Preface

This report, which updates handbooks issued in 1969, 1973, and 1979, reviews the epidemiology of botulism in the United States since 1899, the problems of clinical and laboratory diagnosis, and the current concepts of treatment. It was written in response to a need for a comprehensive and current working manual for epidemiologists, clinicians, and laboratory workers.

We acknowledge the contributions in the preparation of this review of past and present physicians, veterinarians, and staff of the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases (DBMD), National Center for Infectious Diseases (NCID).

The excellent review of Drs. K.F. Meyer and B. Eddie, "Fifty Years of Botulism in the United States,"[1] is the source of all statistical information for 1899-1949. Data for 1950-1996 are derived from outbreaks reported to CDC.

Suggested citation

Centers for Disease Control and Prevention: Botulism in the United States, 1899-1996.
Handbook for Epidemiologists, Clinicians, and Laboratory Workers, Atlanta, GA.
Centers for Disease Control and Prevention, 1998.

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[1] Meyer KF, Eddie B. Fifty years of botulism in the U.S. and Canada. George Williams Hooper Foundation, University of California, San Francisco, 1950.

Dedication

This handbook is dedicated to Dr. Charles Hatheway (1932-1998), who served as Chief of the National Botulism Surveillance and Reference Laboratory at CDC from 1975 to 1997. Dr. Hatheway devoted his professional life to the study of botulism; his depth of knowledge and scientific integrity were known worldwide. He was a true humanitarian and served as mentor and friend to countless epidemiologists, research scientists, students, and laboratory workers.

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I. Emergency assistance

Botulism is a public health emergency. Prompt diagnosis and early treatment of botulism are essential to minimize the otherwise great risk of death. Prompt epidemiologic investigation is critical to prevent further cases from occurring if a hazardous food is still available for consumption. State health departments and the Centers for Disease Control and Prevention (CDC) offer 24-hour diagnostic consultation, epidemic assistance, and diagnostic laboratory services. Trivalent botulinum antitoxin (for *Clostridium botulinum* types A, B, and E) and bivalent botulinum antitoxin (for types A and B) is available from CDC.

Health care providers who suspect they have a patient with botulism should contact their state health department epidemiology offices. The Foodborne and Diarrheal Diseases Branch of CDC (FDDB/DBMD/NCID/CDC) can provide emergency consultation and support to public health authorities.

Foodborne and Diarrheal Diseases Branch

Days	phone	(404) 639-2206 (Monday-Friday, 8:30 AM-4:30 PM, eastern time)
Nights/weekends	phone	(404) 639-2888

Diagnostic laboratory services are available at several state public health laboratories and CDC.

Names of manufacturers and trade names are provided for identification only, and inclusion does not imply endorsement by the U.S. Public Health Service or the U.S. Department of Health and Human Services.

II. Introduction

Botulism is a neuroparalytic illness resulting from the action of a potent toxin produced by the organism *Clostridium botulinum*. This microbe was first described in 1897 by E. van Ermengem after his investigation of a foodborne outbreak in Ellezelles, Belgium. Foodborne botulism is rare but it may kill rapidly, and contaminated products may expose many persons. Foodborne botulism therefore, represents a medical and a public health emergency that places a premium on rapid, effective communication between clinicians and public health officials.(1,2)

"Botulism" comes from the Latin "botulus," meaning sausage. When botulism was first recognized in Europe, many cases were caused by home-fermented sausages. This derivation, although historically important, has lost much of its significance, since plant rather than animal products are more common vehicles. Sausage now is rarely the cause of botulism in the United States.

Four distinct forms of botulism can occur, depending on the mode of acquisition of the toxin. Foodborne botulism results from the ingestion of food containing preformed toxin. Wound botulism is caused by organisms that multiply and produce toxin in a contaminated wound. Infant botulism is due to the endogenous production of toxin by germinating spores of *C. botulinum* in the intestine of the infant. Child or adult botulism from intestinal colonization is represented by those cases in which no food vehicle can be identified, there is no evidence of wound botulism, and there is the possibility of intestinal colonization in a person older than 1 year of age.

C. botulinum is a group of culturally distinct organisms that are alike only in that they are clostridia and produce antigenically distinct neurotoxins with a similar pharmacologic action. *C. botulinum* organisms are straight to slightly curved, gram-positive (in young cultures), motile, anaerobic rods, 0.5-2.0 µm in width, 1.6-22.0 µm in length, with oval, subterminal spores.(3) The seven types of *C. botulinum* (A-G) are distinguished by the antigenic characteristics of the neurotoxins they produce. Types A, B, E, and in rare cases, F cause disease in humans. Types C and D cause disease in birds and mammals. Type G, identified in 1970, has not yet been confirmed as a cause of illness in humans or animals. Important epidemiologic features and some clinical characteristics distinguish the types of botulism that cause human illness. Rare cases of infant and adult botulism have been confirmed to be the result of intestinal colonization by non-*botulinum Clostridium* species that produced botulinum neurotoxin.

The structure and mechanism of action of each of the seven neurotoxins are similar. Each toxigenic Clostridia produces a polypeptide of 150 kDa which is activated by proteases following bacterial lysis. The active toxin consists of a heavy chain (H, 100 kDa) and a light chain (L, 50 kDa). The heavy chain consists of an amino-terminal 50 kDa domain (H_N) and a carboxy-terminal 50 kDa domain (H_C). Neuronal cell intoxication occurs through four steps: (1) binding of H_C to polysialoganglioside (and probably other protein) receptors on the neuronal membrane, (2) internalization of active toxin into endosomal-like compartments, (3) membrane translocation facilitated by H_N, and (4) enzymatic cleavage of target proteins by the L chain to prevent the release of the neurotransmitter acetylcholine from synaptic terminals of the motorneurons in muscle. The L chain of each neurotoxin type is a zinc-endopeptidase which has been shown to cleave a toxin-specific location of at least one of 3 proteins (VAMP, SNAP-25, or syntaxin). Although their absolute functions are unkown, these 3 proteins are members of a group of proteins (SNARE proteins) which are essential to the docking and fusion of synaptic vesicles with the pre-synaptic membrane. The exact mechanism for neurotransmitter release is not known but most likely involves a fusion pore or a complete membrane fusion. Cleavage of one of the SNARE proteins by botulinum neurotoxin inhibits the release of acetylcholine from the synaptic terminal.(4)

The ability of *C. botulinum* to cause food poisoning in humans is directly related to the production of heat-resistant spores that survive preservation methods that kill nonsporulating organisms.(5) The heat resistance of spores varies from type to type and even from strain to strain within each type; although some strains will not survive at 80°C, spores of many strains require temperatures above boiling to ensure destruction.(6,7) The thermal resistance of spores also increases with higher pH and lower salt content of the medium in which the spores are suspended.(8)

In many cases, it is impractical or undesirable to treat a food product in a manner to eliminate all *C. botulinum* spores. As a result, most control methods focus on the inhibition of growth and toxin production. The main limiting factors for growth of *C. botulinum* in foods are: (1) temperature, (2) pH, (3) water activity, (4) redox potential, (5) food preservatives, and (6) competing microorganisms. All of these factors are interrelated and so changing one factor influences the effect of other factors. The interaction of factors may have a positive or negative effect on the inhibition of *C. botulinum*. In general, proteolytic strains grow optimally at 40°C; the lower limit is 10°C, upper limit is 45-50°C. Nonproteolytic strains, including type E can continue to grow even at 3.3°C. The minimum pH range for growth of proteolytic strains is 4.6-4.8; the limit is pH 5.0 for nonproteolytic strains. However, some food proteins, such as soy and beef, may have a protective effect on *C. botulinum* at or below pH 4.6. In addition, certain food preparations may contain low-acid "pockets" in which the pH may be high enough to support the production of toxin. Low water activity (a_w) inhibits the growth of *C. botulinum*. A minimum a_w of ~0.94 is needed to support growth and toxin production. Water activity can be limited by dehydration, but is in general controlled by the addition of NaCl. The minimum a_w of 0.94 corresponds to an approximate 10% NaCl solution. High redox potential (Eh) is usually due to the presence of O_2. The optimum Eh for growth of *C. botulinum* is low (~-350 mV) but toxin production has been observed at Eh of +250 mV. Because of this range, *C. botulinum* growth and toxin production can occur even in products considered to have a high oxygen level. In addition, vacuum-packaging used to lower Eh to preserve food increases anaerobic conditions and so may support the production of toxin. A number of food preservatives (nitrite, sorbic acid, parabens, phenolic antioxidants, polyphosphates and ascorbates) inhibit the growth of *C. botulinum* and limit toxin production. Lactic acid bacteria such as *Lactobacillus*, *Pediococcus*, and *Lactococcus* have been shown to produce acid and so inhibit *C. botulinum*.(5)

