

# Irukandji Syndrome Case Series From Australia's Tropical Northern Territory

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**Study objective:** We describe Irukandji syndrome (a painful hypercatecholaminergic condition caused by jellyfish envenoming) in Australia's Northern Territory.

**Methods:** We collected prospectively a standardized data set on patients presenting to health facilities in the Northern Territory. Additional cases were identified retrospectively. Data collected included demographic, geographic, seasonal, and environmental features, as well as sting details, clinical manifestations, investigations, management, and outcomes.

**Results:** From 1990 to 2007, Irukandji syndrome affected 87 people. Age ranged from 1 to 51 years (64% male victims; 41% children [63% indigenous]). Activities associated with stings included snorkeling or scuba diving (35%) and swimming (29%). Stings commonly occurred in water greater than 2 m deep (63%), with fine weather (73%) and still or light breeze (70%). Seasonal variation was bimodal; peaks in May and October corresponded to prevailing offshore winds in the Darwin and Gove areas, respectively. Pain was severe (65%), with rapid onset (<30 minutes in 79%). Sting lesions (visible in 63%) were mild, and nematocysts (detected in 7 cases) had variable morphology. Systemic features were common, including hypertension and ECG abnormalities. Severe complications included troponin-level increases (2 cases) and cardiomyopathy with ventricular tachycardia (1 case), but no fatalities. Management included vinegar as first aid (66%), parenteral opioids (70%) (range 2 to 82.5 mg morphine equivalents in adults), and magnesium sulfate (3 cases). Hospital admission (49%) and aeromedical retrieval (16%) were commonplace.

**Conclusion:** Irukandji syndrome in the Northern Territory was clinically consistent with previous studies but had distinct seasonal, geographic, and environmental features. Indigenous children in remote coastal communities are at risk, and there is room for improvement in prevention and management. [Ann Emerg Med. 2009;xx:xxx.]

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## INTRODUCTION

### Background

Irukandji syndrome is a poorly understood condition resulting from jellyfish envenoming. It is characterized by severe pain, a state of catecholamine excess, and the potential for life-threatening cardiovascular complications.<sup>1-4</sup> In 1952, Flecker<sup>5</sup> named the syndrome after an Indigenous tribe near Cairns, North Queensland, Australia (Figure 1). In 1961, Barnes<sup>6</sup> identified a jellyfish that caused the syndrome by envenoming himself, his son, and a local lifeguard. Eventually this approximately 20-mm-diameter 4-tentacled box jellyfish was described fully by Southcott<sup>7</sup> and named *Carukia barnesi*.

Early descriptions of Irukandji syndrome noted minor local skin effects as a result of a relatively innocuous contact with a

jellyfish.<sup>6,8-11</sup> Severe systemic features arise within minutes, including "a sense of impending doom," dysphoria and restlessness, generalized diaphoresis, hypertension, nausea and vomiting, and severe often cyclical pain affecting the limbs, back, abdomen, or chest. Most cases resolve quickly; however, a minority of individuals develop severe pain intractable to opioids and are at risk of life-threatening complications such as acute pulmonary edema, transient cardiomyopathy, and cardiogenic shock.<sup>10,12</sup> The 2 reported fatalities<sup>1,8</sup> (one an American tourist visiting the Great Barrier Reef<sup>1</sup>) were both attributed to intracerebral hemorrhage as a result of uncontrolled hypertension, but in only one of these cases was there definitive evidence of jellyfish envenoming. Although the toxin(s) responsible for the Irukandji syndrome remain to be

### Editor's Capsule Summary

#### *What is already known on this topic*

Irukandji syndrome is a potentially lethal condition caused by intense catecholamine surge after jellyfish envenomation.

