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Laboratory Findings in Four Cases of Adult Botulism Suggest Colonization of the Intestinal Tract

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There was laboratory evidence of intestinal colonization in four cases of adult botulism confirmed by the Centers for Disease Control. No preformed toxin was detected in available foods, but *Clostridium botulinum* was isolated from foods in two instances. Botulinal toxin was detected in the sera of all four patients, in one case at 47 days after ingestion of suspected food. *C. botulinum* was demonstrated in the stool of all four patients and persisted for 119 days after the onset of illness in one patient. Two patients had surgical alterations of the gastrointestinal tract, which may have promoted the colonization. The apparent lack of ingestion of preformed toxin in these cases and the persistence of botulinal toxin or *C. botulinum*, or both, for long periods in three of the patients suggest that colonization of the intestinal tract occurred.

There are three clearly defined forms of botulism: food-borne, wound, and infant botulism. Food-borne botulism is caused by the ingestion of preformed toxin, usually in food (9). Wound botulism (5) is due to organisms growing in deep wounds. Infant botulism develops when ingested spores or organisms colonize the digestive tract, multiply, and produce toxin (6, 8).

The growth of *Clostridium botulinum* within the intestine was considered more than 60 years ago as a possible mechanism of intoxication in some cases, but this possibility was difficult to verify experimentally, as concluded by Burke et al. (1). Minervin (7) pointed out clinical evidence of toxin production in the digestive tract in 1966, but intestinal colonization of humans was not clearly documented until the recognition of infant botulism in 1976 (6, 8). However, persons susceptible to infant botulism are usually less than 6 months of age.

Nevertheless, rare cases suggesting intestinal colonization in noninfants have occurred. The clinical aspects of this type of case have been reported, but we wish to provide additional laboratory findings from four incidents that suggest intestinal colonization as the source of botulism in adults.

The four cases were selected from laboratory records on botulism investigations dating back to 1966 in the Centers for Disease Control Botulism Laboratory. In each case, the patient had the typical signs and symptoms of botulism and there was positive laboratory evidence in one or more clinical specimens. No preformed botulinal toxin was detected in any food examined, nor was a wound noted that could have served as a site of infection. Other observations were as follows. Botulinal toxin or *C. botulinum* was detected in clinical specimens for long periods; *C. botulinum* or its spores were found in a food vehicle, but no preformed toxin was detected; and surgery may have altered conditions in the gastrointestinal tract. The mouse neutralization test used to identify botulinal toxin and the methods used to isolate *C. botulinum* are described elsewhere (2).

Case 1: elderly man, Kentucky, October 1973. The incident involved a man and his wife who had both become ill at about the same time; the wife died before the illness was diagnosed. Because botulism was not considered until late in the course of the man's illness (day 22), it was assumed that clinical specimens would be negative for toxin and organisms. Type B botulinal toxin was detected in the patient's stool (day 22), and *C. botulinum* was isolated on days 22 and 32. Type B botulinal toxin was detected in a serum obtained on day 30 (Table 1). A serum obtained on day 37 was negative for toxin. No preformed toxin was found in any of the foods found in the home, but *C. botulinum* type B was isolated from three of four containers of home-canned blackberries. *C. botulinum* is not likely to have grown in the berries because of the high acidity of berries (pH 3.2 to 3.6 [4]).

Case 2: 33-year-old woman, Oregon, March 1978. The patient was admitted to the hospital after suffering dizziness, weakness, and a "thick tongue," and she experienced a respiratory arrest during the initial examination (W. J. English, L. P. Williams, Jr., R. E. Bryant, and M. D. Gillies, Letter, N. Engl. J. Med. **304**:789–790, 1980). Three years before the onset of illness, the patient had undergone a jejunal-ileal bypass for obesity. Type A botulinal toxin was detected in two sera obtained on day 2 of illness. No toxin was detected in the serum on day 3, after the patient had received antitoxin. The stool obtained on day 2 was insufficient in quantity for direct toxin testing, but *C. botulinum* type A was isolated. Two gastric fluid samples were negative for both toxin and organism (Table 1). There was no food history consistent with food-borne botulism and no evidence of an infected wound. Several foods from the patient's refrigerator were negative for botulinal toxin and *C. botulinum*. At 17 days after the onset of illness, the patient died from respiratory complications.

Case 3: 27-year-old man, Iceland, June 1981. An outbreak of botulism was recognized when three children in the family developed signs suggesting botulism within a 2-day period; the diagnosis was subsequently confirmed by the detection of type B toxin in serum and the isolation of *C. botulinum* type B (nonproteolytic) from stool specimens. The mother developed signs of botulism 11 days after the onset of illness in the first child. Serum and stool specimens were obtained from the mother 12 days after exposure. Type B toxin was found in the serum, and *C. botulinum* type B was isolated from her stool.

