

## Note

# Two Cases of Foodborne Botulism Type E and Review of Epidemiology in France

A. Boyer, C. Girault, F. Bauer, J.-M. Korach, J. Salomon, E. Moiro, J. Leroy, G. Bonmarchand

**Abstract** In 1999, two new cases of type E botulism were observed in French hospitals. Since this type of botulism is uncommon in France, the cases prompted a national epidemiological study. Sixteen cases of type E botulism, including the two cases reported here, occurred between 1952 and 1999. The clinical and treatment characteristics of all cases were evaluated, and the results suggest that, despite its rarity, type E botulism should be considered by clinicians in France. Changes in the eating habits of people in France, as in the rest of Europe, with the increased consumption of vacuum-packed fish from endemic areas and decreased consumption of local foodstuffs, could explain the occurrence of the most recent cases.

## Introduction

*Clostridium botulinum* has been classified into four distinct groups (I–IV) and different serotypes [1]. Type E botulism is transmitted by fish and shellfish, food types that require careful storage and culinary preparation. It is endemic in areas such as Canada and Alaska and rare in France. Early identification of type E botulism is important to ensure effective management of this potentially fatal condition. Two cases observed recently in French hospitals prompted us to carry out a national epidemiological study of this type of botulism.

The survey permitted us to re-evaluate the clinical and microbiological characteristics, as well as the treatment methods and changing sources, of type E botulism in metropolitan France.

## Materials and Methods

Following two recent reports of type E botulism observed in French intensive care units (ICUs), we sought to review the epidemiology of these infections in metropolitan France. However, a comprehensive study was almost impossible to complete, despite the fact that notification of botulism cases is compulsory in France.

In order to obtain complete and accurate data, the French Ministry of Health, the National Reference Center (Institut Pasteur, Paris), the Department of Sanitary and Social Affairs (Direction Départementale des Affaires Sanitaires et Sociales) and the National Department of Veterinary Affairs (Direction Nationale des Services Vétérinaires), which examine suspect food or animals, were all contacted. A questionnaire regarding the characteristics, diagnosis and management of previously reported cases was also sent to the microbiology laboratory of each teaching hospital in France. A cross-analysis was then performed on the information obtained from these different sources, and a literature review was conducted.

## Results and Discussion

The first case leading to the present study was that of a 31-year-old patient who was hospitalized for respiratory distress, with difficulty swallowing, muscular weakness in all four limbs and blurred vision. The initial clinical examination showed a symmetrical motor deficit of all limbs, with diminished tendon reflexes, normal superficial sensitivity and a normal level of consciousness. A symmetrical nonreactive mydriasis, together with bilateral ptosis, was also observed. He had dysphonia and was afebrile. Computed tomography scan of the brain and lumbar puncture were normal. Progressive respiratory distress led to intubation in the intensive care unit. Except for a creatine phosphokinase level of 35,000 IU/l (indicating rhabdomyolysis), the laboratory test results were normal, as

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A. Boyer, C. Girault (✉), F. Bauer, E. Moiro, J. Leroy, G. Bonmarchand  
Service de Réanimation Médicale, Hôpital Charles Nicolle,  
Centre Hospitalier Universitaire, 76031 Rouen Cedex, France  
e-mail: Christophe.Girault@chu-rouen.fr  
Tel.: +33-2-32888261  
Fax: +33-2-32828636

J.-M. Korach  
Intensive Care Unit, General Hospital, Châlons-en-Champagne,  
France

J. Salomon  
French Ministry of Health, Paris, France

was the chest radiograph. Electromyography confirmed the presence of a presynaptic neuromuscular conduction block. The serum and stool samples, collected 16 h after the appearance of symptoms, were sent to the National Reference Center for examination. Type E botulin toxin was found in the patient's serum by mouse bioassay. Fecal samples were negative.

Questioning of the patient and his contacts linked the intoxication to a meal shared with his brother, who had remained asymptomatic. The suspect food items were either prawns fished off the Nigerian coast and bought vacuum-packed and frozen from a supermarket, or fresh herring that had been caught off the Channel coast the day before and marinated for 24 h at room temperature. Culture of the herring was no longer possible. A national survey conducted by the Direction Départementale des Affaires Sanitaires et Sociales led to the detection of type E botulin toxin in another packet of prawns from the same batch. This strongly suggested that the prawns were the source of the toxin responsible for the patient's condition; however, this could not be proven conclusively. Weaning the patient from the ventilator was delayed by the development of aspiration pneumonia, but it was finally achieved on day 12. At the time of discharge, the patient still had episodes of orthostatic hypotension and blurred vision.

