigation.

Failure to work up all suspected botulism cases fully could mask a foodborne botulism case as a wound botulism case. Delay in identification of foodborne botulism may endanger others exposed to a contaminated product. Investigators can improve diagnostic work-ups by interviewing the patient or close contacts quickly, especially when foodborne botulism is suspected, so that suspicious food items are gathered quickly. Treating facilities should be encouraged to follow specimen guidelines more carefully.