

# The need for global planned mobilization of essential medicine: lessons from a massive Thai botulism outbreak

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## Introduction

A massive outbreak of botulism in northern Thailand in March 2006 tested international capacity to respond to a public health emergency. Botulism poisoning due to contaminated home-canned bamboo shoots caused illness in 209 villagers, of whom 134 persons were hospitalized and 42 required mechanical ventilation. A global search for *Botulinum* antitoxin began, involving international agencies, embassies, national laboratories, airlines and commercial organizations in seven countries. Sufficient antitoxin was obtained from four sources for treatment of 90 patients, but with delays in treatment of 5 to 9 days from time of exposure. Rapid local outbreak detection and an effective international response likely prevented mortality and additional morbidity. However, the international response to this public health emergency was informal and conducted through professional relationships rather than through predefined protocol for antitoxin acquisition. Stronger commitment through formal international agreements, including creation of global and regional stockpiles of critical medicines and supplies, is urgently needed.

## The outbreak

On Wednesday, 15 March 2006, several patients sought treatment at Ban Luang district hospital with reports of gastroenteritis starting at 13:00. An outbreak of botulism was suspected, and an investigation was begun when another 10 patients presented to the emergency unit, some with bulbar palsies and respiratory compromise.<sup>1</sup> All patients had eaten home-canned bamboo shoots one day earlier, when approximately 330 villagers attended an annual religious rite in a small village in this district, during

which home-canned bamboo shoots from two 20-litre cans were served without heating in small plastic bags for lunch. Over the following week, a total of 209 villagers had the onset of symptoms compatible with botulism. Among the affected villagers, 134 (64%) were hospitalized with paralysis ranging from minor bulbar palsies to quadraparesis; 42 (20%) of patients required mechanical ventilation for respiratory depression. There were no deaths. The epidemiological investigation of this outbreak has been reported previously.<sup>2</sup>

## The response

Authorities in the province declared a public health emergency on Thursday 16 March. Immediately upon establishing a presumptive diagnosis of botulism poisoning, efforts were begun to obtain *Botulinum* antitoxin, which is life-saving if given within 48 hours.<sup>3</sup>

The total number of cases and those with severe neuromuscular impairment requiring ventilatory support increased over the next several days, to 19 patients on ventilators by the third day and 39 by day six. Numbers of patients requiring ventilator support and times of request and deliveries of antitoxin are shown in Fig. 1. The process of obtaining antitoxin was difficult. Telephone and email contacts were established between the Thai public health ministry in Bangkok; embassies in Bangkok, Geneva and London; the World Health Organization in Geneva; the United States Centers for Disease Control and Prevention (CDC) in Atlanta; the National Laboratory in the United Kingdom; and the Japan National Institute of Infectious Disease (NIID) in Tokyo.

Ultimately it was possible to obtain 93 vials (treatment courses) of antitoxin

from the CDC, the United Kingdom's National Laboratory and NIID in Tokyo. An additional 10 vials were purchased from a commercial source in Canada. The first 20 patients with most severe neurological impairment received antitoxin on day five, and 70 more patients were treated by the ninth day after the exposure.

Table 1 shows time intervals from the original exposure, initiation of requests for antitoxin, initiation of procurement from various sources and delivery to the hospital. If Thai authorities had not been able to mobilize 42 ventilators and staff to manage the most severely affected patients, these delays would have certainly resulted in significant mortality. In a previous botulism poisoning episode in the same area eight years earlier, two of four patients requiring mechanical ventilation died; no antitoxin was given to any of the patients.

## Global planned response needed

Based on this experience, there are at least five policy issues that must be addressed to ensure rapid international response to such public health emergencies.

First, adequate health service infrastructure is necessary at every level within each country. This allows local health facilities to respond effectively to initial emergency requests and will reduce the time needed to mobilize support from local agencies or from the capital. This need is evident not only from this botulism case, but also from responses to the massive 2005 Asian tsunami. Most developing countries have inadequate health infrastructures, especially in rural settings.