#### *What question this study addressed*

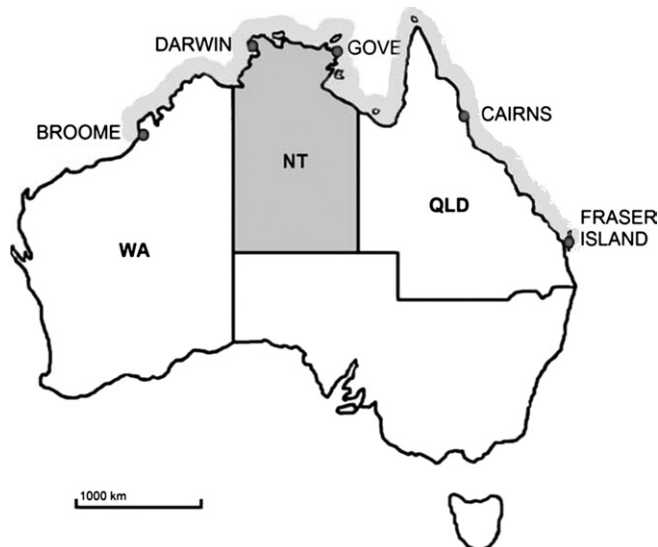
This case series examines findings in likely cases of Irukandji syndrome to understand potential preventive measures and treatments.

#### *What this study adds to our knowledge*

The study confirms characteristics of pain and signs of catecholaminergic excess. Irukandji syndrome is most common when prevailing winds are offshore. This series includes cases of priapism and pancreatitis, conditions that not been previously reported in association with Irukandji syndrome.

#### *How this might change clinical practice*

The ability to anticipate seasonal variation could allow more effective primary prevention. Additional education efforts can increase the use of effective first aid measures such as application of vinegar.



**Figure 1.** Geographic distribution of Irukandji syndrome in Australia. Key: NT, Northern Territory, QLD, Queensland, WA, Western Australia. Shaded coastline indicates geographic distribution of Irukandji syndrome.

### Goals of This Investigation

This study investigates the demographic, geographic, seasonal, and environmental features, as well as the sting details, clinical presentations, investigations, management, and outcomes associated with cases of Irukandji syndrome diagnosed in the Northern Territory between 1990 and 2007 and compares these with previously published studies from Western Australia and north Queensland.

## MATERIALS AND METHODS

### Study Design

The study is a case series of 87 cases of Irukandji syndrome occurring in the Northern Territory of Australia between 1990 and 2007.

### Setting

This region has a coastline of 10,950 km and is serviced by Royal Darwin Hospital, a 350-bed tertiary referral center, Gove District Hospital, which is a small regional hospital at Nhulunbuy on the Gove peninsula, servicing east Arnhem Land (Figure 1), and numerous health centers in small remote Aboriginal communities along the coast and on offshore islands.

### Selection of Participants

The study intended to include all identifiable cases of Irukandji syndrome in the Northern Territory between 1990 and 2007. Between April 1991 and May 2004, standard data collection forms were available at Royal Darwin Hospital, Gove District Hospital, and the coastal community health centers across the region, allowing the prospective collection of data on all suspected jellyfish stings at presentation to these sites.<sup>29</sup> From the 606 forms returned, 70 cases were identified as consistent

fully characterized, the clinical features probably result from a massive endogenous catecholamine surge.<sup>13-16</sup>

Irukandji syndrome occurs along Australia's northern coastline from Fraser Island (25° 15' south) in Queensland, across the Northern Territory to Broome (17° 58' south) in north Western Australia. "Irukandji-like" syndromes also occur worldwide, including reports from Thailand, the Caribbean, and Hawaii.<sup>6,17-20</sup> Thus far, only *C barnesi*, which is rare or absent in the Northern Territory and Western Australian waters, is conclusively proven to cause Irukandji syndrome, although other jellyfish species have been implicated.<sup>9,21-27</sup> Previous studies from Cairns<sup>28</sup> and Broome<sup>11</sup> suggest variations in syndrome severity and in environmental conditions, possibly reflecting different jellyfish species or stages of maturity.

### Importance

Jellyfish envenoming is a well-known public health threat in tropical Australian waters that affects the commercial and recreational activities of locals and tourists.<sup>29</sup> In north Queensland<sup>28</sup> and north Western Australia,<sup>11</sup> cases of Irukandji syndrome outnumber envenoming by the potentially lethal multi-tentacled box jellyfish *Chironex fleckeri*. In the Northern Territory, *C fleckeri* envenoming predominates,<sup>29</sup> and a gap remains in our understanding of Irukandji syndrome. Similarly, the global significance of Irukandji syndrome is unknown.

with Irukandji syndrome<sup>9</sup> by one author (B.J.C.). Explicit criteria were not used. Data collection forms were also used to perform chart reviews of a further 17 cases retrospectively identified from clinical record databases of Royal Darwin Hospital and Gove District Hospital for patients with *International Classification of Diseases* 10 code “X26.01 Contact with Irukandji jellyfish” during January 1990 to December 2007. Diagnosis was made by the treating physician and confirmed by the abstractors as consistent with Irukandji syndrome.<sup>9</sup>

