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# ARTICLE

# Global Occurrence of Infant Botulism, 1976–2006

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#### What's Known on This Subject

Infant botulism has been recognized in some, but not all, countries.

#### What This Study Adds

We present the global occurrence of infant botulism from 1976 to 2006 and document substantial variation in recognition that exists between continents and between countries within continents. Epidemiological information on the non-US cases, including the frequency of feeding honey, is also included.

#### ABSTRACT -

OBJECTIVE. To summarize the worldwide occurrence of reported infant (intestinal toxemia) botulism cases since first recognition of the disease in 1976.

PATIENTS AND METHODS. We collected information on infant botulism cases by active and passive surveillance, by provision of therapeutic Human Botulism Immune Globulin to suspected cases, and by searching the medical literature. We defined a case as laboratory-confirmed botulism that occurred in an infant  $\leq 12$  months of age that was not caused by the ingestion of botulinum toxin in food.

RESULTS. Twenty-six countries representing 5 continents reported the occurrence of at least 1 case of infant botulism among their residents. The United States, Argentina, Australia, Canada, Italy, and Japan, in this order, reported the largest number of cases. A history of honey exposure was significantly more common among case subjects hospitalized outside of the United States than among those who were recently hospitalized in California.

CONCLUSIONS. Most countries have not yet reported cases of infant botulism. This limited reporting of the disease to date contrasts with the known global occurrence of *Clostridium botulinum* spores in soils and dust and suggests that infant botulism may be underrecognized, underreported, or both. When bulbar palsies, hypotonia, and weakness are present, physicians should consider the possibility of infant botulism even if the patient has not been fed honey. Publication of additional case reports and surveillance summaries will enhance understanding of the occurrence and extent of this underrecognized disease. *Pediatrics* 2008;122:e73–e82

NFANT BOTULISM IS an uncommon disease that occurs when ingested spores of the common soil-dwelling bacterium *Clostridium botulinum* (or, rarely, toxigenic *Clostridium butyricum* or *Clostridium baratii*) germinate and produce botulinum neurotoxin in the colon. The resulting illness varies in severity from outpatient mild hypotonia to hospitalized systemic flaccid paralysis to sudden unexpected death.<sup>1-4</sup> The broad

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#### Key Words

*Clostridium botulinum*, infant botulism, botulinum toxin, epidemiology, Human Botulism Immune Globulin, BabyBIG

#### Abbreviations

BIG-IV—Botulism Immune Globulin Human (Intravenous) CDC—Centers for Disease Control and Prevention CDHS—California Department of Health Services CDPH—California Department of Public Health IBTPP—Infant Botulism Treatment and Prevention Program UCBSPH—University of California-Berkeley School of Public Health Accepted for publication Feb 25, 2008

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spectrum of severity and nonspecific presentation may make infant botulism difficult to diagnose and result in its being underrecognized and underreported.<sup>2</sup>

To assess the global occurrence of infant botulism, we identified countries that have reported infant botulism cases, summarized the cases reported, and compared selected epidemiological and clinical features of cases identified outside of the United States with those identified inside the United States.

### PATIENTS AND METHODS

#### **Case Definition**

We defined a case as laboratory-confirmed botulism that occurred in an infant  $\leq 12$  months of age that was not caused by the ingestion of botulinum toxin in food. (Two laboratory-proven cases of foodborne botulism in infants [1 in the United States caused by home-canned baby food<sup>5</sup> and 1 in Hungary caused by commercially canned baby food<sup>6</sup>] have occurred.) All cases included in this report had the diagnosis of infant botulism established by use of the

mouse-neutralization bioassay7 that used either monovalent, toxin-type-specific botulinum antitoxin (eg, anti-A, anti-B, anti-F, etc) or, when these reagents were not available, polyvalent antibotulinum toxin antitoxin. We excluded case reports<sup>3,4,8-11</sup> of deceased infants who were found postmortem to have C botulinum toxin or organism in their intestines, because neither the United States nor other countries have a systematic method for ascertaining the presence of *C* botulinum among infants who die unexpectedly. A case was designated as occurring in a particular country if the infant had onset of illness in that country or had spent at least 2 weeks before the onset of illness in that country. If the location of the infant during or before the onset of illness was unavailable, the case was assigned to the infant's country of residence.