The detection and verification of this outbreak was impressively rapid

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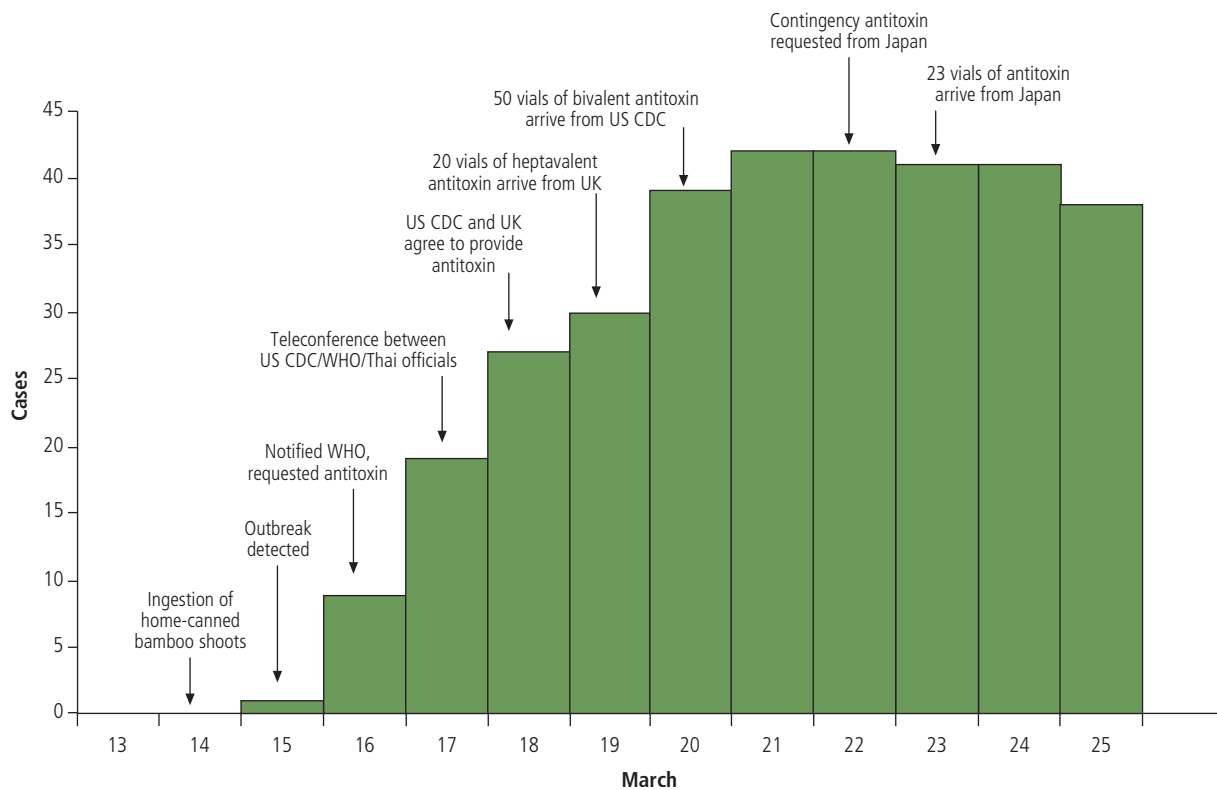
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Fig. 1. Daily number of botulism outbreak patients on respirators and steps in managing the outbreak



UK, United Kingdom; US CDC, United States Centers for Disease Control and Prevention.  
Source: Number of patients from Nan Provincial Health Office, Thailand.

given that the typical incubation period for botulism is 1 to 3 days.<sup>4</sup> Prompt detection and reporting was facilitated by the Thai system of Surveillance and Rapid Response Teams (SRRTs), of which there are 1030 at district level, supported by SRRTs at provincial, regional and national levels. A similar response would not be possible in countries that lack such infrastructure, particularly specialized epidemiological surveillance capacity. This episode validated Thailand's policies of investing in human resources for health and supporting SRRTs and the Field Epidemiology Training Program.

Second, it is necessary to institute communication and response systems with international partners before emergencies arise. Though the multiple agencies' responses were exceptionally rapid, the time needed to acquire and deliver antitoxin ranged from 5 to 9 days. Communication difficulties contributed significantly to these delays, highlighting the importance of pre-arranged communication channels not only with international agencies, but also with technical partners, embassies, airlines and relevant commercial partners. Involvement of foreign affairs ministries as well as health agencies would greatly

improve communication and response efficiency.