### Data Collection and Processing

The data collected included demographic features, geographic location, and environmental features, including weather and sea conditions. Sting details, clinical manifestations, investigations, first aid, management, and outcomes were also recorded. The National Tidal Centre provided tidal information, predominant wind direction, and hourly water temperatures.<sup>30</sup> Analgesic requirements included calculation of morphine equivalents, such that 1 mg morphine was considered equipotent to 10 mg meperidine.<sup>31</sup> Skin scrapings or sticky tape samples were performed on some patients for microscopy for stinging organelles (nematocysts) as previously described.<sup>28,32</sup> Children were defined as younger than 15 years.

Data abstraction was performed by 2 abstractors (C.P.N. and E.B.W.). Formal interrater reliability was not assessed. The abstractors were self-trained and not blinded. The investigators communicated periodically by e-mail.

Variables not mentioned on the data collection forms were assumed to be absent rather than unknown, except where indicated in the “Results” section by a reduction in the denominator from the total 87 cases. This particularly applies to the data on clinical manifestations, investigations, and management. Information from ambulance forms, medication charts, and observation charts was used preferentially to resolve any discrepancies between information from different sources (eg, referral letters and clinical notes). Data were collated and analyzed with Microsoft Office Excel 2002 (Microsoft, Redmond, WA) and Intercooled Stata 9.0 (StataCorp, College Station, TX). The study was approved by the Human Research Ethics Committee of the Menzies School of Health Research and the Northern Territory Department of Health and Community Services.

## RESULTS

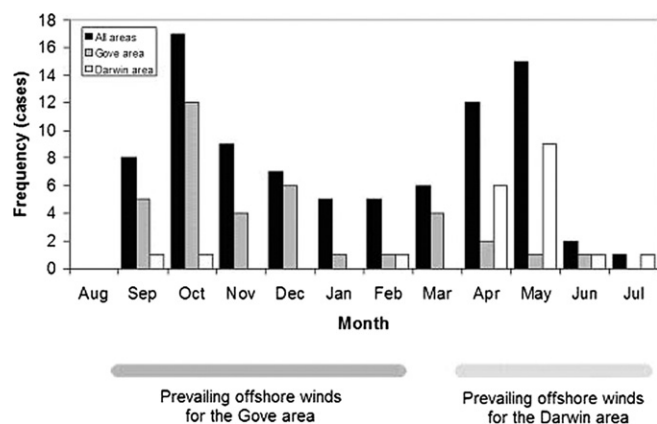
### Characteristics of Study Subjects

Geographic locations and demographic and environmental data for 87 cases of Irukandji syndrome in the Northern Territory are shown in Table 1. Cases were reported in all years, with the exception of 2001. A median of 4.5 case patients presented each year (range 0 to 13 cases), peaking at 13 in 1992. People fishing or boating offshore accounted for 9 cases, with the most remote case occurring in a commercial fisherman 650 km west of Darwin in the Timor Sea (12° 07' south).

**Table 1.** Geographic location and demographic and environmental data for Irukandji syndrome in the Northern Territory.