## **Case Ascertainment**

#### In the United States

We collected information on infant botulism cases that occurred in the United States by using 3 methods: (1) nationwide surveillance through the provision of Botulism Immune Globulin Human (Intravenous) (BIG-IV) for suspected infant botulism cases<sup>12,13</sup>; (2) statewide surveillance in California; and (3) collaboration with the Centers for Disease Control and Prevention (CDC).

Since its creation in 1992, BIG-IV has been available, initially as an investigational new drug and later as a licensed product, through the California Department of Public Health (CDPH) (until July 1, 2007, the California Department of Health Services [CDHS]) Infant Botulism Treatment and Prevention Program (IBTPP) for the treatment of patients with infant botulism who are hospitalized in the United States.<sup>12,13</sup> Physicians who suspect that their patients may have infant botulism can telephone the IBTPP (510-231-7600) for diagnostic and treatment consultation that includes the provision of BIG-IV. Through this process the IBTPP has collected demographic, clinical, and laboratory information on each patient with infant botulism it has treated.

The CDPH has provided diagnostic laboratory services for all patients with infant botulism in California since 1976, the year in which infant botulism was first recognized to be a distinct clinical entity.<sup>14,15</sup> As a consequence, the IBTPP has been able to investigate all laboratory-confirmed infant botulism cases in California. For most California cases, a detailed parental interview was completed regarding environmental and dietary exposures, including exposure to honey.

The CDC collects information on infant botulism cases through passive surveillance based on annual reporting of cases by state health departments.<sup>16</sup> Each year the IBTPP and the CDC compare data collected from their separate, but overlapping, surveillance activities to create a complete line listing of all laboratory-confirmed infant botulism cases in the United States. History of honey exposure is not systematically collected by the IBTPP or CDC among cases outside of California. Accordingly, statistics presented in this article regarding honey exposure among cases inside the United States are based

on the experience of California cases only. Differences over time in the proportion of California cases with a history of honey exposure were evaluated by using the Mantel-Haenszel  $\chi^2$  test.

# Outside of the United States

We collected information on cases that occurred outside the United States by using 3 methods: (1) active and passive surveillance through correspondence with colleagues in other countries; (2) provision of BIG-IV for suspected infant botulism cases; and (3) scientific literature searches.

During the years immediately after the initial recognition of infant botulism in the United States, the CDHS conducted active surveillance for infant botulism cases outside the United States by contacting physicians and public health officials in other countries to determine if they had identified cases. In recent years, the IBTPP has learned about cases of infant botulism worldwide from physicians who were treating patients with infant botulism and had contacted the IBTPP through its Web site (www.infantbotulism.org) for advice on the diagnosis, treatment, and investigation of infant botulism cases. Since 2005, the IBTPP has made BIG-IV available to patients with infant botulism who are hospitalized outside of the United States.

We searched scientific literature databases by using PubMed on March 2, 2006, March 21, 2007, and January 18, 2008, and restricted our search to articles on humans using the following search terms: ("botulism" [Medical Subject Heading (MeSH)] or "*Clostridium botulinum*" [MeSH]) and ("infant" [MeSH] or infant or infantile). To identify relevant articles that were not indexed in PubMed, we searched PubMed on November 7, 2006, March 21, 2007, and January 18, 2008, by using the following search terms: [(botuli\*[tiab] or clostridium\*[tiab]) and infant\*[tiab]] not Medline[sb].

To find relevant articles not available through PubMed, the University of California-Berkeley School of Public Health (UCBSPH) library searched additional databases on August 3, 2006, and January 18, 2008, by using key words "infant" and "botulism." The databases searched included PapersFirst, Global Health, Web of Science, CAB Abstracts, Biosis Previews, Environmental Science and Pollution Management, Lilacs, IndMed, KoreaMed, NiPAD, Agricola, and Africa-Wide. In addition to these literature searches, we reviewed articles collected by the IBTPP since 1976 through other literature searches.

