

# AN OUTBREAK OF TETRODOTOXIN POISONING FROM CONSUMING HORSESHOE CRABS IN SABAH

M Suleiman<sup>1</sup>, J Muhammad<sup>2</sup>, J Jelip<sup>1</sup>, T William<sup>3</sup> and TH Chua<sup>4</sup>

<sup>1</sup>Sabah State Health Department, Kota Kinabalu, Sabah; <sup>2</sup>Kudat Area Health Office, Kudat, Sabah; <sup>3</sup>Jesselton Medical Centre Sdn Bhd, Metro Town, Kota Kinabalu, Sabah;

<sup>4</sup>Department of Pathobiology and Medical Diagnostics, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia

**Abstract.** The horseshoe crab (*Carcinoscorpius rotundicauda*) is consumed by those residing near the coastal areas of Kota Marudu District in Malaysia, as it is considered a delicacy. During June to August, 2011 thirty cases of tetrodotoxin poisoning were reported from Kota Marudu District following ingestion of horseshoe crabs caught in Kota Marudu Bay. The purpose of this study is to describe this case series in order to determine risk factors to prevent further outbreaks. There were six confirmed and 24 probable cases of tetrodotoxin poisoning identified in the study area during the study period as diagnosed by clinical presentation and laboratory findings. Symptoms included dizziness (80%), circumoral and lingual numbness (80%), hand and feet numbness (63.3%), nausea and vomiting (30%) and weakness and difficulty in breathing (26.6%). Three cases (10%) died while 27 cases recovered. Forty-seven percent of the cases had onset of symptoms within 30 minutes of ingestion and 14% 31-60 minutes after ingestion of horseshoe crab meat. Urine samples were collected from the cases, while horseshoe crabs, cockles and sea water from the epidemic area were also taken for analysis. Tetrodotoxin was detected in the urine of six cases; the highest concentrations recorded were among the three cases who died. High tetrodotoxin concentrations were found in the hepatic cecum and eggs of the tested horseshoe crabs. Dinoflagellates were not detected in the sea water or cockle samples. Intensive health education was initiated quickly to stop other members of the Marudu Bay community from consuming the horseshoe crabs. This is the first documented epidemic of tetrodotoxin poisoning in Sabah.

**Keywords:** tetrodotoxin poisoning, horseshoe crab, Sabah

## INTRODUCTION

Although tetrodotoxin poisoning has often been associated with eating puffer

fish, many other marine organisms and terrestrial animals may also have tetrodotoxin. Noguchi and Arakawa (2008) wrote a comprehensive review and listed organisms which accumulate the toxin in their bodies including many species of puffer fish, platyhelminthes, marine gastropods, celphalopads, starfish, newts, frogs and horseshoe crabs.

Most reported tetrodotoxin poisoning cases are from eating puffer fish (espe-

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Correspondence: Dr TH Chua, Department of Pathobiology and Medical Diagnostics, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, 88400 Kota Kinabaru, Sabah, Malaysia.

