

# A Queensland Family with Ciguatera after Eating Coral Trout

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## ABSTRACT

A family of 4 developed symptoms of ciguatera poisoning after a meal of coral trout; symptoms appeared to be dose-related. The father, who had a previous history of Hodgkin's disease for which he had radiotherapy to the chest and upper abdomen nine months prior, having eaten the most, had the most severe symptoms. The mother, who was 11 weeks pregnant at the time, had moderately severe symptoms, while the children ate a smaller amount and had only minor symptoms. Both family cats developed severe symptoms typical of ciguatera. Mannitol I.V. relieved all the symptoms of the mother and gave transient relief from most symptoms experienced by the father. Mannitol again proved effective at relieving the father's symptoms when repeated a week later. Laboratory analysis confirmed that the sample of coral trout was contaminated with relatively high levels of ciguatoxin. Pregnancy progressed uneventfully to term, followed by a normal delivery. Although the baby developed lung complications within 24 hours of birth, these appeared unrelated to the previous ciguatera episode.

## INTRODUCTION

Ciguatera is poisoning caused by eating fish contaminated with lipid-soluble toxins called ciguatoxins.<sup>1 2</sup> Ciguatoxins are not inactivated by cooking and poisoning usually occurs soon after ingestion of the contaminated fish, causing short-term gastrointestinal, but often distressing long-term neurological symptoms.<sup>1 3</sup>

Ciguatera poisoning is a major public health problem in the tropical and subtropical Pacific region.<sup>3 4 5</sup> Deaths have occurred but may have been previously overestimated,<sup>6 7</sup> with Bagnis<sup>7</sup> suggesting the fatality rate was 0.1 per cent (3 in 3009 cases) during 1964-70 in the South Pacific. In 1994 ninety-eight deaths were attributed to ciguatera poisoning when some 500 cases of poisoning were reported after most of a local population in Madagascar ate contaminated shark flesh - a fatality rate of almost 20 percent.<sup>8</sup> However, further toxicological study suggested that ciguatoxin was not the cause.<sup>9</sup> Two or three deaths have also been reported recently from Fiji (Pearn 1996, pers. comm.).

The incidence of ciguatera in Queensland is approximately 0.16 cases per 10, 000 population. Similar figures are reported from other parts of Australia, but may be inaccurate, due to non-reporting of confirmed cases and wrong diagnoses.<sup>3</sup>

Fish repeatedly causing ciguatera in Queensland include coral trout, narrow-barred Spanish mackerel, reef cod, barracuda, emperor, grouper, trevally, queenfish and kingfish. Others have been implicated, but evidence is currently lacking. Red bass, chinaman and paddletail are presently not regarded as suitable for consumption because of the perceived risk of ciguatera.<sup>1</sup>

Ciguatoxins may be present throughout tropical or sub-tropical seas, but with two main problem areas in Queensland. The first extends from Bowen north to Port Douglas (Great Barrier Reef), and the second from Maryborough north to Gladstone - especially on the inside coast of Fraser Island, where the capture and sale of narrow-barred Spanish mackerel and barracuda in Platypus Bay is banned, as these fish are frequently toxic.<sup>10</sup> A third high-risk area for ciguatera in Australia is the reefs around Gove (Nhulunbuy) in the Northern Territory. Many tourist areas in the South Pacific also experience outbreaks and with the export and rapid transport of fresh reef fish to other areas in the world, the problem is likely to occur in places far from tropical oceans.

The ciguatoxins arise from gambiertoxins which are produced in some strains of the benthic dinoflagellate, *Gambierdiscus toxicus*, a small bottom-living algae<sup>11</sup> These algae are eaten by herbivorous fish and the ingested gambiertoxins apparently oxidised to the ciguatoxins as they pass through fish at each trophic level. The toxins are then slowly accumulated in the tissues of these fish. If humans then eat these contaminated fish, ciguatera poisoning may occur to a greater or lesser degree depending on the levels of the various toxins accumulated and individual susceptibility.

In this report we present the clinical records of one family who suffered ciguatera poisoning in which the presence of ciguatoxins was confirmed by bioassay.

#### **Clinical Records**

A family of four fried and ate coral trout fillets approximately 250g pieces in size in September 1995; two of the family cats were also given the fish. Shortly after one cat started dragging its back legs around and was vomiting. The other cat was vomiting and disappeared for 4 days. When it returned, it was weak in the back legs and was meowing continuously in pain. Both cats had to be put down.