III. Foodborne botulism

A. Incidence

For the purpose of surveillance, we defined a foodborne outbreak as one or more cases of botulism in which a contaminated food source was implicated. In the period 1899-1949, 477 foodborne botulism outbreaks were recorded in the United States, and in the period from 1950 through1996, an additional 444 outbreaks were reported to CDC for a total of 921. The average number of outbreaks per year has changed little, 9.7 per year for the earlier time period and 9.4 per year since 1950.

For the period 1899-1949, 1281 cases of botulism were reported, and in the time from 1950 through 1996, and additional 1087 cases were reported, bringing the total to 2368 cases. The average number of cases per outbreak has remained constant: 2.6 cases/outbreak in the first half of this century and 2.5 cases/outbreak so far in the second half.

Of the 444 foodborne botulism outbreaks since 1950, 37.6% were caused by type A botulinum toxin, 13.7% by type B, 15.1% by type E, 0.7% by type F, and 32.9% were unidentified with respect to toxin type (Table 1). The proportion of outbreaks for which the toxin type was not determined is decreasing. In 76.9% of the outbreaks for the period 1950-1959, the toxin type was not determined, compared with 59% of outbreaks for the period 1960-1969, 12.5% for 1970-1979, 2.5% for 1980-1989, and 3.6% for 1990-1996. From 1990 through 1996, outbreaks were most often caused by type A (44.6%), followed by type E (35.7%)and type B (12.5%).

B. Mortality

For the period 1899-1949, the case-fatality ratio was high at approximately 60%, but since about 1950, mortality has gradually decreased (Table 2). For the period 1950-1996, the case-fatality ratio was 15.5%. This decline in case-fatality ratio is due primarily to improvements in supportive and respiratory intensive care and perhaps to the prompt administration of antitoxin. The case-fatality ratio has generally declined over the years for all toxin types.

C. Geographic distribution

Foodborne botulism outbreaks have been reported from 46 states, Puerto Rico, and Washington D.C. from 1899 through 1996; only four states have never reported any foodborne botulism: Delaware, New Hampshire, South Carolina, and Vermont. Five western states (California, Washington, Colorado, Oregon, and Alaska) have accounted for more than half (53.8%) of all reported foodborne outbreaks since 1950 (Figure 1). Alaska alone accounts for 16.2% of outbreaks nationwide. This is because of the distinctive public health problem among the Alaska Native population, in which all botulism cases have been associated with improper preparation and storage of traditional Alaska Native foods.(1,9)

There is a distinctive geographic distribution of botulinum toxin types in the United States. Of the 167 type A outbreaks recorded from 1950 through 1996, 144 (86.2%) occurred in states west of the Mississippi River. California, Washington, Oregon, and Colorado accounted for 58.7% of all reported type A outbreaks. Twenty states, most of them in the East, have not reported type A outbreaks (Figure 2).

Outbreaks of type B botulism have been reported by 26 states. Of the 61 type B outbreaks documented from 1950 through 1996, 37 (60.7%) were reported from eastern states; New York and Kentucky reported 13 of these Type B outbreaks (Figure 3).

Type E outbreaks have been reported from 10 states (Figure 4). The geographic distribution shows a predilection for Alaska, with 56 (83.6%) reported outbreaks from 1950 through 1996.

This regional distribution of outbreaks by toxin type is in keeping with the findings of a survey of soil samples which demonstrated a predominance of type A spores in soil specimens from the West and predominance of type B spores in soils of the northeast and central states.(10) Type E spores have been found in marine life and sediment from the Pacific Northwest and the Great Lakes.(11,12)

D. Food sources and products causing outbreaks

Until the early 1960s nearly all outbreaks of botulism in which toxin types were determined were caused by type A or B toxins and were usually associated with ingestion of home-canned vegetables, fruits, and meat products. Type E botulism was not recognized as a major problem in the United States until 1963, when 22 cases were reported.(13,14) Sixty-one of the 67 outbreaks of type E botulism reported from 1950 through 1996 have been traced to marine products (fish or marine mammals); several cases have been attributed to beaver. The remainder are of an undetermined source. Only three outbreaks of Type F botulism have been reported in this country with one being traced to home-prepared venison jerky.(14-16)

From 1950 through 1996, 289 (65.1%) botulism outbreaks have been traced to home-processed foods and 31 (7%) to commercially processed foods, including foods served in restaurants. The type of food processing responsible for 124 (27.9%) outbreaks is unknown (Table 3).

Vegetables were the most important vehicle for the botulism toxin in the Untied States from 1950 through 1996. Fish and marine mammals were also responsible for a large number of the botulism outbreaks during this period. Of the 87 outbreaks caused by marine products (fish, or marine mammals), 61 were due to type E, 15 to type A, 8 to type B, and 3 were unknown. Beef, milk products, pork, poultry, and other vehicles caused fewer outbreaks.

E. Prevention and control

In the United States, foodborne botulism due to commercial foods has been largely controlled by safe canning and food manufacturing processes. Commercial canned foods are heated to a sufficient temperature and for a sufficient time to kill the spores. Unheated commercial foods in cans or jars can be made safe by acidification or other manipulations that inhibit the growth of the organism (e.g., addition of phosphoric acid to garlic in oil). Occasionally, commercial foods still cause botulism if they are prepared in a way that permits toxin production.

Many outbreaks of foodborne botulism in the United States result from eating improperly preserved home-canned foods.(18) Persons doing home canning and other food preservation should be educated about the proper time, pressure, and temperature required to destroy spores, the need for adequately refrigerated storage of incompletely processed foods, and the effectiveness of boiling, with stirring, home-canned vegetables to destroy botulinum toxins.(19) A pressure cooker must be used to can vegetables at home safely because it can reach temperatures above boiling (>212°F [>100°C]), which is necessary to kill botulism spores.(19) Although botulism spores are heat stable, botulinum toxin is heat labile. Botulinum toxin can be inactivated by heating to 176°F (80°C). Therefore, heating home-canned foods before consumption can reduce the risk of botulism intoxication.

C. botulinum may cause container lids to bulge and the contents to have “off-odors.” Commercial cans or home-canned products with bulging lids should not be opened, and foods with off-odors should not be eaten or “taste tested.” (19) For more information about safe home-canning procedures, contact your local county extension home economist or see the website the Extension Service of the U.S. Department of Agriculture (USDA) at http://nchfp.uga.edu/publications/publications_usda.html .(20)

IV. Infant botulism

Since 1980, infant botulism has been the most common form of botulism reported in the United States. It is epidemiologically distinct from foodborne botulism, representing not ingestion of toxin preformed in contaminated foods but colonization (infection) of the intestine by spores of *C. botulinum*, with subsequent in vivo toxin production.(21) Although infant botulism was first described in 1976,(22,23) earlier cases have been identified retrospectively, and its detection only in recent years might reflect advances in diagnostic capabilities rather than the emergence of a new clinical syndrome.

The disease is characterized by the onset of constipation, which is followed shortly by neuromuscular paralysis that begins with the cranial nerves and progresses to peripheral and respiratory musculature. The spectrum in severity has ranged from mild lethargy and slowed feeding to severe hypotonia and respiratory insufficiency.