Tel:+6012 602 9046

E-mail: thchua@ums.edu.my

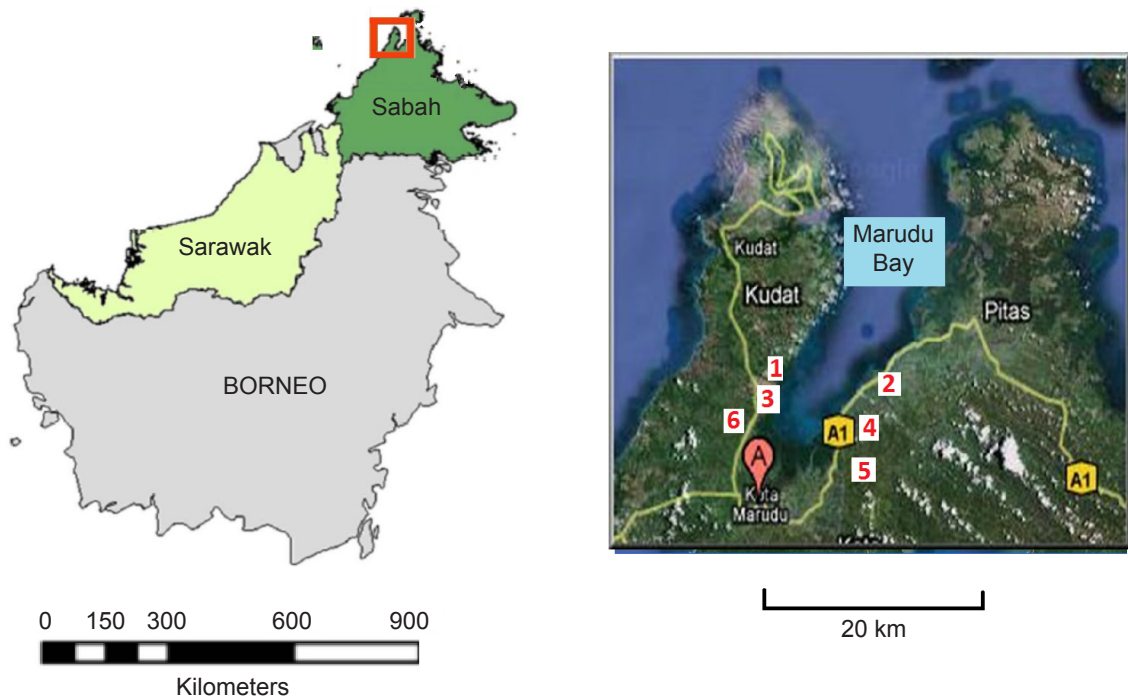


Fig 1—Locations of tetrodotoxin poisoning cases at Marudu Bay. (1) Kampong Toporoi (episode 1), (2) Teritipan (episode 2), (3) Kampong Bingkungan (episode 3), (4) Kampong Tandek (episode 4), (5) Kampong Nolotan (episode 5), (6) Kampong Bintasan (episode 6).

cially *Takifugu rubripes*) in Japan where fugu is considered a delicacy; tetrodotoxin is especially found in the liver and ovaries of puffer fish (Noguchi and Arakawa, 2008). During 1980-1999, 554 cases of fugu poisoning involving 912 persons were reported in Japan, of whom 106 died (Fukushima and Ohtsuka, 2005). Consumption of another puffer fish species (*Lagocephalus sceleratus*) has been reported to cause tetrodotoxin poisoning on Reunion Island (Puech *et al*, 2014), in the Mediterranean Sea (Kheifets *et al*, 2012) and in Singapore (Yong *et al*, 2013).

In western Malaysia, the only reported case of tetrodotoxin poisoning was from a lady who consumed the roe of a puffer fish (Loke and Tan, 1997). In eastern Malaysia, puffer fish poisoning has been reported more frequently. In

1985, a family of 4 had tetrodotoxin poisoning where one died from eating the roe of *Tetraodon lunaris* (Lyn, 1985), although this could have been a misidentification of *Canthigaster valentini* Bleeker. In 1987, 18 persons were poisoned from eating the roe of an unidentified puffer, of whom 9 died within 60 minutes (Kan *et al*, 1987).

Tetrodotoxin poisoning from consuming the round tail horseshoe (*Carcinoscorpius rotundicauda*) is less common than from consuming puffer fish. However a notable occurrence affecting 71 persons in Chon Buri Province, Thailand due to consuming horseshoe crab eggs was reported by Kanchanapongkul and Krittaypoosipot (1995). Similar poisonings have been reported from Japan (Noguchi and Arakawa, 2008), China (Liao and Li, 2001) and Cambodia (Ngy *et al*, 2007).

In Sabah, Malaysia, horseshoe crabs are consumed by residents near coastal areas, especially in Kota Marudu District, where it is considered a delicacy. Various dishes are prepared from the eggs and meat of horseshoe crabs either by barbecuing or boiling it. Locals claim to know which organs need to be removed when preparing a dish of horseshoe crabs (Robert *et al*, 2014).

We present here a case series of 30 patients who developed tetrodotoxin poisoning in 2011 after consuming horseshoe crabs from Marudu Bay, Kota Marudu District, Malaysia. This information may help inform future control and prevention efforts.

CASE SERIES

This paper describes 30 tetrodotoxin cases from Kota Marudu, Sabah (Fig 1), who were admitted to Kota Marudu Hospital during June to August, 2011, and referred to the Queen Elizabeth Hospital in Kota Kinabalu.

Although the cases were from different villages (Table 1), they all had consumed horseshoe crabs caught from Marudu Bay and had symptoms of dizziness and numbness. Six were confirmed to have tetrodotoxin poisoning (as defined by CDC, 2005) while another 24 were probable cases who had clinical symptoms of stage 1 poisoning. Three of the confirmed cases died from tetrodotoxin poisoning. In two episodes, only one person was involved, while in the others the whole family was poisoned. The attack rate was usually 100% (Table 1).