The second case leading to our investigation was that of a 32-year-old patient who was hospitalized for a combination of nausea, vomiting, headaches and dizziness. On neurological examination, a nonreactive left mydriasis was found. Computed tomography scan of the brain and lumbar puncture were normal. On day 1, the mydriasis became bilateral, and visual difficulties and mouth dryness developed, which suggested botulism. At admission to the intensive care unit, the patient required intubation for neuromuscular respiratory distress. Laboratory tests showed only an increased level of serum amylase (1,295 IU/l), and chest

radiograph was normal. Electromyographic investigation revealed signs of presynaptic bloc. Serological tests, carried out on serum collected 48 h after the symptoms appeared, confirmed the presence of type E botulism by mouse bioassay, but fecal samples were negative. Progressive motor recovery permitted extubation on day 20; as in the first case, this was delayed by the development of aspiration pneumonia. After several weeks, the patient still had headaches and dysuria requiring intermittent catheterization.

Subsequent questioning revealed that vacuum-packed frozen scallops imported from China had been consumed after being pan-fried several hours after thawing. The dish had been shared with three other people, all of whom remained asymptomatic. No foodstuffs were available for culture. Packets from the same lot were subsequently sent to the National Reference Center laboratory for culture, but proved negative.

Including these two cases, 16 cases of botulism E have been identified in France since 1951, the year in which the first antitoxin E serum was made [2]. The microbiological and epidemiological characteristics of these cases are presented in Table 1 [3–5]. Eleven of the 16 cases were identified by the National Reference Center. Two-thirds of the microbiology laboratories of French teaching hospitals replied to our survey; none of which had experienced any cases of type E botulism. The French Ministry of Health was the source of information in only 7 of 16 cases, because not all cases had been systematically notified. Only one case was reported and diagnosed by the National Department of Veterinary Affairs.

The clinical picture of type E botulism does not present any defining feature other than a short incubation period (1 day on average), which is linked to the need for mechanical ventilation [6]. Diagnosis was made by isolating the E toxin from serum in 11 of the 16 cases. Since it was apparently easier to confirm the diagnosis

**Table 1** Epidemiological characteristics of 16 cases of foodborne botulism type E occurring in France from 1951 to 1999

Month/year	Type of botulism	No. of cases	No. of deaths	Suspected (S) or confirmed (C) food source	Source of isolated toxin	Source of information	Mechanical ventilation
March 1951	E	3	0	canned pilchards (S)	NA	IP, PD [3]	NA
August 1974	B + E	2	1	ham (S)	serum	IP, MH	NA
August 1977	E	2	0	canned crab from Russia (C)	food	VD	NA
February 1980	E	3	2	salted herrings (C)	food/serum	NA, PD [4]	yes 2/3
July 1980	E	1	0	fried carp (C)	food/serum	IP, PD [5]	no
June 1997	E	1	0	fish (S)	serum	IP, MH	yes
January 1998	E	1	0	scallops from China (S)	serum	IP, MH	yes
April 1998	E	1	0	fried shrimps from coastal waters of Nigeria (S)	serum	IP, MH	yes
April 1999	E	1	0	salmon or fish soup (S)	serum	IP, MH	yes
October 1999	E	1	0	grey mullet (C)	food/serum	IP, MH	yes
Total (%)		16	3 (18)	7 (C) / 9 (S)	serum: 11(68)	–	7 (44)

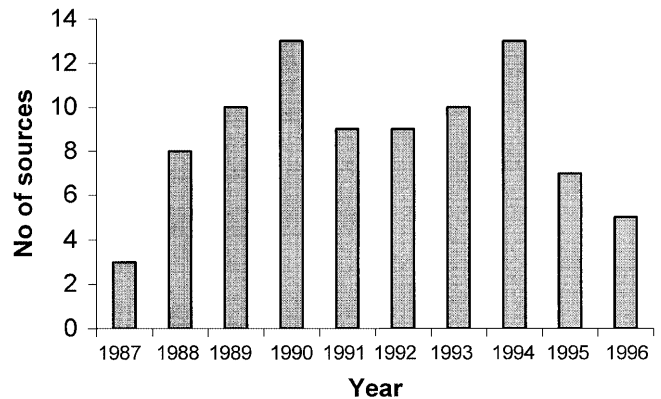
IP, Institut Pasteur; NA, not available; PD, published data; MH, French Ministry of Health; VD, veterinary department