## Case Studies – Ciguatera poisoning

Case	Presentation	Clinical Features /response	Management
<b>Case One</b>	<u>Initial</u>		
Father, 34-year-old male - ate 3 or 4 pieces of contaminated fish (up to 1000g)	Severe diarrhoea, nausea, burning feeling inside his mouth, on palms soles. Generalised arthralgia and myalgia. Cold water seemed to further 'burn' his mouth, cool-to-warm water was tolerated.	By end of mannitol infusion, symptoms improved rapidly but left with minor mouth burning of the mouth and hands, less arthralgia and myalgia; somewhat lethargic. Diarrhoea improved.	Oral imodium, two litres of 4% dextrose and N/5 saline (given over a couple of hours, with 250 ml of 20% mannitol over 30 minutes.
	<u>7<sup>th</sup> day</u>		
	Severe pruritis anxiety, depression, mouth and palms burning, arthralgia, lethargy & diarrhoea	Improved: - arthralgia, Burning mouth and Feet by end of Infusion; no ease in pruritis	Another 250ml of 20% mannitol IV. Doxepin 50 – 100mg nocte eased pruritis & anxiety
<b>Case Two</b>	<u>Initial</u>		
Mother, 33-year-old female – ate 2 pieces of contaminated fish (500g)	Distressed, vomiting dehydrated, 11 weeks pregnant.	Symptoms settled by end of mannitol -no further treatment.	2l IV 4% dextrose and N/5 saline – 250 ml 20% mannitol between.
	<u>7<sup>th</sup> Day</u>		
		Very slight burning of hands & mouth, mild itchy skin.	None
<b>Cases 3 &amp; 4</b>			
Children, male 4 years, female 6 years – ate small piece contaminated fish.	nausea, vomiting, profuse, watery diarrhoea for 24 hours.	Minor burning of the mouth. Later – legs aching.	Glucose and electrolyte fluids, fat-free diet. Paracetamol.

### Case Five

A male infant was born to the mother (Case 2) by elective caesarean section at 39 weeks gestation (i.e. 28 weeks, after the initial poisoning). Apgar score was 9 and 9, birth weight 3.42kgs. He developed mild respiratory distress by three hours of age and was placed in 28% oxygen with an average oxygen saturation of 95% over the next twelve hours. He was noted to be a very irritable baby dropping his oxygen saturation with handling or spontaneous crying. He had increasing oxygen requirements. By 28 hours in 100% oxygen his PO<sub>2</sub> was 65 mm/Hg with a pH of 7.35 and pCO<sub>2</sub>, of 42 mm/Hg. Initially CXR suggested retained foetal lung fluid with a subsequent CXR showing an increased interstitial markings with pulmonary congestive oedema.

He was diagnosed as having persistent pulmonary hypertension of the new-born (PPHN). He was intubated paralysed and received high frequent ventilation. Hypotension was managed with dopamine, adrenaline and volume expansion; exosurf, tolazoline and magnesium sulphate were given with little improvement. On day four he developed an episode of acute haemorrhagic oedema. He required a total of seven days ventilation, with maximum pressure being 27/10 and maximum  $\text{FiO}_2$  70%. Post extubation he had evidence of pulmonary interstitial emphysema and bronchopulmonary dysplasia, managed with dexamethasone and diuretics. Blood cultures were negative and alpha 1 antitrypsin and surfactant protein levels were normal; echocardiography showed a small ventricular septal defect. Oxygen was ceased by day 24 and diuretics by day 60. At follow-up the baby is behaving normally with no residual symptoms.

## **MATERIALS & METHODS**

A portion of the coral trout (585 g) implicated in the poisoning was obtained for laboratory analysis. A 482-g portion of this sample was extracted with acetone and partially purified according to the standard procedure for ciguatoxins<sup>12</sup>. A portion of the ether soluble fraction was dried, emulsified in Tween 60/0.9% saline and 24 mg (0.5 ml) injected i.p. into two 24 g Quackenbush mice. Signs of intoxication were monitored and time to death recorded. Potency of the extract was estimated from the dose vs. time to death relationship  $\log(\text{MU}) = 2.3\log(1 + 1/T)$ , where one mouse unit (MU) is the  $\text{LD}_{50}$  dose for a 20 g mouse and T is the time to death in hours.<sup>2</sup>

## **RESULTS**

The ether extract yielded 1.23 g of material which upon intra-peritoneal injection into mice, induced laboured respiration, lacrimation, abdominal compression, diarrhoea, hypersalivation, wobbly/staggering gait, hind-limb paralysis and convulsions just prior to death (170 and 181 min). The estimated potency of the injected extract was 0.25 MU/g flesh or 1.3 ng ciguatoxin-1/g flesh, a relatively high level of ciguatoxin for coral trout.