For each citation identified in the database searches, we reviewed the title, country of origin, abstract, and key words. Articles chosen for manual review were case reports, case series, reviews, original research studies, or summaries of infant botulism cases published by authors outside the United States or pertaining to cases that occurred outside the United States. Articles without abstracts, ambiguous abstracts, or abstracts not in English were also collected for manual review. We excluded articles with detailed abstracts that did not mention botulism in an infant or that only mentioned cases within the United States. Information on individual or groups of infant botulism cases were abstracted from the articles chosen for manual review by using a standard abstraction form. Articles not published in English were abstracted by people who are fluent readers of these languages. For case reports of infant botulism, we abstracted for each case subject the country of residence, age at disease onset, gender, honey exposure, history of travel, laboratory confirmation of diagnosis, *C botulinum* toxin type, intubation or ventilation of patient, death, and length of hospital stay. For articles that reported groups of cases, we abstracted the country reporting the cases, time period, number of cases, and *C botulinum* toxin type.

From the abstracted articles we compiled and summarized information on cases of infant botulism according to country. If a case was found to be reported in more than 1 article, we used the most detailed account of the case. If it was impossible to determine if a case in a particular article was a duplicate of another case report or a duplicate of a report from personal correspondence, we contacted (when possible) surveillance officials in the country in which the case was reported for clarification. In instances when we were unable to verify duplicate reports, we assumed that the cases in question were duplicates so that we would not overstate the number of cases reported per country.

## RESULTS

In the United States from 1976 through 1991, 1070 infant botulism cases (511 diagnosed by the IBTPP laboratory and 559 reported through passive surveillance to the CDC) were identified. From 1992 (when the pivotal clinical trial of BIG-IV in California began<sup>12,13</sup>) through 2006, the IBTPP provided BIG-IV to 789 patients with infant botulism who were living in the United States. During the same period, 560 patients with infant botulism who were not treated with BIG-IV (87 confirmed by the IBTPP laboratory and 473 cases reported through passive surveillance to the CDC) were identified. In total, case ascertainment within the United States identified 2419 cases (average incidence: 2.1 cases per 100 000 live births). The numbers of male and female case subjects were approximately equal. The mean age at onset of infant botulism cases was 13.8 weeks (median: 12.0 weeks [interquartile range: 7.0-19.0 weeks]) and ranged from 0 to 52 weeks. Nine case subjects (0.4%) were identified in outpatient settings and did not require hospitalization during the course of illness. Twenty (0.8%) case subjects died after hospital admission for infant botulism, with the most recent death occurring in 2004. Two (10%) of the infants who died had received BIG-IV. One case subject experienced a sustained cardiopulmonary arrest at home before treatment with BIG-IV, and the other was diagnosed postmortem with illness caused by C baratii type F neurotoxin (which BIG-IV does not neutralize) and succumbed to Clostrid*ium difficile* colitis. Among those diagnosed in California, the proportion of cases that included a history of honey exposure decreased significantly over time from 39.7% in the 1970s to 14.7% in the 1980s, 5.3% in the 1990s,

and just 4.7% in the 2000s (P < .0001; Mantel-Haenszel  $\chi^2$  test for trend).

Outside of the United States, active and passive surveillance for infant botulism identified cases that were not reported in the literature as well as cases that were reported. Cases not reported in the literature included 17 cases in Canada (John Austin, PhD, Health Canada Bureau of Microbial Hazards, written communication, May 2007), 15 cases in Australia (James Manson, MD, written communication, August 1980; Lloyd Shield, MD, written communication, January 1987; Paul Roche, PhD, Australian Government Department of Health and Ageing, written communication, September 2006; and John Carnie, MD, written communication, January 2007), 5 cases in Japan (Chie Monma, PhD, Tokyo Metropolitan Research Laboratory of Public Health, verbal communication, November 2006; and Motohide Takahashi, PhD, Japan National Institute of Infectious Disease, verbal communication, October 2007), 4 cases in Italy (Lucia Fenicia, PhD, Istituto Superiore di Sanità, written communication, May 2007), and 2 cases in Sweden (Ninna Gullberg, MD, written communication, August 2003; Bjorn Stjernstedt, MD, written communication, March 2006; and Theresa Smith, US Army Research Institute of Infectious Diseases, written communication, January 2008).