in ventilated patients by the presence of toxin in serum, there could be a direct correlation between the quantity of toxin ingested and the severity of clinical signs [6]. In one report, two serotypes were identified in the serum of two patients who shared the same meal. Ham was the only suspected foodstuff, but the source animal could have been contaminated by animal feed containing fish meal [7]. In all other cases, the food source, whether confirmed (7 of 16 cases) or suspected (9 of 16 cases) was nearly always fish or shellfish. When performed, stool cultures remained negative. Since constipation is a frequently observed symptom of this type of infection, the collection and culture of stools is not always possible; nevertheless, this may be attempted up until 1 week after the onset of clinical signs [6]. Culture of gastric fluid can also be of diagnostic value, and should be attempted routinely, because it was the only examination that permitted diagnosis in 4 of 309 patients in Alaska [6].

The definite source of infection with type E botulism can only be confirmed by detecting the toxin in the foodstuff itself; the presence of *Clostridium botulinum* alone in the foodstuff not being sufficient for diagnosis [6]. Our study revealed that the diagnosis of botulism was difficult to confirm in 25% of cases, probably because of the delay in producing cultures and/or the lack of sensitivity of the laboratory tests [8]. Type E botulism appears to have a severe prognosis: in our study, 7 of 16 patients required mechanical ventilation, and the observed mortality rate was 18.7%, while in an American series, 9 of 32 patients required ventilation and the mortality rate was 8% [8]. The improvement in the prognosis of type E botulism observed during the present century seems partly linked to earlier diagnosis, but it is mostly due to the development of intensive care techniques, including mechanical ventilation.

Regarding specific treatment, the use of antitoxin serum remains debatable. In a retrospective study of type A botulism, the neutralization of circulating toxins appeared to stop the progression of the illness, to reduce the duration of hospitalization and even to improve the prognosis [9]; however, its real efficacy remains unknown, since no prospective, randomized, controlled study has ever been performed. Furthermore, treatment is costly and is not free of secondary allergic effects (serum sickness). For these reasons, serum therapy is no longer administered in France; however, it is still provided to most of the patients with botulism in the USA [10]. Antibiotics targeting the clostridium are also not recommended [1].

In France, botulism still occurs and is essentially due to type B (Figure 1). Type E botulism has a greater tendency to result in epidemics compared to other serotypes, as demonstrated by the fact that, in the USA, 78% of botulism cases are caused by type E compared with 60% by type A [11]. *Clostridium botulinum* resists



**Figure 1** Evolution of the changing sources of type E or type B botulism in France from 1987 to 1996

temperatures as low as 4°C and as high as 80°C. Therefore, the different methods of preparing fish (dried, marinated or salted) may help explain the geographic distribution of type E botulism and its comparative rarity in France. However, type E botulism does occur in France and must be considered, as supported by the five most recent cases (Table 1).

One possible explanation for the recent cases of type E botulism in France is the increased use of vacuum-packaging for food that is distributed commercially. This method encourages the growth of anaerobic bacteria, and the problem is probably exacerbated when the packaged fish originate from areas in which type E botulism is endemic (e.g., Japan, China and Alaska). To illustrate this point, from 1997 to 1999 five cases of type E botulism were reported, two of which were suspected to have been caused by the consumption of vacuum-packed fish, while from 1974 to 1980 eight cases were reported, and only two of them were suspected to have the same cause. Even though the probable source of infection was not always confirmed by bacteriological analysis, the incidence has risen in recent years. Indeed, these cases are sporadic, and the source of contamination remains a hypothesis. Nevertheless, the importance of systematically verifying and supervising these foodstuffs is highlighted. The increasing influence of animal botulism on the incidence of human cases could also be invoked, but for the moment, this only concerns serotypes C and D [12].

In conclusion, although type E botulism is rare in France, it should be considered when signs of paralysis develop within hours of ingesting fish or shellfish. Currently, the transmission of type E botulism might be facilitated by the ever-increasing consumption of vacuum-packed foodstuffs originating from endemic zones. Prevention will, therefore, depend on the screening of foodstuffs at risk in the alimentary chain.

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