A. Epidemiology

Since the recognition of infant botulism in 1976, cases have been identified with increasing frequency. In the United States, 1442 cases were reported to CDC from 46 states between 1976 and 1996 (Figures 5 & 6). Type A accounted for 46.5% of these cases (Figure 7) and type B for 51.9% (Figure 8). Since reporting began to stabilize in 1980, the average annual incidence of reported infant botulism in the United States has been approximately 1.9/100,000 live births. Since 1976, 47.2% of all infant botulism cases have been reported from California. Between 1976 and 1994, the incidence of infant botulism was highest in Delaware, Hawaii, Utah, and California (9.0, 8.8, 6.3 and 5.7 per 100,000 live births, respectively). The reasons for the apparent geographic variation are unknown.

The characteristics of infant botulism cases have been clarified in recent years. Infants hospitalized with the disease tend to have had higher birth weights than other infants, and their mothers tend to be white, older, and better educated than mothers in the general population. Affected infants are also more commonly breast-fed,(24,25) and breast-feeding is associated with an older age at onset in type B cases.(25) In general, affected infants are the product of normal gestation and delivery. No congenital abnormalities have been shown to be associated with infant botulism, and the children were generally healthy until the onset of botulism. Approximately the same number of males as females have been affected. The mean age at onset has been 13 weeks, the range from 1 to 63 weeks. Clustering of cases of infant botulism has been noted in some suburban areas in the eastern United States and in some small towns and rural areas in the West.(26-29)

B. Source of *C. botulinum*

Infant botulism occurs when an infant ingests spores (less likely vegetative cells) of *C. botulinum* which in turn colonize the intestinal tract and produce toxin.(21) In a prototypical case, type B organisms, but no toxin, were isolated from honey fed to an infant with infant botulism whose fecal specimens contained type B organisms and toxin. Family members who ate some of the same honey did not become ill. In several studies, more than 20% of affected infants had ingested honey before the onset of botulism.(25,29,30) In many cases, *C. botulinum* spores of the same type were cultured from honey in the same households.

However, since most infants with infant botulism have had no exposure to honey, the risk factors and vehicles of transmission of *C. botulinum* for the majority of cases remain unclear. (21,31) A survey of foods commonly fed to infants revealed *C. botulinum* in specimens of corn syrup as well as honey, but in no other category of foods tested.(32) In other studies, the same types of *C. botulinum* that caused disease were isolated from soil in an infant's yard and from vacuum cleaner dust. Investigators have also frequently noted environmental conditions that might expose infants directly to environmental sources of *C. botulinum* spores, such as a shared crib, dusty or windy locales, nearby building construction, or outdoor activities.(26,28) These exposures have not, however, been fully evaluated by controlled studies. Infants hospitalized with botulism have also more typically been breast-fed than have control infants.(25,31,33,34) Breast-feeding is known to affect the fecal flora differently than formula feeding; in mice, the fecal flora have been shown to be an important susceptibility factor in challenge experiments with *C. botulinum* type A spores.(35)

C. Prevention and control

The risk factors for infant botulism are poorly described, but possible sources of spores include foods and dust. Honey should not be fed to infants because it has been identified as a food source. (19)

V. Wound botulism

Wound botulism is a rare disease resulting from the growth of *C. botulinum* spores in a contaminated wound with in vivo toxin production.(36) Neurologic findings are indistinguishable from those seen in foodborne botulism; however, gastrointestinal symptoms do not occur. Wounds might not be obvious or grossly infected. Between 1943, when the syndrome was first recognized, through 1985, 33 cases of wound botulism were reported in the United States. Of these, 25 were laboratory confirmed; 17 cases were type A, 7 type B, and 1 a mixture of type A and type B organisms.(37) The median age of patients was 21 years (range 6-44 years); 81% were male. The wounds were usually deep and contained avascular areas; many patients had compound fractures, and four had extensive crush injuries of the hand. The median incubation period in cases of trauma was 7 days (range 4-21 days).(38) Since 1980, wound botulism cases have occurred in persons who used illicit drugs; these were associated either with needle puncture sites or with nasal or sinus lesions due to chronic cocaine sniffing.(39) From 1986 through 1996, 78 cases of wound botulism were reported in the United States; the majority were linked to injectable drug use, particularly with so-called “black tar heroin.” Sixty-six cases were type A, 9 were type B, and the remaining 3 were of unknown toxin type. The median age of patients was 38 years (range 5-65 years); 60% were male.

VI. Child or adult botulism from intestinal colonization

Isolated cases of botulism in which extensive investigation failed to implicate a specific food as the cause of the disease have been recorded by CDC since 1978 as cases of "undetermined origin" rather than of foodborne botulism; through 1996, all of these cases have been in adults. Although there has been speculation since the 1920s, careful investigation has now demonstrated that some of these cases are caused by colonization of the gastrointestinal tract by *C. botulinum* or *C. baratii* with in vivo production of toxin, analogous to the pathogenesis of infant botulism.(40,41) Support for the diagnosis of botulism from intestinal colonization is provided by the demonstration of the prolonged excretion of toxin and *C. botulinum* in the stool, and by the demonstration of spores of *C. botulinum* but not preformed toxin in suspected foods. In some cases of botulism strongly suspected of representing intestinal colonization, the patients had a history of gastrointestinal surgery or illnesses such as inflammatory bowel disease, which might have predisposed them to enteric colonization.(42) No other specific risk factors have been identified.

VII. Clinical syndrome

The clinical syndrome of botulism, whether foodborne, infant, wound, or intestinal colonization, is dominated by the neurologic symptoms and signs resulting from a toxin-induced blockade of the voluntary motor and autonomic cholinergic junctions and is quite similar for each cause and toxin type.(21,34,38,43) Incubation periods for foodborne botulism are reported to be as short as 6 hours or as long as 10 days,(44) but generally the time between toxin ingestion and onset of symptoms ranges from 18 to 36 hours.(45) The ingestion of other bacteria or their toxins in the improperly preserved food or changes in bowel motility are likely to account for the abdominal pain, nausea and vomiting, and diarrhea that often precede or accompany the neurologic symptoms of foodborne botulism. Dryness of the mouth, inability to focus to a near point (prompting the patient to complain of "blurred vision"), and diplopia are usually the earliest neurologic complaints. If the disease is mild, no other symptoms may develop and the initial symptoms will gradually resolve. The person with mild botulism may not come to medical attention. In more severe cases, however, these initial symptoms may be followed by dysphonia, dysarthria, dysphagia, and peripheral-muscle weakness. If illness is severe, respiratory muscles are involved, leading to ventilatory failure and death unless supportive care is provided. Recovery follows the regeneration of new neuromuscular connections. A 2- to 8-week duration of ventilatory support is common, although patients have required ventilatory support for up to 7 months before the return of muscular function.(43) Death occurs in 5%-10% of cases of foodborne botulism; early deaths result from a failure to recognize the severity of disease or from secondary pulmonary or systemic infections, whereas deaths after 2 weeks are usually from the complications of long-term mechanical ventilatory management.(43)

Perhaps because infants are not able to complain about the early effects of botulinum intoxication, the neurologic dysfunction associated with infant botulism often seems to develop suddenly. The major manifestations are poor feeding, diminished suckling and crying ability, neck and peripheral weakness (the infants are often admitted as "floppy babies"), and ventilatory failure.(21,24,34) Constipation is also often seen in infants with botulism, and in some, has preceded the onset of neurologic abnormalities by many days. Loss of facial expression, extraocular muscle paralysis, dilated pupils, and depression of deep tendon reflexes have been reported more frequently with type B than with type A infant botulism.(34) Treatment with aminoglycoside antimicrobial agents may promote neuromuscular weakness in infant botulism(46) and has been associated with an increased likelihood of the requirement of mechanical ventilation.(21,34) Fewer than 2% of reported cases of infant botulism result in death.