## **DISCUSSION**

Symptoms of ciguatera have been carefully documented in Australia<sup>1 13 14</sup> and can be divided into 2 main classes, gastrointestinal and neurological. Gastrointestinal symptoms are diarrhoea (>60% of patients), abdominal pain, nausea (>50%) and vomiting (>30%). The neurological symptoms include myalgia (>80% of patients), burning sensation of skin on contact with cold water, pruritis, arthralgia (>70%), paraesthesia of hands, feet, mouth and lips, headache (>60%), mood disorders (depression, irritability, anxiety) (50%), ataxia or vertigo, sweating, eye pain (>40%), dental pain, tremor (>30%), neck stiffness, decreased strength in certain muscle groups (>20%), salivation (10% of patients). Other non-specific symptoms reported include fatigue and lassitude (90% of patients), chills (40%), skin rash, exertional breathlessness and dysuria (20%).<sup>5</sup> A recent case of coma due to ciguatera poisoning was reported from Rhode Island, USA.<sup>15</sup>

Victims may develop any of the above signs and symptoms, often depending on the amount of contaminated fish eaten, or the concentration of ciguatera toxin in the fish itself. Gastrointestinal symptoms characteristically last for one or two days, whereas some neurological symptoms persist for several weeks or longer - as experienced by case 1, above. In some victims the neurological symptoms can persist for many months, or even years. Victims should avoid eating reef fish for three to six months to avoid a possible relapse.

Intravenous (IV) mannitol solution is recommended in a dose of 1 g/kg IV infusion of 10% or 20% mannitol solution over 30 minutes, given as soon as possible after ciguatera has been diagnosed to reduce the severity and duration of ciguatera symptoms.<sup>16 17 18 19</sup> However, some people do not respond to mannitol,<sup>20</sup> a fact needing further study. This may be related to any delayed timing of the treatment (although not in *Case 1* above), inadequate dosage, or different responses among cases. A recurrence of symptoms may occur about 24 hours after a first administration of mannitol and a second infusion of mannitol is recommended, again as occurred with *Case 1*.

The mannitol infusion repeated a week after the original envenomation produced beneficial effects, although outside the acute-phase treatment suggested by Pearn.<sup>18</sup> It has been two of the authors (PJF & RJL) personal experience with previous cases that some beneficial effects can often be experienced using mannitol up to a week after ciguatera poisoning (personal observations 1994 and earlier).

Doxepin was useful in *Case 1* to treat the itching skin. Lethargy and depression have previously described for ciguatera (see above), and have been treated with fluoxetine.<sup>21</sup>

The 'burning' feeling of the mouth in the mother and father has been described in the literature in the past as 'temperature reversal' although recent experiments showed temperature perception was intact in ciguatera poisoning and reversal of temperature does not occur,<sup>22</sup> the study showing these sensations are generated in C-polymodal nociceptor fibres in skin and deep structures with the intensity of the sensations depending on the intensity of discharge in these fibres. Ciguatera causes persistent sodium channel opening in nerve membrane resulting in oscillations in membrane potential and runs of spontaneous discharges.<sup>1</sup>

Two cases of severe ciguatera poisoning in pregnancy have been previously reported in the literature,<sup>23 24</sup> one in the second trimester with no problems at the full-term delivery, but in the other severe ciguatera poisoning occurred at term and after delivery the baby suffered fascial palsy, and possible myotonia of the hands, although no long-lasting problems occurred.<sup>24</sup>

In our *Case 2* pregnancy proceeded uneventfully. Despite problems with the baby within 3 hours of birth, we have no knowledge of foetal exposure to ciguatera toxin causing postnatal morbidity except the term pregnancy mentioned.<sup>24</sup> It is most likely that this baby had retained foetal lung fluid, and had episodic hypoxia associated with his extreme agitation producing severe PPHN, with ventilation and high O<sub>2</sub> likely to have caused lung damage. We feel this could not be correlated with early maternal exposure to ciguatera toxin.

Ciguatera toxin can affect cats by causing paralysis of the pelvic and hind leg muscles (as occurred with this family's cats), and has been used to detect if ciguatera toxins are present in fish.<sup>25</sup>

Confirmation that the coral trout was contaminated with ciguatoxins was obtained by extracting the toxin and bioassay in mice. Signs in mice induced by the extract were typical of those reported for Pacific ciguatoxins,<sup>26</sup> confirming the presence of ciguatoxins in the sample. The level of ciguatoxin (1.3 ng ciguatoxin-1/g flesh) found in the flesh sample was high,<sup>25</sup> consistent with the severe cases of poisoning that resulted from ingestion of this fish.

### Treatment - Ciguatera poisoning

Symptoms	Treatment
<p><u>Gastrointestinal</u> Diarrhoea, abdominal pain, nausea, vomiting.</p> <p><u>Neurological</u> Myalgia, burning skin on contact with cold water, pruritus, arthralgia, paraesthesia of hands, feet, mouth and lips, headache, mood disorders (depression, irritability, anxiety), ataxia or vertigo, sweating, eye pain, dental pain, tremor, neck stiffness, decreased muscle strength, salivation.</p> <p><u>Non-specific</u> Fatigue and lassitude, chills, skin rash, exertional breathlessness, dysuria, coma</p>	<p>Resuscitation, if necessary Rehydration, by IV infusion if necessary Mannitol 20% - up to 250ml Anti-emetics (eg metoclopramide) Anti-diarrhoeals (eg loperimide) Anti-pruritic medications (eg doxepin, anti-histamines) Anti-anxiolytics (eg doxepin, benzodiazepines) Non-specific – paroxetine</p>

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