Sixteen cases (53%) were males. The highest percentages of subjects were from the age groups 0-10 (30%) and 31-40 years old (30%) (Table 2).

Table 1  
Cases of tetrodotoxin poisoning from eating horseshoe crabs during June-August 2011, Kota Marudu, Malaysia.

Episode	Date (2011)	Number of cases		Case information	Clinical outcome	Attack rate (%)
		Confirmed	Probable			
1	3 Jun	1	-	Kampong Toporoi, 41 year old male.	Died	100
2	4 Jun	1	-	Kampong Teritipan, 62 year old male.	Died	100
3	15 Jun	1	18	Kampong Bengkongan	All recovered	100
4	16 Jul	2	-	Kampong Tandek.	One died	100
5	26 Jul	1	-	Kampong Nolotan, 38 year old male, one of four persons who consumed the same dish.	Recovered	25
6	12-Aug	-	6	Kampong Intasan Darat	All recovered	100

Table 2  
Tetrodotoxin poisoning cases by age groups.

Age group in years	Number of cases	Percent of total
0-10	9	30.0
11-20	0	0
21-30	4	13.3
31-40	9	30.0
41-50	3	10.0
51-60	0	0
≥61	5	16.7

The cases comprised three ethnic groups; the Bajaus (70%) who are mainly fishermen and reside near coastal areas, the Rungus (26.7%) and the Kadazan Dusun (3.3%) (Table 3). The occupations of cases included fishermen, self-employed and housewives.

For 47% of the cases, the onset of symptoms of tetrodotoxin poisoning occurred within 30 minutes. Only three individuals had symptoms that developed as much as 3 or more hours later (Table 4).

Most cases developed circumoral and lingual numbness (80%), hands and feet numbness (63.3%), as well as dizziness and vertigo (80%), nausea and weakness (Table 5). Three cases developed respiratory paralysis and died.

Urine samples were collected from the patients by the hospital during their stay and sent to the National Poison Institute in Penang to quantify the level of tetrodotoxin in the urine using a gas chromatography-mass spectrometry assay.

A total of five horseshoe crabs were collected from Kampong Bandau around Marudu Bay after the third episode of tetrodotoxin poisoning and sent to the Sabah Fisheries Department for toxicological testing. Samples were taken from different

body parts of the crabs for tetrodotoxin analysis.

Samples of sea water and cockles were also taken from Kampong Teritipan, Kampong Bintasan, Kampong Kuala Bandau and Kampong Tanjung Batu to check for the presence of dinoflagellates (*Pyrodinium bahamense var. compressum* and *Cochlodinium polykrikoides*).

#### Toxicological findings

The tetrodotoxin concentrations in the horseshoe crab body varied by tissue type, with the highest concentration of tetrodotoxin (4,113 ng/ml) in the hepatic cecum of the male crabs (Table 6).

The concentrations of tetrodotoxin in the urine of affected patients varied from 0 to 602 ng/ml (Table 7). Higher concentrations were found in the urine of the cases who died.

Analysis of samples of sea water and cockles taken from Kampong Teritipan, Kampong Bintasan, Kampong Kuala Bandau and Kampong Tanjung Batu did not show the presence of dinoflagellates.

#### DISCUSSION

The horseshoe crab is considered a delicacy in Kota Marudu District. Its consumption has presumably been going on for a long time, especially among those residing in coastal areas. However tetrodotoxin poisoning cases from consuming these crabs have been few until the case series described here. This is the first report from Sabah of a tetrodotoxin poisoning cluster resulting from consuming horseshoe crabs.

The tetrodotoxin concentrations in the sampled horseshoe crabs in our study varied by tissue type, being highest in the hepatic cecum. Ngy *et al* (2007) also found the highest concentration of tetrodotoxin

Table 3  
Distribution of tetrodotoxin cases by ethnicity and occupation.

Category	Number	Percentage
Ethnicity		
Bajau	21	70.0
Rungus	8	26.7
Kadazan Dusun	1	3.3
Occupation		
Dependent (child)	9	30.0
Housewife	7	23.3
Self employed	6	20.0
Fisherman	7	23.3
Fisherman and farmer	1	3.3

Table 4  
Time in minutes from consumption to onset of symptoms of tetrodotoxin poisoning.