VIII. Diagnosis

Botulism is probably substantially underdiagnosed. The diagnosis is not difficult when it is strongly suspected, as in the setting of a large outbreak, but since cases of botulism most often occur singularly, the diagnosis may pose a more perplexing problem. Findings from many outbreaks have suggested that early cases are commonly misdiagnosed. They may be diagnosed only retrospectively after death, when the subsequent clustering of cases of botulism-like illness finally alerts public health personnel to an outbreak of botulism.(47-49) Other cases are undoubtedly missed entirely. Entire outbreaks may even go undetected despite severe illness in patients; for example, one outbreak was recognized retrospectively only after a second cluster of cases was associated with the same vehicle.(44)

Botulism should be suspected in any adult with a history of acute onset of gastrointestinal, autonomic (e.g., dry mouth, difficulty focusing), and cranial nerve (diplopia, dysarthria, dysphagia) dysfunction or in any infant with poor feeding, diminished sucking and crying ability, neck and peripheral muscle weakness, and/or ventilatory distress.(50) The demonstration of bilateral cranial nerve findings and the documentation of neurologic progression (descending peripheral muscle weakness, ventilatory compromise) increase the level of suspicion. The diagnosis is even more likely if an adult patient has recently eaten home-canned foods or if family members are similarly ill, or both. If the typical clinical syndrome is present and no food item can be pinpointed as a means of transmission, a contaminated wound should be sought. If the typical syndrome is seen and a wound is identified, the wound should be explored and specimens taken for culture and toxicity testing even if the wound appears clean.

The differential diagnosis includes myasthenia gravis, stroke, Guillain-Barré syndrome, bacterial and chemical food poisoning, tick paralysis, chemical intoxication (e.g., from carbon monoxide, barium carbonate, methyl chloride, methyl alcohol, organic phosphorus compound, or atropine), mushroom poisoning, medication reactions (e.g., from antibiotics such as neomycin,

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XIV. Tables and Figures

Table 1. Outbreaks of foodborne botulism by toxin type, 1950-1996

	1950-1959	1960-1969	1970-1979	1980-1989	1990-1996	Total
Toxin type	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
A	14 (13.5)	12 (15.4)	68 (53.5)	48 (60.8)	25 (44.6)	167 (37.6)
B	3 (2.9)	10 (12.8)	28 (22.0)	13 (16.5)	7 (12.5)	61 (13.7)
E	7 (6.7)	9 (11.5)	15 (11.8)	16 (20.3)	20 (35.7)	67 (15.1)
F	0	1 (1.3)	0	0	2 (3.6)	3 (0.7)
Unknown	80 (76.9)	46 (59.0)	16 (12.6)	2 (2.5)	2 (3.6)	146 (32.9)
Total	104	78	127	79	56	444

CDC, by toxin type, 1950-1996

	1950-1959	1960-1969	1970-1979	1980-1989	1990-1996	Total
Toxin Type A						
Cases	39	30	164	119	60	412
Deaths	18	8	26	14	4	70
Case fatality ratio	46.2	26.7	15.9	11.8	6.7	17.0
Toxin Type B						
Cases	4	23	110	28	11	176
Deaths	2	4	6	1	0	13
Case fatality ratio	50.0	17.4	5.5	3.6	0.0	7.4
Toxin Type E						
Cases	21	35	28	62	47	193
Deaths	8	15	3	1	3	30
Case fatality ratio	38.1	42.9	10.7	1.6	6.4	15.5
Toxin Type F						
Cases	0	3	0	0	2	5
Deaths	0	0	0	0	0	0
Case fatality ratio	-	0.0	-	-	0.0	0.0
Total, toxin known						
Cases	64	91	302	209	120	786
Deaths	28	27	35	16	7	113
Case fatality ratio	43.8	29.7	11.6	7.7	5.8	14.4
Total, toxin unknown						
Cases	169	89	34	6	3	301
Deaths	30	15	11	0	0	56
Case fatality ratio	17.8	16.9	32.4	0.0	0.0	18.6
Percent cases due to unknown toxin type	72.5	49.4	10.1	2.8	2.4	27.7
Total						
Cases	233	180	336	215	123	1087

Table 3. **Number (%) of foodborne botulism outbreaks, by place of food processing, 1950-1996**

Process location	1950-1959 No. (%)	1960-1969 No. (%)	1970-1979 No. (%)	1980-1989 No. (%)	1990-1996 No. (%)	Total No. (%)
Home processed	51 (49.0)	44 (56.4)	85 (66.9)	69 (87.3)	40 (71.4)	289 (65.1)
Commercially processed	2 (1.9)	10 (12.8)	9 (7.1)	6 (7.6)	4 (7.1)	31 (7.0)
Unknown	51 (49.0)	24 (30.8)	33 (26.0)	4 (5.1)	12 (21.4)	124 (27.9)
Total	104	78	127	79	56	444

Table 4. Number (%) of foodborne botulism outbreaks, by food category and toxin type, 1950-1996

Toxin type	Vegetables	Fruits	Condiments	Dairy product	Beef	Pork	Poultry	Fish	Marine mammal	Other	Unknown	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
A	102 (61.1)	3 (1.8)	3 (1.8)	2 (1.2)	5 (3.0)	1 (0.6)	4 (2.4)	14 (8.4)	1 (0.6)	9 (5.4)	23 (13.8)	167
B	35 (57.4)	2 (3.3)	2 (3.3)	0	0	4 (6.6)	1 (1.6)	4 (6.6)	4 (6.6)	2 (3.3)	7 (11.5)	61
E	0	0	0	0	0	0	0	36 (53.7)	25 (37.3)	2 (3.0)	4 (6.0)	67
F	0	0	0	0	0	0	0	0	0	1 (33.3)	2 (66.7)	3
Unknown	43 (29.5)	3 (2.1)	1 (0.7)	1 (0.7)	1 (0.7)	2 (1.4)	1 (0.7)	3 (2.1)	0	3 (2.1)	88 (60.3)	146
Total	180 (40.5)	8 (1.8)	6 (1.4)	3 (0.7)	6 (1.4)	7 (1.6)	6 (1.4)	57 (12.8)	30 (6.8)	17 (3.8)	124 (27.9)	444

Table 5. Method of testing serum for botulinum toxin

Tube number	Volume of serum (ml)	Volume of antitoxin[a] (ml)	Type of antitoxin	Volume drawn into syringe	Volume injected into each mouse (ml)
1	1.0	0.0	None	0.8	0.4
2	1.0	0.25	A	1.0	0.5
3	1.0	0.25	B	1.0	0.5
4	1.0	0.25	E	1.0	0.5
5	1.0	0.25	F	1.0	0.5
6	1.0	0.25	ABCDEF[b]	1.0	0.5

[a] Mix antitoxin with serum and incubate 30 to 60 minutes at room temperature.

[b] Since type F toxin is rarely encountered, a trivalent antitoxin (types A, B, and E) reagent will be sufficient to confirm most cases of botulism; and tube number 5 (type F) can be prepared later if necessary.

Table 6. Method of testing extracts and culture fluids for botulinum toxin

Tube number	Volume of specimen (ml)	Treatment[a]	Type of antitoxin	Volume drawn into syringe (ml)	Volume injected into each mouse (ml)
1	1.0	None	None	0.8	0.4
2	1.0	Heat 100°C for 10 min	None	1.0	0.5
3	1.0	0.25 ml trypsin	None	1.0	0.5
4	1.0	0.25 ml antitoxin	A	1.0	0.5
5	1.0	0.25 ml antitoxin	B	1.0	0.5
6	1.0	0.25 ml antitoxin	E	1.0	0.5
7	1.0	0.25 ml antitoxin	F	1.0	0.5
8	1.0	0.25 ml antitoxin	ABCDEF[b]	1.0	0.5

[a] Mix antitoxin or trypsin with specimen and incubate 30 to 60 minutes at room temperature.