<b>Geographic location, Demographic data, and environmental data</b>	<b>Cases (%)</b>
<b>Geographic location</b>	
Gove area (Nhulunbuy)	37/85 (44%)
Darwin area	20/85 (24%)
Offshore islands* and fishing vessels	20/85 (24%)
Mainland remote communities	8/85 (9%)
<b>Sex</b>	
Male	56/87 (64%)
<b>Ethnicity</b>	
Nonindigenous Australian	53/86 (62%)
Indigenous Australian	29/86 (34%)
Overseas national	4/86 (5%)
<b>Age, y (median 20; range 1–51)</b>	
Adult	51/86 (59%)
Children (<15)	35/86 (41%)
Stung at Gove	30/35 (86%)
Indigenous Australian	22/35 (63%)
<b>Sting time (median 1:45 PM)</b>	
6–8:59 AM	7/82 (9%)
9–11:59 AM	19/82 (23%)
Noon–2:59 PM	29/82 (35%)
3–5:59 PM	19/82 (23%)
6–8:59 PM	4/82 (5%)
9 PM–5:59 AM	4/82 (5%)
<b>Activity when stung</b>	
Snorkeling or scuba diving	30/86 (35%)
Swimming	25/86 (29%)
Standing/wading/playing in shallow water	18/86 (21%)
Fishing, offshore, hauling in net or line	8/86 (9%)
Fishing, from shore	2/86 (1%)
Boating, hauling in anchor	1/86 (1%)
Jumping off a jetty	1/86 (1%)
“Skurfing” (water skiing with a surfboard)	1/86 (1%)
<b>Water depth, m (median 3; range 0.2–30)</b>	
<1	11/48 (23%)
1 to <2	7/48 (15%)
2 to <5	11/48 (23%)
>5	19/48 (40%)
<b>Wind conditions</b>	
Still	13/37 (35%)
Slight breeze	13/37 (35%)
Moderate breeze	9/37 (24%)
Strong wind	2/37 (5%)
<b>Weather conditions</b>	
Fine	45/62 (73%)
Cloudy	14/62 (23%)
Raining	3/62 (5%)
<b>Tide cycle (excludes the 14 cases of envenoming that occurred offshore)</b>	
High	24/73 (33%)
Outgoing	19/73 (26%)
Low	10/73 (14%)
Incoming	20/73 (27%)
<b>Water temperature: median 29.9°C; range 25–32.3°C (known for 77 cases)</b>	

\*Includes divers off Groote Eylandt (n=3) and Tiwi Islands (n=2).



**Figure 2.** Seasonal variation of Irukandji syndrome in the Northern Territory. There is a distinct bimodal seasonal pattern. This pattern largely reflects distinct unimodal distributions for the Gove and Darwin areas associated with prevailing offshore winds. Prevailing winds were consistent in different locations throughout the Northern Territory. From September to February, the prevailing winds were northwesterly (ie, offshore winds for the predominantly northeast-facing Gove area), and from April to July the prevailing winds were southeasterly (ie, offshore winds for the predominantly northwest-facing Darwin area). During March, winds were low and had little pattern, whereas in August the prevailing winds were southwesterly. There were no cases of Irukandji syndrome during August, when the prevailing wind was not offshore for either Darwin or Gove. These peak periods also correspond to transitions between the “wet” and “dry” seasons. Furthermore, whereas cases persistently presented through the “wet” season (December to February), they were rare once the “dry” season was established (June to August).

### Main Results

Geographic location and demographic and environmental data are shown in Table 1. Seasonal variation was bimodal; peaks in May and October corresponded to prevailing offshore winds in the Darwin and Gove areas, respectively (Figure 2).

The clinical manifestations, investigations, management, and outcomes are summarized and compared with other studies in Tables 2 and 3. Pain was severe (65%), with rapid onset (within 30 minutes in 79%). Sting lesions (visible in 63%) were mild (Figure 3), and nematocysts (detected in 7 cases) had variable morphology (Figure 4). Systemic features were common, including hypertension and ECG abnormalities. The ECG changes included atrial and ventricular ectopy, atrioventricular conduction defects, ST-segment elevation, T-wave abnormalities, and 1 case of nonsustained ventricular tachycardia. There were severe complications, including troponin-level elevations (2 cases) and cardiomyopathy with acute pulmonary edema and nonsustained ventricular tachycardia (1 case). One patient, a 10-year-old indigenous girl, experienced complications because of pneumonia and

pancreatitis with ileus, resulting in an 11-day hospital admission. There were 2 cases of acute renal impairment and 1 case of priapism. No patient required mechanical ventilation, developed intracranial hemorrhage, or died.

Management included vinegar as first aid (66%), parenteral opioids (70%) (range 2 to 82.5 mg morphine equivalents in adults), and magnesium sulfate (3 cases). Hospital admission (49%) and aeromedical retrieval (16%) were commonplace. Epinephrine was administered to 1 patient for a possible allergic reaction. Two ampules of *C. fleckeri* antivenom were administered to 1 patient, with no clinical improvement observed. One patient re-presented to hospital with severe generalized pain 29 hours after the sting occurred. This patient was originally discharged with incomplete resolution of pain. Four cases of severe Irukandji syndrome are described in Table 4.