In addition, the IBTPP provided BIG-IV to 1 resident of Mexico who was hospitalized in the United States and to 4 residents of Canada who were hospitalized there.

Through the PubMed searches, 368 citations were identified. Of these, 33% (n = 122) met the criteria for manual review and were abstracted. The UCBSPH library search yielded 44 citations, 37 of which were available for abstraction. In addition, 37 case reports and 14 summary reports collected by the IBTPP over the years were abstracted. A total of 210 articles were abstracted (122 from the PubMed search, 37 from the UCBSPH library search, and 51 from the IBTPP files). Seventy percent (n = 147) of these articles were found to contain information about cases of infant botulism that occurred in countries other than the United States.

Through the 3 search methods, a total of 524 infant botulism cases from 25 countries in Asia, Australia, Europe, North America, and South America were identified (Table 1). Argentina reported the largest number of cases (n = 366), 11 times more than the number of cases reported by Australia (n = 32), which was the country with the second highest number of cases. Canada (n = 27), Italy (n = 26), and Japan (n = 22) reported the next highest numbers of cases, respectively.

Recognition of infant botulism cases spread globally after its initial recognition in the United States in late 1976 (Fig 1). The first non-US infant botulism cases became known  $\sim$ 1 year later when England and Australia identified their first cases. In the subsequent 3 decades, other European, North American, South American, and Asian countries identified their first cases.

Demographic and clinical information was available for  $\sim$ 20% of the cases reported outside the United States (Table 2). Among these cases, the numbers of male and female patients were almost equal. On average, the case

Location	Time Period	Total No. of Infant Botulism Cases	Type A, n	Type B, n	Other Type(s), n	Toxin Type Not Reported or Not Determined
Global total, excluding the United States	1976–2006	524	437	56	12	19
Asia						
China <sup>17,18</sup>	1986–1989	2	0	1	0	1ª
Japan <sup>19–21</sup>	1986–2006	22	14	3	2 <sup>b</sup>	3
Taiwan <sup>22</sup>	1987	1	0	1	0	0
Australia <sup>23–36</sup>						
Total	1978–2006	32	12	15	1c	4ª
New South Wales		7	_	—	—	—
South Australia		9	—	—	—	—
Victoria		9		—	—	—
Queensland		5			—	—
Northern Territory		1	—	—	_	_
Unknown		1	—	—	—	—
Europe						
Czech Republic <sup>37</sup>	1979	1	0	1	0	0
Denmark <sup>38,39</sup>	1995-2000	2	0	0	1 <sup>d</sup>	1e
France <sup>40–42</sup>	1983-2006	4	1	3f	0	0
Germany <sup>43–46</sup>	1993-2000	4	2	0	0	2 <sup>e</sup>
Greece47	2006	1	1	0	0	0
Hungary <sup>48,49</sup>	1995-2002	2	0	0	19	1e
Italy <sup>49–58</sup>	1984-2006	26	4	17	5 <sup>h</sup>	0
Netherlands <sup>59</sup>	2000-2005	3	1	2	0	0
Norway <sup>39,60</sup>	1997-1999	4	4	0	0	0
Spain <sup>49,61–63</sup>	1985-2002	9	2	2	0	5 <sup>e</sup>
Sweden <sup>64</sup>	1985-2006	3	2	0	1 <sup>i</sup>	0
Switzerland <sup>65</sup>	1987	1	1	0	0	0
United Kingdom <sup>66–70</sup>	1978-2001	5	2	2	1 <sup>i</sup>	0
Middle East						
Israel71-73	1994-2006	2	0	2	0	0
Kuwait <sup>74</sup>	2005	1	0	0	0	1ª
Yemen <sup>75</sup>	1989	1	0	1	0	0
North America						
Canada <sup>76–81</sup>						
Total	1979–2006	27	22	5	0	0
Alberta	1996-2006	2		_	_	_
British Columbia	1985-1997	3		_	_	_
Ontario	1979-2006	3		_	_	_
Quebec	1985	1		_	_	_
New Brunswick	2006	1			_	_
Unknown	1996-2006	17			_	_
Mexico	1990 2000					
Baja California	2001	1	1	0	0	0
United States, all states, except Rhode Island	1976–2006	2419	1079	1310	28 <sup>j</sup>	2ª
South America						
Argentina <sup>82–86</sup>	1982-2005	366	366	0	0	0
, agentina						0
Chile <sup>87–89</sup>	1984–1995	3	2	0	0	1a