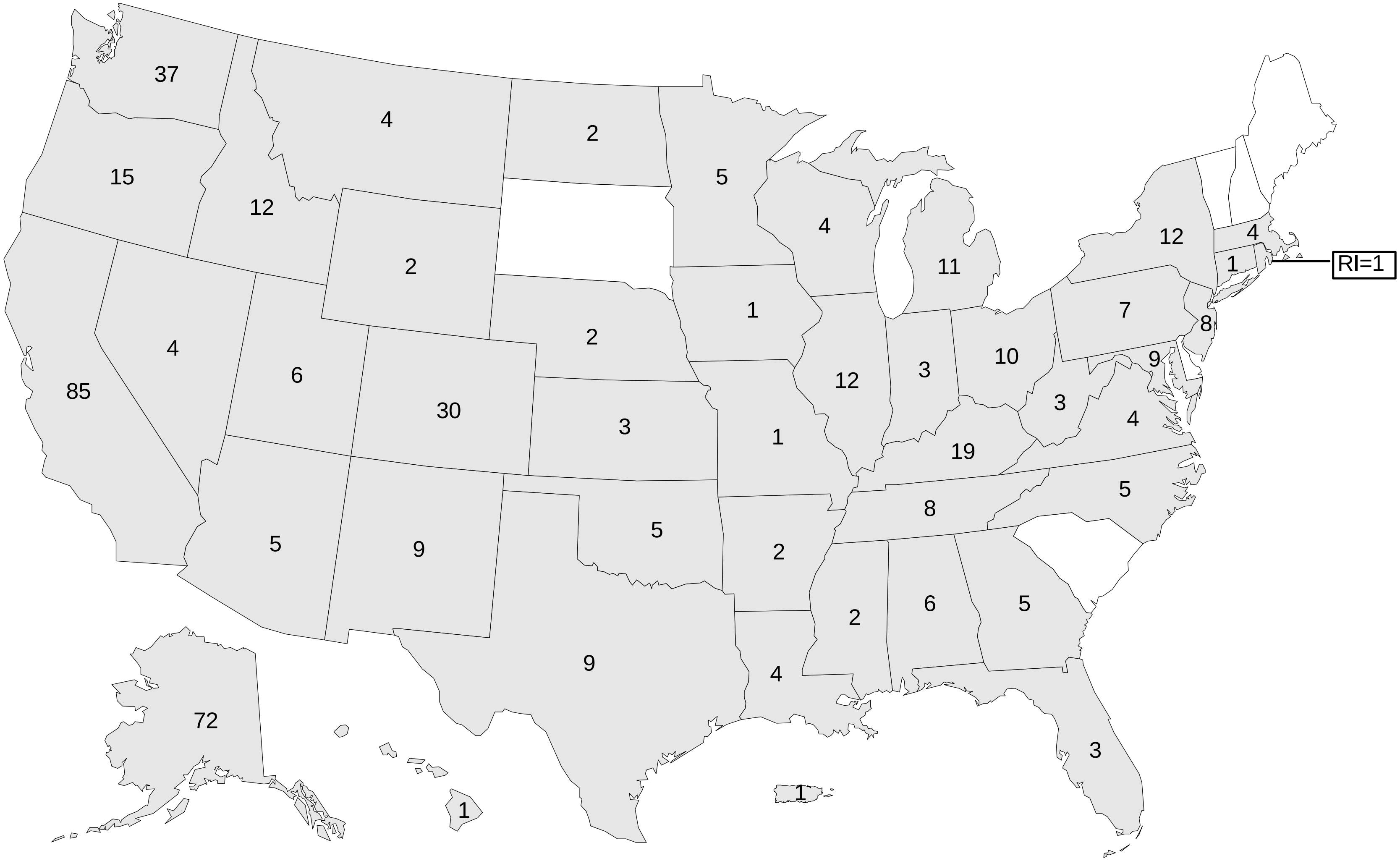
[b] Since type F toxin is rarely encountered, a trivalent antitoxin (types A, B, and E) reagent will be sufficient to confirm most cases of botulism; and, tube number 5 (type F) can be prepared later if necessary.

Table 7. Neutralization tests on trypsinized[a] extracts and culture fluids

Tube number	Volume of trypsinized[a] test material (ml)	Volume of antitoxin (ml)	Type of antitoxin[b]	Volume drawn into syringe (ml)	Volume injected into each mouse (ml)
1	1.25	0.25	A	1.2	0.6
2	1.25	0.25	B	1.2	0.6
3	1.25	0.25	E	1.2	0.6
4	1.25	0.25	F	1.2	0.6
5	1.25	0.25	ABCDEF	1.2	0.6

[a] Trypsinization: 6 ml test material + 1.5 ml 0.5% trypsin; incubate 30 minutes at 37ºC.

[b] Mix trypsinized test material and antitoxin and incubate 30 minutes at 37ºC.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12
4
12
4
2
11
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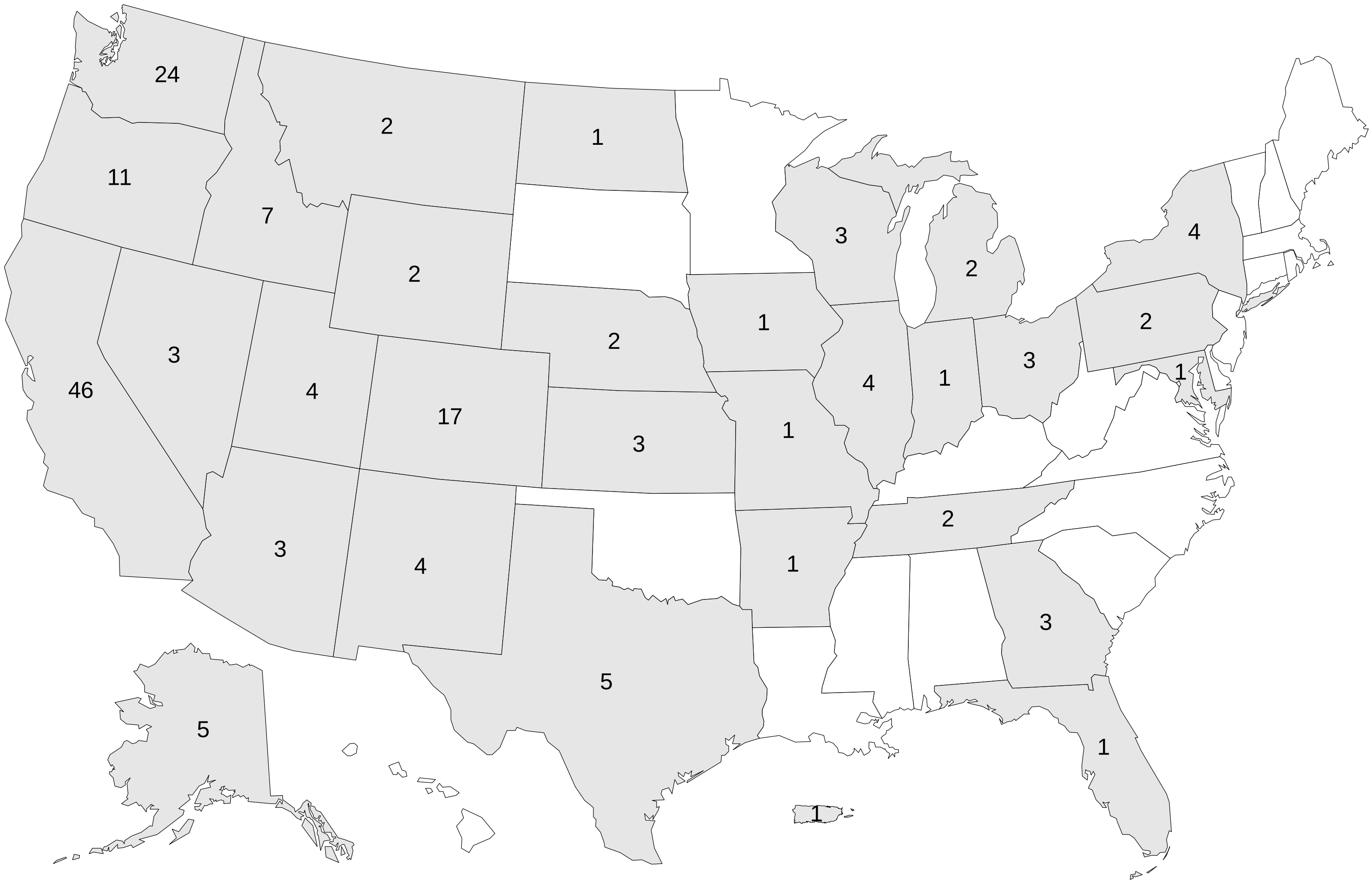
7
8
2
4
6
10
9
12
3
85
30
3
3
4
1
19
5
8
5
5
9
2
6
5
2
9
4
72
3
1
1

Figure 1. Outbreaks of foodborne botulism by state, 1950-1996*

* Multistate outbreaks are added to each involved state's total.