### LIMITATIONS

Our study used combined prospective and retrospective data, with data limited to information recorded by treating clinicians. It may not be representative of the illness spectrum because some patients with Irukandji syndrome who presented at remote clinics may not have been included in the study, some patients may not have sought medical attention, and others may have been incorrectly diagnosed. Sting lesion data may be unreliable because the patient-reported site could not be confirmed in the absence of an identifiable lesion, and in some cases the sting lesion may have resolved before clinician assessment. Geographic locations were based on information given by patients. Pain scores and severity can be difficult to determine in children and, for cultural reasons, indigenous Australians. “Second-rank” symptoms and signs may have been underreported because of other priorities. Investigations may have been underreported if not written in the notes. The study extended back as far as 1990, so variations in management over time are expected. Total opioid requirements were not recorded for many cases, and weights were not available for calculating mg/kg doses for children. Finally, the length of stay for admissions may be biased by long transit times and aeromedical transfers from remote locations.

### DISCUSSION

Although Irukandji syndrome has been noted previously in the Northern Territory of Australia,<sup>33</sup> to our knowledge this is the first comprehensive published case series from the Northern Territory. It bridges the geographic distribution of Irukandji syndrome presentations along Australia’s northern coast.<sup>11,23,28</sup> The study identifies indigenous children in remote coastal communities as especially at risk of Irukandji syndrome, as they are for *C. fleckeri* envenoming.<sup>29</sup>

The characteristic pattern of seasonal variation of Irukandji syndrome in the Northern Territory appears to reflect prevailing offshore winds in different regions. Closer interpretation of the data from Broome shows a similar pattern: during December to

**Table 2.** Clinical manifestations of Irukandji syndrome in the Northern Territory compared with previous case series.

Clinical manifestations	NT, 1990–2007	Broome, <sup>11</sup> 2001–2003	Cairns, <sup>28</sup> 1996	Cairns, <sup>6</sup> 1964
Total cases*	87	88	62	60
<b>Sting lesions (%)</b>				
Sting lesion visible	53/84 (63)	70/88 (80)	—	—
<b>Sting contact sites (%)<sup>†</sup></b>				
Limbs	47/101 (47)	—	—	—
Head and neck	29/101 (29)	—	—	—
Trunk	25/101 (25)	—	—	—
<b>Pain (%)</b>				
Severe or “10/10” pain	46/71 (65) (Severe pain)	40/88 (45) (10/10 Pain)	—	—
Pain onset from time of sting	Median 9 min (63/87 known)	—	—	—
Pain onset <30 min	50/63 (79)	—	—	—
Pain onset >60 min	6/63 (10)	—	—	—
<b>Anatomic location of pain (%)</b>				
Abdominal pain	46/87 (53)	50/88 (57)	25/62 (40)	55/60 (92)
Chest pain/tightness	37/87 (43)	27/88 (31)	16/62 (26)	—
Back pain	34/87 (39)	51/88 (58)	24/62 (39)	24/60 (40)
Generalized pain	32/87 (37)	—	—	—
Leg or limb pain	30/87 (34)	43/88 (49)	21/62 (34)	35/60 (58)
<b>Cardiovascular features</b>				
Tachycardia (%) (>99 beats/min)	20/87 (23)	—	—	—
Hypertension (%) <sup>‡</sup>	39/51 (76)	43/88 (49)	31/62 (50)	—
Mean peak systolic blood pressure, mm Hg <sup>§</sup>	153 (adults, range 110–240)	—	—	144 (range 115–180)
Pulmonary edema (%) <sup>  </sup>	1/87 (1)	2/88 (2)	2/62 (3)	—
<b>Other features (%)</b>				
Nausea and vomiting	41/87 (47)	29/88 (33)	24/62 (39)	34/60 (57)
Diaphoresis	28/87 (32)	19/88 (22)	—	—
Distress or generally unwell	23/87 (26)	74/88 (84)	15/62 (24)	—
Dyspnea	23/87 (26)	—	—	—
Restlessness or agitation	15/87 (17)	—	—	—
Headache	11/87 (13)	—	—	—
Piloerection	9/87 (10)	—	—	—
Flushing	5/87 (6)	25/88 (28)	—	—
Drowsiness	5/87 (6)	—	—	—
Pulse oximetry <95% SaO <sub>2</sub>	4/87 (5)	—	—	—

—, No data published in paper for this variable.

\*If the denominator shown for the frequency of Northern Territory cases is less than 87, then the denominator is the number of cases for which data were known.