## TABLE 1 Reported Infant Botulism Cases According to Continent and Country, 1976–2006

- indicates that the distribution of toxin types by state/province was not available.

<sup>a</sup> C botulinum toxin or organisms were identified in feces by polyvalent antitoxin, but the individual toxin type was not reported.

<sup>b</sup> One neurotoxigenic *C butyricum* type E, 1 type C.

<sup>c</sup> "C. botulinum type A and type B were isolated from faecal samples from the infant."<sup>25</sup>

d "A strain of C. botulinum producing toxin type A and E was identified in stool initially. Further identification of the toxin was not possible."38

<sup>e</sup> Toxin type was confirmed by polyvalent antitoxin but not typed by monovalent antitoxins.

<sup>f</sup>One type B case was reported to have the characteristics of an "AB" type.<sup>42</sup>

<sup>9</sup> Neurotoxigenic *C baratii* type F.

<sup>h</sup> Four neurotoxigenic *C butyricum* type E, 1 type Ab.

<sup>i</sup> Type Bf.

<sup>j</sup> One type A and B (most likely a Ba or Ab from today's perspective), 14 type Ba, 4 type Bf, 1 type E, and 8 type F cases, in 6 of which C baratii was isolated.

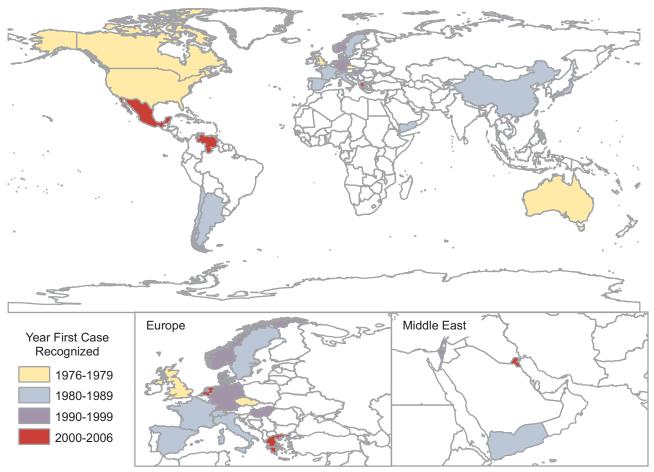


FIGURE 1

Global recognition of infant botulism according to country: 1976-2006.

subjects were 14.3 weeks old at disease onset and received inpatient hospital care for 7.3 weeks. While hospitalized, 68% of the 91 case subjects with information available required intubation or ventilation. Honey exposure was reported in more than half (59%) of the 106 cases with this information available. Illness caused by type A toxin was reported most commonly (83.4%), followed by disease caused by type B toxin (10.7%), *C butyricum* type E toxin (0.9%), and other less common toxin types (Table 2). Death after hospital admission for infant botulism was infrequently reported (n = 6 [1.1%]).