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11
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7
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2
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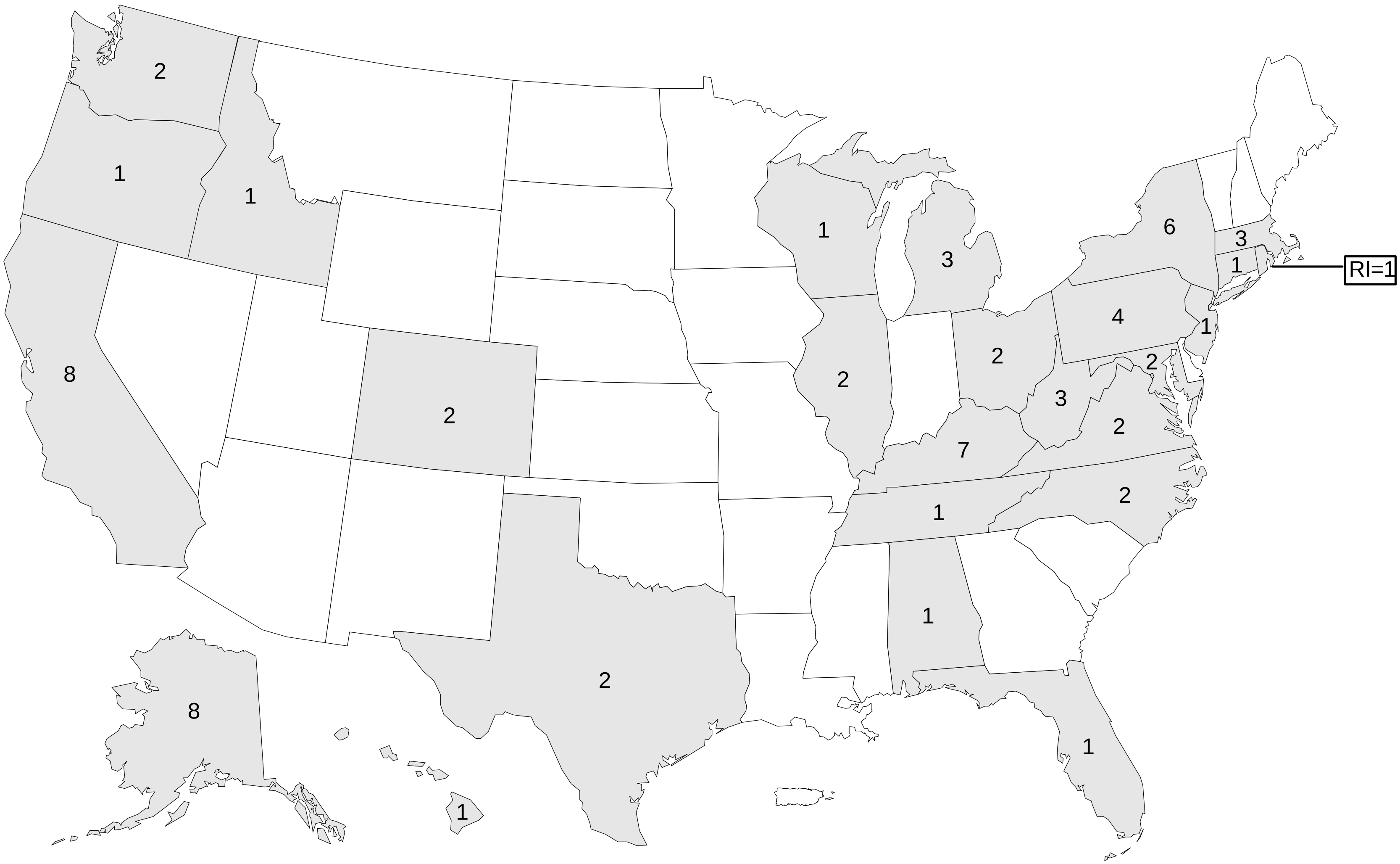
1
4
17
3
4
2
3
5
1
1
1
1
4
3
2
1
3
2
1
4
2
1
2
3
1
5
1

Figure 2. Outbreaks of foodborne botulism, toxin type A, by state, 1950-1996*

* Multistate outbreaks are added to each involved state's total.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2
2
3
2
7
1
2
1
1

Figure 3. Outbreaks of foodborne botulism, toxin type B, by state, 1950-1996*

* Multistate outbreaks are added to each involved state's total.

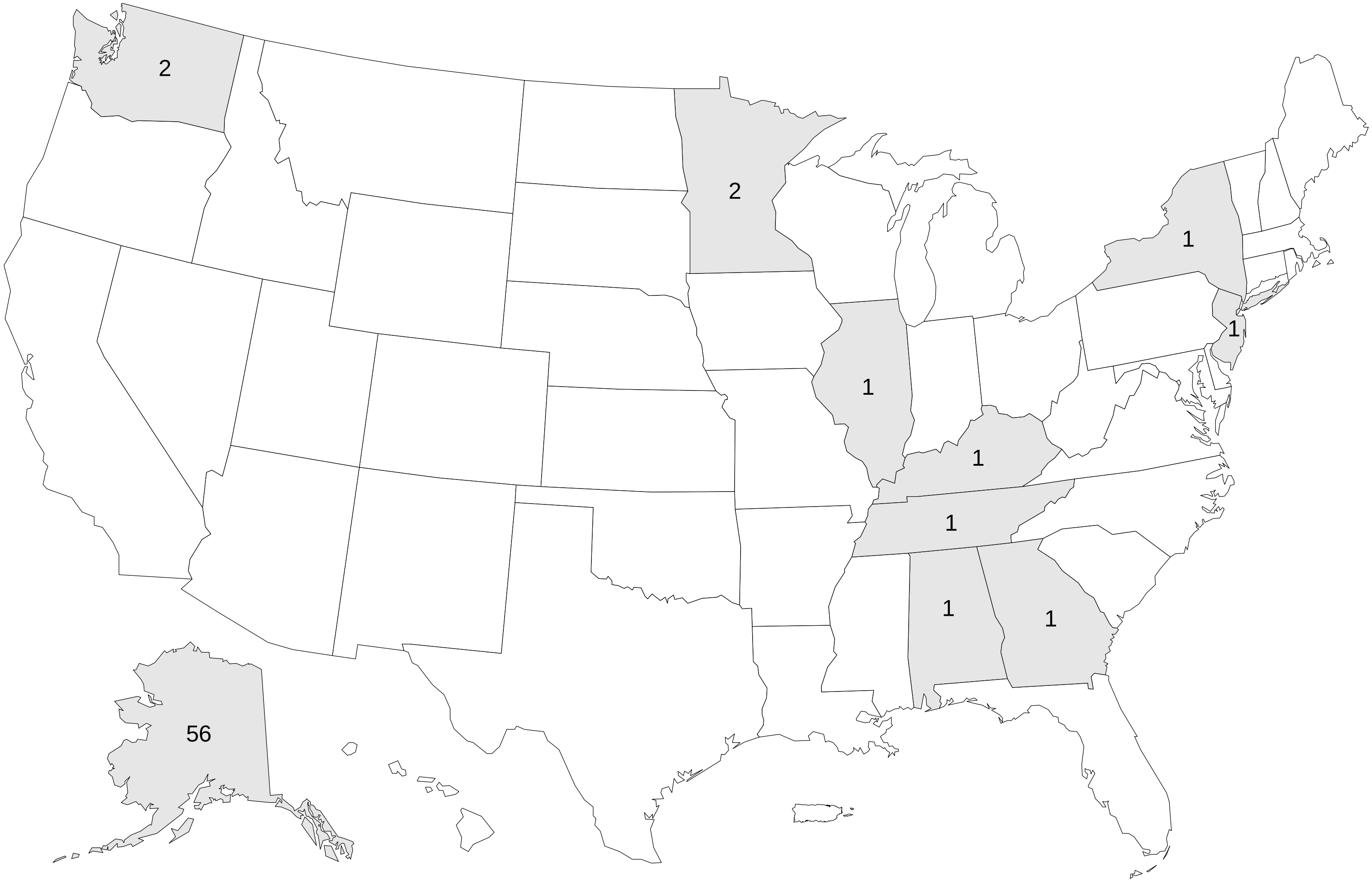


Figure 4. Outbreaks of foodborne botulism, toxin type E, by state, 1950-1996*

* Multistate outbreaks are added to each involved state's total.