<sup>†</sup>In 7 cases, sting contact site location(s) were unknown. A total of 101 sting sites were reported from 80 cases, taking into account cases with multiple sting sites.

<sup>‡</sup>Hypertension is defined as peak systolic blood pressure >139 mm Hg. Only Northern Territory data for adults are shown.

<sup>§</sup>The 2001 to 2002 study from Cairns<sup>23</sup> (116 patients) reported no cases of pulmonary edema, and the mean systolic blood pressure was 145 mm Hg (range 100 to 230 mm Hg).

<sup>||</sup>Diagnosis based on clinical findings and a chest radiograph result consistent with acute pulmonary edema.

March, 90% of stings occurred in east-facing Roebuck Bay when there were prevailing offshore winds, and during March to June, 95% of stings were from west-facing Cable Beach, which in turn had prevailing offshore winds during these months.<sup>11</sup> The pattern in Cairns is distinct: Irukandji syndrome peaks during northerly prevailing winds and predominantly onshore currents.<sup>6,28</sup> Further studies are required to determine why there is an association with offshore prevailing winds in Broome and the Northern Territory. The seasonal pattern may allow appropriate timing of clinician and public health awareness measures.

The diurnal variation of stings, as well as the tidal and weather conditions for the Northern Territory Irukandji syndrome cases, was generally similar to that of the Broome series.<sup>11</sup> Most cases involved activities where water depth exceeded 2 m, which contrasts with *C fleckeri* envenoming in

the Northern Territory, where 84% of cases occur at a depth of less than 1 m,<sup>29</sup> as well as reports from Cairns, where Irukandji syndrome stings occur close to the beach.<sup>6,23</sup> Indeed, 63% of patients in Cairns were swimming inside stinger nets,<sup>28</sup> which are designed to exclude *C fleckeri*, but through which *C barnesi* and other small jellyfish can penetrate. There are no stinger nets currently in the Northern Territory or Broome, and the network of Surf Life Saver–patrolled nets in north Queensland enables swimming during the summer months when *C fleckeri* are present. The varying regional patterns of sting occurrences might reflect differences in the behavior and lifecycle of the envenoming jellyfish species, as well as human activities.

Irukandji syndrome remains a clinical diagnosis and a case definition has been proposed.<sup>11</sup> Because stings from numerous jellyfish species may result in local pain with nonspecific

**Table 3.** Investigations, management, and outcomes of Irukandji Syndrome in the Northern Territory compared to previous case series

Investigations, management, and outcomes	NT, 1990–2007	Broome, <sup>11</sup> 2001–2003	Cairns, <sup>28</sup> 1996	Cairns, <sup>23</sup> 2001–2002
Total cases*	87	88	62	116
<b>Investigations (%)</b>				
Troponin result positive	2/6 (33)	—	—	25/116 (22)
Abnormal ECG result	10/45 (22)	—	—	12/116 (10%)
Abnormal echocardiograph result	1/3 (33)	—	—	6/18 (33)
Skin scrapings/sticky tape samples taken	46/87 (53)	—	—	50/116 (43)
Nematocysts seen	7/46 (15)	—	—	40/50 (80)
<b>Management (%)</b>				
Vinegar use	57/87 (66)	51/88 (58)	43/53 (81)	—
Analgesic medication use	79/84 (94)	—	—	—
Parenteral opioid use	59/84 (70) <sup>†</sup>	79/88 (90)	38/62 (61)	—
Mean morphine equivalents, mg	16.1 <sup>†</sup> (Adults, median 10, range 1–82.5)	20 (Adults, median 13, range 5–90)	—	31 (Adults, range 0–255)
Meperidine use	39/84 (46)	—	30/62 (48) <sup>§</sup>	—
Morphine use	17/84 (20)	—	2/62 (3) <sup>§</sup>	—
Chlorpromazine use	13/87 (15)	—	—	—
Promethazine use	7/87 (8)	—	16/62 (26)	—
Other antiemetic use	22/87 (25)	—	—	—
<b>Outcomes</b>				
Admission rate (%)	41/84 (49)	15/88 (17)	35/62 (56)	74/116 (64)
Aeromedical retrievals (%)	14/87 (16)	—	6/62 (10)	—
Length of stay, days	Mean 1.8 (95% confidence interval 1.3–2.3, range 1–11)	—	—	Mean 1.6 (max 5)

\*If the denominator shown for the frequency of Northern Territory cases is less than 87, then the denominator is the number of cases for which data were known.