### DISCUSSION

To date, all inhabited continents except Africa have reported cases of infant botulism. The lack of reported cases in Africa probably results from difficulty in diagnosing cases rather than from absence of the illness, because *C botulinum* is known to exist in African soil<sup>91</sup> and has caused foodborne botulism there.<sup>92</sup>

Although infant botulism has been detected on almost all continents, reports of cases have been distributed unevenly. For example, excluding North America, South America has reported more cases than any other continent, although the reports have come from just 3 of its 13 countries. Also, almost all South American cases were reported from Argentina. In contrast, no cases have been reported from Brazil or Colombia despite their having larger populations and greater birth rates.<sup>93</sup> In addition, *C botulinum* types A and B are known to exist in Brazilian soil.<sup>94</sup>

In contrast to South America, reports of cases were distributed somewhat more evenly among European countries, which may indicate a comparable ability among European countries to detect cases, a similarity in environmental distribution of spores, or both. The intercountry and intracountry variability in reporting infant botulism cases may reflect differing environmental distributions of C botulinum. In Argentina, the occurrence of infant botulism and the prevalence of botulinum toxinproducing clostridia in the soil were associated in some but not all regions.<sup>86</sup> Other explanations for the variability in the reporting of cases may include differing abilities to detect and report cases, differing cultural practices in the feeding of honey and other foods to infants, differing levels of exposure to dust or soil, and differing susceptibility of patients attributable to other presently unknown factors.

Ingestion of honey, a recognized vehicle for *C botulinum* spores,<sup>95–99</sup> remains the only identified avoidable

TABLE 2 Demographic Characteristics of 524 Infant Botulism Cases Reported Outside of the United States, 1978–2006

Demographic	Value
Age at disease onset	
n	139
Mean, wk	14.3
Median, wk	12.9
Interquartile range, wk	8.9–19.0
Minimum, wk	2
Maximum, wk	52
Gender, <i>n</i> (%)	
Male	63 (12.0)
Female	58 (11.0)
Not reported	403 (77.0)
Total	524 (100.0)
History of honey exposure, n (%)	
Yes	63 (12.1)
No	43 (8.3)
Not reported	418 (79.6)
Total	524 (100.0)
Toxin type, n (%)	
A	437 (83.4)
Ab	1 (0.2)
A and B <sup>a</sup>	1 (0.2)
A and E <sup>b</sup>	1 (0.2)
В	56 (10.7)
Bf	2 (0.4)
C	1 (0.2)
Ec	5 (0.9)
F	1 (0.2)
Not determined	19 (3.6)
Total	524 (100.0)
Intubated/ventilated, n (%)	
Yes	61 (11.6)
No	30 (5.7)
Not reported	433 (82.7)
Total	524 (100.0)
Length of hospital stay <sup>d</sup>	
n	78
Mean, wk	7.3
Median, wk	4.8
Minimum, wk	0.4
Maximum, wk	36.6
Died, n (%)	
Yes <sup>e</sup>	6 (1.1)
No	518 (98.9)
Total	524 (100.0)

<sup>a</sup> "C. botulinum type A and type B were isolated from faecal samples from the infant."<sup>25</sup>

 $^{\rm b}$  "A strain of C. botulinum producing toxin type A and E was identified in stool initially. Further identification of the toxin was not possible."  $^{\rm Y38}$ 

<sup>c</sup> Neurotoxigenic *C butyricum* type E was isolated.

<sup>d</sup> Excludes length of stay for the patients who died while in the hospital.

<sup>e</sup> Deaths reported in Argentina<sup>85</sup> (n = 5) and the Netherlands<sup>59</sup> (n = 1); excludes cases of SIDS in which *C* botulinum was identified.<sup>34,8–11</sup>

risk factor for acquiring infant botulism.<sup>100,101</sup> Illness in case subjects without a history of honey exposure is presumed to be a result of ingestion of spores from environmental sources, such as microscopic dust,<sup>1,3,102</sup> because extensive study of food and nonfood items in various laboratories has consistently found *C botulinum* only in honey.<sup>97,103</sup> However, rare exceptions to this general finding are known. A recent case in the United Kingdom was traced to *C botulinum* spores in powdered infant formula,<sup>70,104</sup> and in a single instance in Canada not associated with illness, *C botulinum* spores were identified in an infant cereal.<sup>97</sup> In Argentina, *C botulinum* has been isolated from herbal (chamomile) tea<sup>105</sup> and from 5 species of medicinal herbs commonly given to infants in that country (María I. Bianco, PhD, Carolina Lúquez, PhD, Rafael A. Fernández, PhD, written communication, 2008).<sup>106</sup>