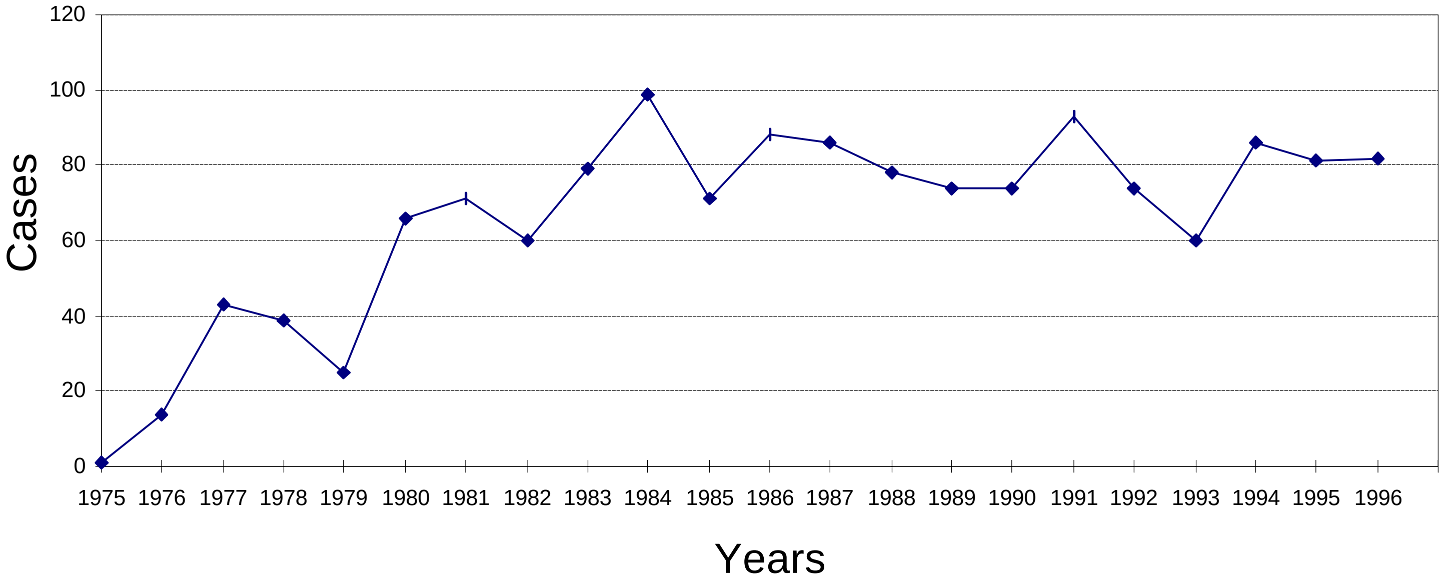
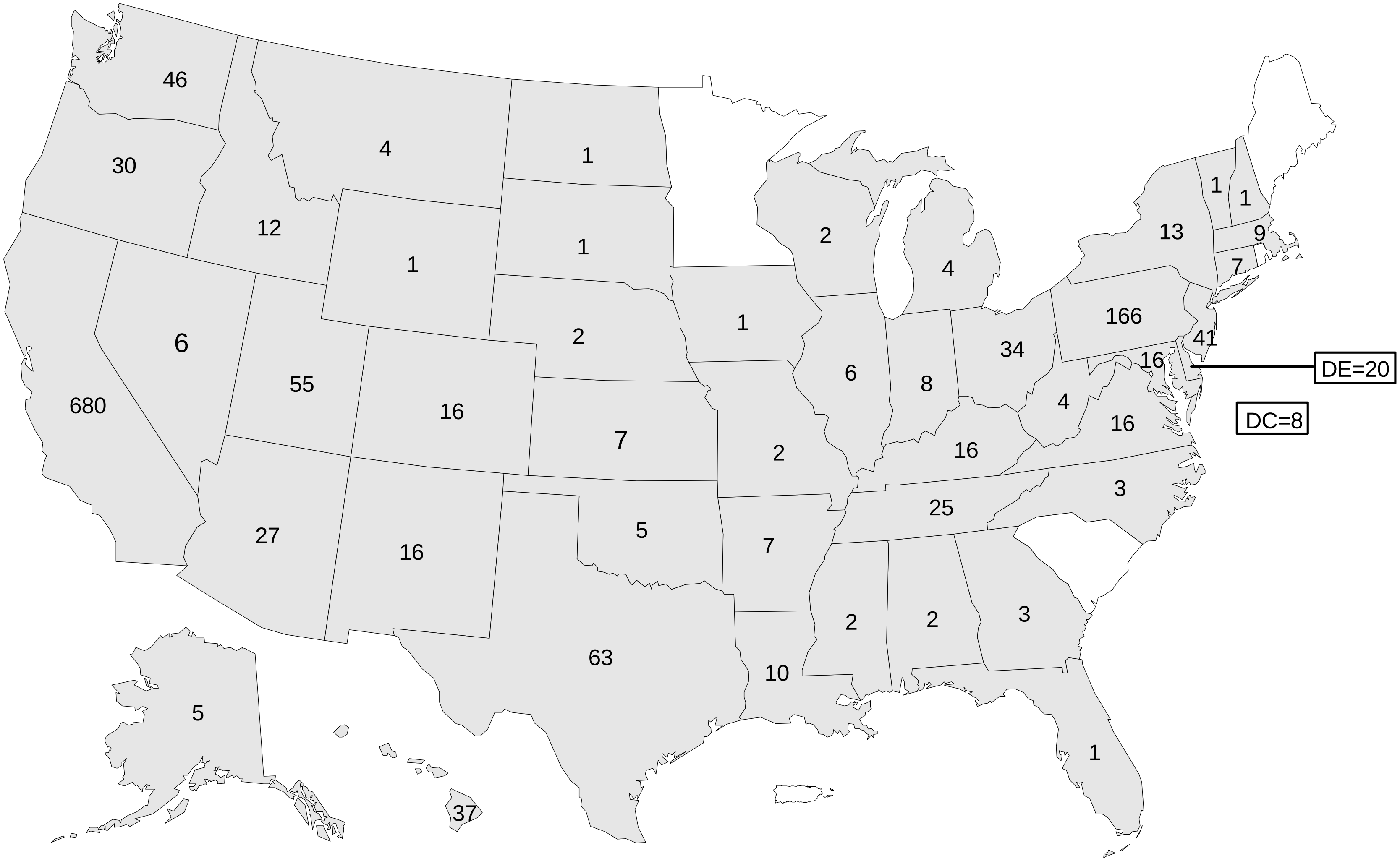