The third imperative of effective response efforts is the establishment of stockpiles of medications, equipment and supplies with clear procedures for release and transport. There are no pre-arranged sources of antitoxin for southeast Asian countries. Readily available information on where and how to procure antitoxin would have increased the speed of acquisition by at least several days. This applies equally to all other "orphan medications" that are life-saving but scarce in quantity, such as diphtheria antitoxin or drugs and supplies needed to respond to pandemic influenza. Stockpiles should be strategically located along air routes and supervised by WHO to ensure readiness of crucial drugs for rapid deployment. This stockpile system could be integrated with individual national stockpile systems in a "virtual stockpile" arrangement so that delivery could occur within 24 hours of requests.

Fourth, the revised International Health Regulations provide a "decision instrument" algorithm for determining whether WHO must be notified of a public health event.<sup>5</sup> In this outbreak, reporting criteria in this algorithm (sever-

ity, unexpectedness, risk of international spread and likelihood of international travel or trade restrictions) were applied, and WHO was notified based on the event's severity and unexpectedness. We strongly support adoption, implementation and enforcement of all provisions of the recently revised International Health Regulations. As shown in this case, this process requires collaboration beyond the health sector, and is ultimately an international and foreign policy issue.

This leads to the fifth response criterion: international response to public health emergencies as a foreign policy as well as a health issue.

Most Thai initiatives for improved international response to public health emergencies have been undertaken at the health ministries level. Ministry of Public Health personnel have worked with neighbouring countries on epidemiological training and have provided emergency drugs for human cases of avian influenza. The Association of Southeast Asian Nations (ASEAN) health ministers' group has reached agreements on regional data sharing and joint outbreak investigations. In 2005, Thailand agreed to commit 5% of its oseltamivir (a drug for treatment of avian influenza)

Table 1. Time periods between events in obtaining *Botulinum* antitoxin for treatment of patients in botulism outbreak

Events	Time to respond	Comment
1) From consumption of home-canned bamboo shoots to establishing of diagnosis	32 hours	Includes incubation period and time until cases presented at local health-care facilities
2) From diagnosis to request for antitoxin from Ministry of Public Health	14 hours	Includes time until diagnosis was made and patients were referred to provincial hospital; antitoxin was requested in late evening
3) From receipt of antitoxin request to procurement efforts	4 hours	The outbreak's extent and the requests' urgency may have been underestimated
4) From start of procurement effort to success in confirming identification of United Kingdom and United States antitoxin sources	48 hours	Thailand lacked antitoxin and procurement procedures were unclear. Delays occurred in communication across time zones. The Thai permanent mission in Geneva and Thai Embassy in London were not instructed to facilitate antitoxin procurement and air transportation
5) From procurement of antitoxin from United Kingdom source until arrival at hospital	18 hours	Commercial shipment
6) From confirmation of antitoxin United States supply to procurement and arrival at hospital	36 hours	Hand-carried on private and commercial aircraft
7) Request for antitoxin from Japan until arrival at hospital	48 hours	Hand-carried on commercial aircraft

supply to initiate a regional drug stockpile. Although the proposal has not yet taken effect, contribution of small percentages from each country's stocks should be considered as a future policy option.

In the emergency described here it was necessary to involve partners beyond government health sectors; these included embassies, airlines and other commercial partners. It is increasingly accepted that public health emergencies can have global consequences beyond the health sector.<sup>6</sup> The social and political impact of the HIV/AIDS (human immunodeficiency virus/acquired immunodeficiency syndrome) epidemic, the effects of a potential H5N1-derived human influenza pandemic and the threat of deliberate release of infectious agents or biotoxins (for example, *Botulinum* toxin or anthrax) have alerted policy-makers to these public health emergencies' implications for national security. Establishing sustainable global capacity for responses to such potential hazards will require action beyond health ministries and global health agencies.

In the 2006 Thai botulism outbreak, a large number of patients received

mechanical ventilation and antitoxin that proved life-saving, thanks to the extraordinary efforts of health professionals and others around the world. The response succeeded in part because it went beyond the usual health-sector partners, although in an improvised way. If efficient detection, confirmation, communication, response and reporting capacity are not expanded through policy commitment beyond the health sector, victims of the next public health emergency may not be so fortunate. ■

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