As occurs in the United States,<sup>107</sup> in most countries the toxin types of C botulinum that caused cases of infant botulism reflected the geographical distribution of toxin types of C botulinum spores found in that country's environment.<sup>108–116</sup> However, some cases with a history of honey exposure were found to be affected by C botulinum toxin types that are not native to their environment. For example, all 4 cases reported in Norway showed a history of honey exposure and were type A, although C *botulinum* type A has not been found in soil in Norway<sup>111</sup> or in honey produced in Norway.96 The honey consumed by 1 of the Norwegian case subjects originated in Argentina,60 where C botulinum type A has commonly been found in soil<sup>109</sup> and in locally produced honey. C botuli*num* spores have also been found in honeys produced in Asia, Europe, and North America.95,99

Although the information was available for only 20% of case subjects living outside the United States, honey exposure was reported ~12 times more frequently in these cases than in cases diagnosed in California since 2000. A history of feeding honey was particularly common among case subjects living in the Middle East, Germany, Norway, Spain, and Venezuela. This observation suggests that either physicians in these regions are recognizing mainly those infant botulism cases that have a history of honey exposure or exposure to environmental C botulinum spores is a less common means of acquiring the disease in these countries. The latter possibility seems unlikely in light of the US experience. Hence, physicians should consider the possibility of infant botulism in a patient with bulbar palsies, hypotonia, and weakness even if there is no history of honey ingestion.

The significant decline over 3 decades in the proportion of California cases with a history of honey exposure may reflect an increasing familiarity with the illness among California health care providers during this period. In the 30 years since the first cases of infant botulism were recognized in California, physicians in California have diagnosed and treated almost 1000 patients with infant botulism. Developing familiarity with infant botulism in low-incidence countries by sharing case histories through grand rounds or regional educational seminars may lead to an enhanced ability to recognize the illness in the absence of a history of honey exposure.

Information on intubation and ventilation was available for only 17% of case subjects who were hospitalized outside the United States. These patients seemed somewhat more likely to require intubation or ventilation than did patients hospitalized within the United States. Sixty-seven percent of the case subjects hospitalized outside of the United States required intubation or ventilation, compared with 56% of patients with infant botulism in California who were hospitalized in the placebo group of the 1992–1997 randomized, controlled trial of Human Botulism Immune Globulin.<sup>12</sup> These observations suggest that outside of the United States, case subjects with severe disease are recognized more often than are those with less severe disease and that mild-to-moderate cases of infant botulism may be occurring undetected. Alternatively, these observations may represent a possible publication bias, in that case reports of more severely ill patients may be more likely to be published.

Patients with infant botulism who were hospitalized inside and outside of the United States were similar in their distributions of age and gender. The age distribution of infant botulism, centering around 3 to 4 months of age and spanning from the first weeks of life to  $\sim 1$ year of age, continues to be a defining feature of the disease.<sup>2</sup> Perhaps coincidentally, the age distribution of hospitalized patients with infant botulism is essentially indistinguishable from the age distribution of victims of sudden infant death syndrome (crib death) cases.<sup>1,2,117–119</sup> In addition to the United States, <sup>120</sup> 5 countries<sup>3,4,8–11</sup> have documented the presence of *C botulinum* in the intestinal contents of infants who died suddenly. These findings are consistent with the possibility that *C* botulinum may cause a portion of the deaths now classified as SIDS in some,<sup>1,3,4,8–11</sup> but not all,<sup>121</sup> parts of the world.

## CONCLUSIONS

Aside from honey-associated cases, the occurrence of infant botulism in the United States, and presumably the rest of the world, is thought to reflect the environmental distribution of the spores and the ability of physicians to identify and report the disease.<sup>2</sup> More accurate case ascertainment worldwide would be possible by mandating the reporting of infant botulism to each country's national health agency. Publication of additional case reports and surveillance summaries will enhance knowledge of the global epidemiology of infant botulism and enable its improved prevention, treatment, and control.

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# **Global Occurrence of Infant Botulism, 1976 2006**

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