Figure 5. Cases of infant botulism, 1975-1996



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2
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680
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1
1
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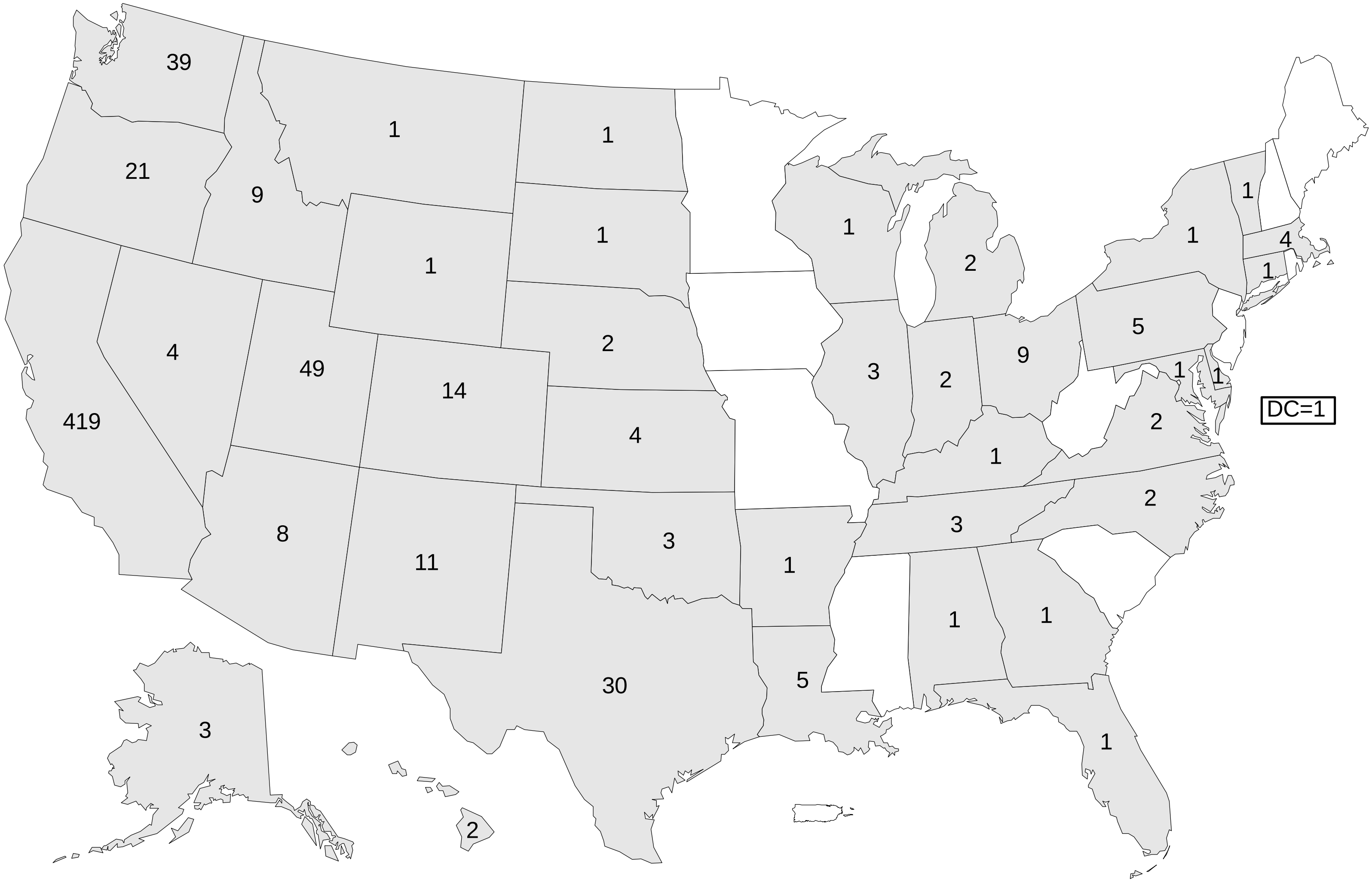
9
7
166
41
16
DE=20
DC=8
4
16
16
2
5
7
25
3
27
16
63
10
2
2
3
1
5
37

Figure 6. Outbreaks of infant botulism, by state, 1976-1996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1
4
419
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DC=1
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2
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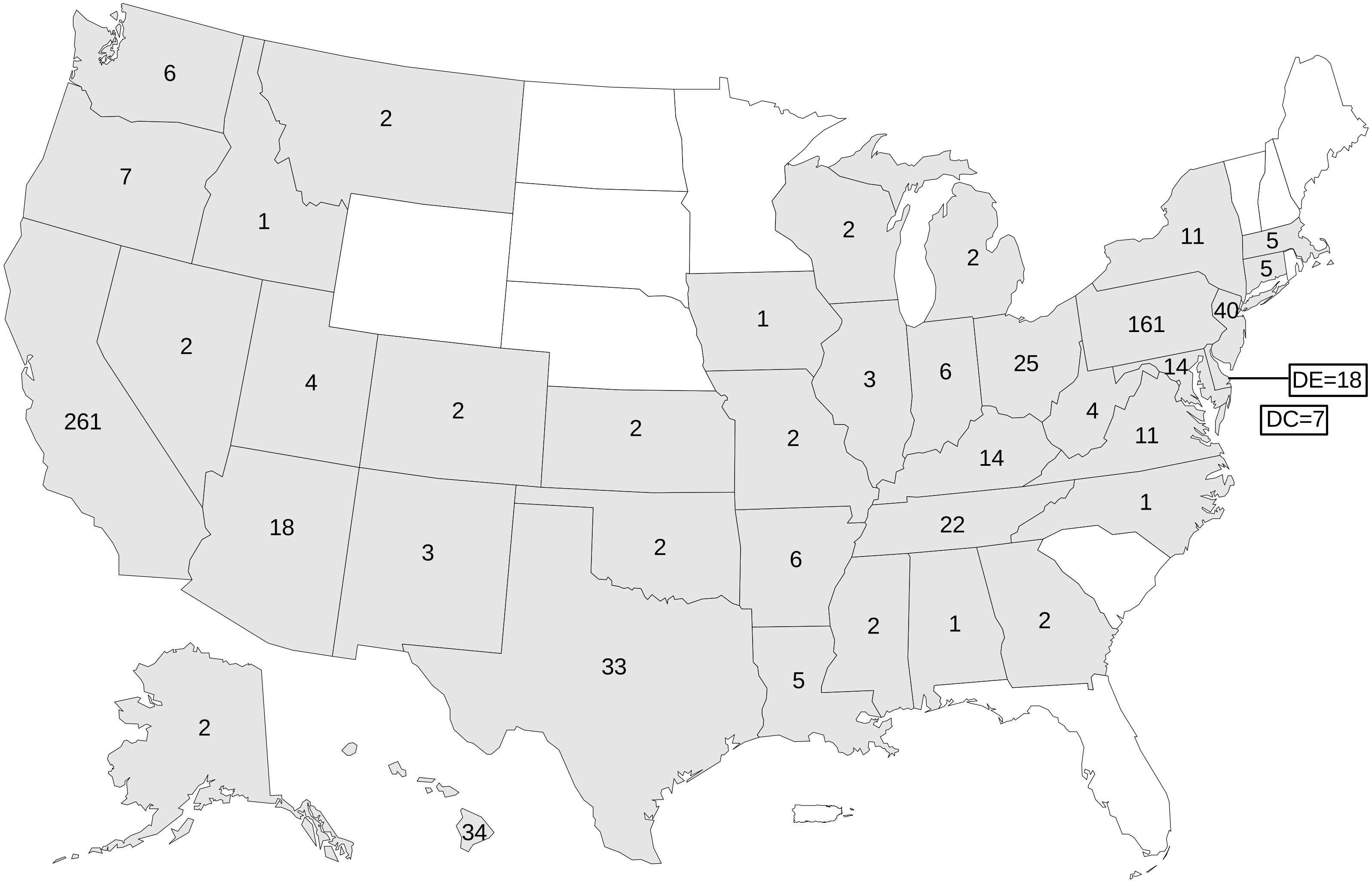
2

Figure 7. Outbreaks of infant botulism, type A, by state, 1976-1996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14
DE=18
DC=7
2
4
11
14
18
3
2
6
22
1
33
2
1
2
5
2
34

Figure 8. Outbreaks of infant botulism, type B, by state, 1976-1996

XV. Appendix