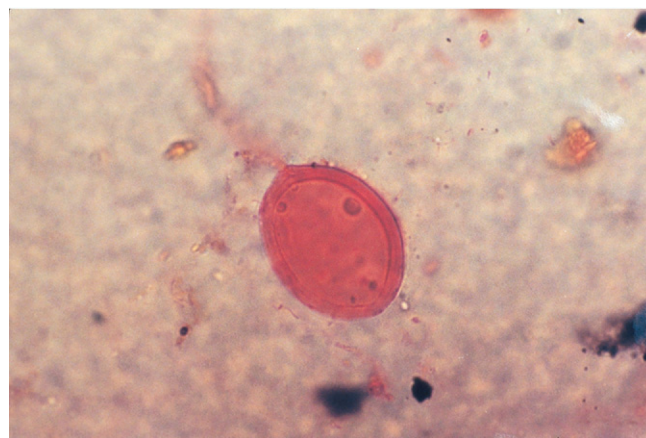
<sup>†</sup>Both morphine and meperidine were given to 2 patients, and it was uncertain which narcotic was used in 5 cases. There were no instances of fentanyl use.

<sup>†</sup>There were 21 adults with known doses of parenteral opioids. Doses could not be calculated as mg/kg amounts for the children because weights were rarely obtainable during data collection.

<sup>§</sup>A further 6 patients (10%) received both meperidine and morphine.



**Figure 3.** Skin lesion from contact with jellyfish bell in a case of Irukandji syndrome. Skin lesions were variously described as “goose pimples,” erythema, raised welts, and edema. The lesions were generally diffuse and ranged from less than 1 cm to 15 cm in diameter. Adherent tentacles were found in a few cases, and in a few others linear lesions were described.



**Figure 4.** Scraping of sting lesion of patient in Figure 3 showing eosin-stained bell nematocyst; magnification  $\times 1000$ . Nematocyst morphology was variable, with some but not all having nematocysts wider than the classical cigar-shaped *C fleckeri* nematocysts<sup>32</sup> and a bell (circular) nematocyst seen in one case.

systemic upset, criteria for the diagnosis of Irukandji syndrome are needed to preserve its status as a useful clinical entity. Key features include recent contact with seawater, a relatively minor initial sting followed by a progressive syndrome (over minutes

to hours) characterized by generalized pain and distress, and features of catecholamine excess such as hypertension. On this basis, case reports from Hawaii,<sup>20</sup> Florida,<sup>18</sup> and Thailand<sup>17</sup> appear consistent with a true Irukandji syndrome, whereas other