	Time in minutes							
	0-30	31-60	61-90	91-120	12-180	181-210	211-240	>241
No. of cases	14	4	6	3	0	1	1	1
Percent	47	14	20	10	0	3	3	3

Table 5  
Symptoms among tetrodotoxin poisoning patients.

Clinical stage of poisoning	Symptoms and signs	Number	%
Stage 1	Circumoral, lingual numbness	24	80.0
Stage 1	Nausea, vomiting	9	30.0
Stage 2	Hand and feet numbness	19	63.3
Stage 2	Body weakness	8	26.7
Stage 2-3	Dizziness, vertigo	24	80.0
Stage 4	Respiratory paralysis, cardiovascular collapse	3	10.0

in horseshoe crabs in the hepatic cecum, followed by the other viscera, the eggs, muscles, intestines and testes. Since there is little muscular tissue in the crabs, it is likely the tetrodotoxin poisoning resulted from consuming the hepatic cecum or the eggs, which are considered the tastiest parts.

Tetrodotoxin is a potent poison; consuming 100 g of the eggs, if they have a tetrodotoxin concentration >100 MU/g, can be fatal (Ngy *et al*, 2007). The urine tetrodotoxin concentration among the cases who died ranged from 93 to 602 ng/ml, suggesting they probably had ingested a substantial quantity of tetrodotoxin.

Table 6  
Concentration of tetrodotoxin by horseshoe crab body part examined.

Gender of horseshoe crab examined	Horseshoe crab body part	Concentration of tetrodotoxin
Female	Eggs	257.49 ng/ml
	Stomach	186.65 ng/ml
	Hepatic cecum	113.39 ng/ml
Male	Hepatic cecum	4,113.89 ng/ml
	Stomach	782.34 ng/ml

Table 7  
Concentrations of tetrodotoxin in the urine of tetrodotoxin poisoning cases.

Case number per episode	Date	Tetrodotoxin concentration	Case outcome
Case 1 of episode 2	4 June 2011	93.4 ng/ml	Died
Case 1 of episode 3	15 June 2011	Not detected	Recovered
Case 7 of episode 3	15 June 2011	1.3 ng/ml	Recovered
Case 8 of episode 3	15 June 2011	2.3 ng/ml	Recovered
Case 17 of episode 3	15 June 2011	17.3 ng/ml	Recovered
Case 1 of episode 4	16 June 2011	602.3 ng/ml	Died
Case 2 of episode 4	16 June 2011	236.2 ng/ml	Died

Tetrodotoxin poisoning from the consumption of horseshoe crabs in Sabah has not been previously reported, presumably due to removal of the toxic organs prior to consumption (Robert *et al*, 2014). This case series might be due to other factors, such as unusually high tetrodotoxin levels in the horseshoe crabs in the study area during that period. A study from Thailand (Kanchanapongkul, 2008) reported seasonal variation in the number of cases of horseshoe crab tetrodotoxin poisoning, with a peak from December through March, which falls within the dry season. There were more cases of tetrodotoxin poisoning associated with consumption of horseshoe crabs in Cambodia during the rainy (April-May) and dry (December-January) seasons (Ngy *et al*, 2007). The same study found the total mean tetro-

dotoxin concentration of the viscera and intestines to be 17.7 MU/g in female crabs and 6.5 MU/g in male crabs in the dry season, 116.0 MU/g in female crabs and 28.7 MU/g in male crabs in the wet season, suggesting the toxicity level in that study area was higher in the wet season. In Kota Marudu District, our study area, there was an increase in rain fall during November to March, but the tetrodotoxin poisoning cluster occurred during June to August 2011. It is possible rain changed the environment, increasing the population of tetrodotoxin-producing bacteria such as *Vibrio alginolyticus*. These bacteria can create a symbiotic relationship with the horseshoe crabs and accumulate inside their bodies, increasing the level of tetrodotoxin (Kungsuwan *et al*, 1987). More studies are needed to investigate the

relationship between rain and the level of tetrodotoxin in horseshoe crabs.

This report describes a case series of tetrodotoxin poisoning that occurred in a cluster, causing fatalities from consuming horseshoe crabs in Sabah. Appropriate health education is needed to prevent this tragedy from recurring. Physicians and district medical officers need to be trained to recognize and respond appropriately to these cases.

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