No botulinal toxin was detected in the serum obtained from the asymptomatic father 19 days after the suspected family exposure. Type B toxin was detected in an enrich-

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TABLE 1. Laboratory findings in four cases of adult botulism with evidence of intestinal colonization

Case no.	Specimen (no. of samples)	No. of days after onset or exposure	Botulinal toxin[a]	*C. botulinum*[a]
1	Serum	30	B	
		37	–	
	Stool	22	B	B
		32	NS	B
	Blackberries (3)		–	B
2	Gastric fluid (2)	2–4	–	–
	Serum	2	A	
	Posttreatment serum	3	–	
	Stool	2	QNS	A
3	Serum	19[b]	–	
		47	B	
	Stool	19[b]	NS	B[c]
		47	NS	B
	Sausages (6)		–	–
4	Serum	14	A	
	Posttreatment serum (8)	15–77	–	
	Stools			
	(4)	14–20	A	A
	(5)	14–20	–	A
	(11)	21–119	–	A
	(9)	26–67	–	–
	Cream of coconut		–	A

[a] Positive results indicated by A or B, referring to toxin type. –, Negative result; NS, nonspecific toxicity; QNS, quantity not sufficient.
[b] No symptoms at 19 days after suspected exposure.
[c] Toxin detected in enrichment culture, but organism could not be isolated.

ment culture of the stool (day 19), but *C. botulinum* could not be isolated. Twenty-five days later, the father developed classic signs of botulism. Serum and stool specimens were obtained on day 47. Type B toxin was detected in the serum, and *C. botulinum* type B was isolated from the feces. No botulinal toxin was detected in the stools of any of the patients in this incident. A nonspecific toxic factor which caused mouse deaths was present. It did not cause signs of botulism in the test mice, nor was it neutralized by botulinal antitoxin. The suspected food was homemade blood sausage consumed by the family the day before the onset of illness in the first child. Neither toxin nor *C. botulinum* was detected in six samples of sausages. The secondary cases involving the mother and the father were probably not due to later exposure, since the family was aware of the hazard of home-preserved foods by that time. The long interval between the suspected exposure and onset of symptoms, the detection of the organism in the feces while the subject was asymptomatic, and the subsequent appearance of toxin in the serum coincidentally with the onset of symptoms strongly suggest that the father's illness was due to the gradual buildup of toxigenic organisms in the intestine (Table 1). The mother's illness may also have been due to intestinal colonization, but the evidence is not as strong, since her case lacked the tests on preonset specimens and the interval between the onset of her illness and those of the children was not so great.

Case 4: 37-year-old woman, Maryland, January 1985. Five weeks before admission to the hospital for botulism, the patient had undergone a Billroth I surgical procedure for ulcer disease to remove the pyloric valve. She was on a vegetarian diet. No home-canned foods were consumed. No botulinal toxin was detected in the many foods tested by the U.S. Food and Drug Administration but *C. botulinum* type A was isolated from canned cream of coconut. No positive evidence was found in spinal or gastric specimens.

The patient was treated with antitoxin on day 15. Posttreatment sera obtained over the next 9 weeks showed demonstrable levels of antitoxin. During a 119-day period, 29 stool and enema washings were tested (Table 1). Type A botulinal toxin was detected in four of the stools obtained before day 20. No botulinal toxin was detected in the other 25 stools. *C. botulinum* was isolated consistently from all 10 stools obtained before day 26 and intermittently from 10 of 19 stools obtained on days 26 through 119. Toxin was detected in the stool 2 days after antitoxin treatment, and organism was detected 104 days posttreatment. Metronidazole administered on days 20 and 25 may have aided in temporarily eradicating the organism, thus explaining the intermittent detection of *C. botulinum* after day 26. The patient survived until day 240, after which she died of complications (3). The extreme persistence of the organism in the intestinal tract of this patient provides irrefutable evidence for colonization of the intestinal tract of an adult human. It would seem likely that the prior surgical alteration of the gastrointestinal tract provided the conditions necessary for the establishment of the toxigenic agent.

The four cases of adult botulism presented here were confirmed by positive laboratory evidence. The patients had the typical signs and symptoms of botulism, but there was no evidence of an infected wound and no apparent vehicle for preformed toxin. *C. botulinum* was isolated from foods in two cases, suggesting a source of spores.

Two patients had experienced surgical alteration of the gastrointestinal tract, which may have favored spore outgrowth and toxin production. Botulinal toxin was detected in the sera of all patients, 30 days after suspected exposure in case 1 and 47 days after suspected exposure in case 3. *C.*

botulinum was present in the stool of all four patients, persisting for 32, 47, and 119 days in cases 1, 3, and 4, respectively.

In case 3, the initiation of the incidence appeared to be a classical food-borne outbreak, with secondary cases, possibly because of a combination of mild intoxication and intestinal colonization, as evidenced by the late development of symptoms and appearance of toxin in the serum of the last patient.

Between 1973 and 1985, approximately 300 noninfant patients with botulism were confirmed in our laboratory. For at least 15 of the confirmed cases, including the 4 in this report, no source of preformed toxin was detected. Other cases of adult colonization may be in this group, but the four cases presented were selected because these cases more fully met the criteria for selection.

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