**Table 4.** Four cases of severe Irukandji syndrome from the Northern Territory, Australia.

Case	Symptoms
<b>Patient A</b>	29-year-old man stung while hauling in a fishing net in deep sea near Groote Eylandt.
Clinical	Mild sting on right arm progressed during 20 min to severe whole body aches, headache, chest tightness, respiratory distress, and hypertension (185/112 mm Hg). Symptoms persisted for 72 h, including intermittent sinus tachycardia and chest pains unresponsive to GTN infusion.
Investigations	ECG: progressive T-wave inversion in leads II, III, aVF, V2–V6 during the first 48 h. Troponin I level elevated (2.57 $\mu\text{g/L}$ at 24 h). Normal CXR and TTE results (day 5) and Myoview scan result (day 13).
Management	Morphine (total 24.5 mg IV), chlorpromazine, aspirin, clopidogrel, enoxaparin, and GTN infusion.
Length of stay	6 days
<b>Patient B</b>	21-year-old man stung while scuba diving to 30 m depth in Darwin Harbor.
Clinical	Tingling sensation in his face progressed to agonizing abdominal, loin, facial, and leg pain during 10 min; then profuse vomiting, tremor, and diaphoresis during the next 30 min. He had hypertension (220/120 mm Hg), tachycardia (140 beats/min), and tachypnea (40 breaths/min). Symptoms resolved during 24 h.
Investigations	ECG: sinus tachycardia. CXR and troponin I (<0.3 $\mu\text{g/L}$ ) normal.
Management	Morphine (total 82.5 mg IV), chlorpromazine, metoclopramide, and labetalol. Pain subsided after $\text{MgSO}_4$ (10 mmol during 30 min) at 3 h. Pain returned during the next 2 h (treated with 10 mg morphine IV) until further $\text{MgSO}_4$ (10 mmol during 2 h) was given. Although improved, pain persisted and another 10 mg morphine IV was required during the next 7 h.
Length of stay	2 days
<b>Patient C</b>	35-year-old man stung while hauling in ropes on a fishing boat near Bathurst Island.
Clinical	Stinging sensations in legs and back and welts progressed to excruciating abdominal, chest, and limb pains and vomiting. Arrived at Royal Darwin Hospital 16 h post-envenoming, with ongoing pain, tachycardia (100 beats/min), hypertension (154/79 mm Hg), and tachypnea (25 breaths/min), $\text{SO}_2$ 100% on air, and with bibasal lung crepitations.
Investigations	ECG: sinus rhythm with T-wave flattening in aVL and 1-mm ST elevation in V2–V3. Nonsustained VT for 2 min. Troponin I level increased (2.74 $\mu\text{g/L}$ at 24 h). Mild hyperglycemia and hyperlactemia. CXR: diffuse bilateral alveolar opacities consistent with pulmonary edema. TTE: Diffuse cardiomyopathy with mildly decreased left ventricular function. Follow-up TTE and CXR results were normal (day 5).
Management	Morphine (total 5 mg IV), chlorpromazine, and metoclopramide. $\text{MgSO}_4$ (10 mmol IV during 30 min) given at 18 h, ECG normalized. Further $\text{MgSO}_4$ (10 mmol IV during 2 h) given when pain recurred at 20 h.
Length of stay	4 days
<b>Patient D</b>	30-year-old man stung while preparing fish next to patient C.
Clinical	Burning sting with erythema behind his right knee, followed by abdominal cramps, agonizing whole-body pains, severe occipital headache, and continual vomiting. Arrived at Royal Darwin Hospital at 16 h with ongoing pain and hypertension (148/89 mm Hg).
Investigations	Serial ECGs: concave-upwards 1-mm ST elevation in leads II, III, aVF, with ongoing chest pain. Trop I result negative (<0.3 $\mu\text{g/L}$ ). CXR result normal. Mild hyperglycemia and hyperlactemia.
Management	Morphine (total 2.5 mg IV). Treated with $\text{MgSO}_4$ (10 mmol IV during 30 min) at 18.5 h postenvenoming for pain recurrence—pain free at 19 h. Generalized pain (9/10 severity) recurred at 24 h. $\text{MgSO}_4$ (10 mmol IV during 30 min; then 5 mmol/h IV) given at 26 h. Pain improved but persisted (2–4/10) until 42 h, and then the $\text{MgSO}_4$ infusion was weaned.
Length of stay	4 days

GTN, Glyceryl trinitrate; CXR, chest radiograph; TTE, transthoracic echocardiograph; IV, intravenously;  $\text{MgSO}_4$ , magnesium sulfate; VT, venous thrombosis.

reports<sup>34</sup> have some “Irukandji-like” features but may be distinct clinical entities.

Not all *C barnesi* stings cause full-blown Irukandji syndrome,<sup>23</sup> and debate about which jellyfish species actually cause Irukandji syndrome is highly contentious.<sup>21,22,24,25</sup> Some species attributions have been based on microscopic appearances of nematocysts from patient skin samples.<sup>23,26</sup> Our experience of more than 15 years of examining skin samples from jellyfish sting victims cautions against this practice<sup>29,32</sup> because variable nematocyst appearances from a single species are possible because of normal variations in shapes and sizes and nematocyst distortion during discharge or in sampling and processing. Microscopy of skin scrapings has been used to suggest that other species caused an Irukandji syndrome fatality<sup>23</sup> and another severe envenoming with cardiogenic pulmonary edema.<sup>26</sup> However, we believe the photographs published do not definitively exclude *C barnesi*. Nevertheless, other Carybdeid

jellyfish may well be responsible for Irukandji syndrome in the Northern Territory and Western Australia.

The clinical features of Irukandji syndrome, including severity and onset, were similar in the Northern Territory to those reported from Broome and Cairns.<sup>11,28</sup> Priapism and pancreatitis have not previously been recognized as complications of Irukandji envenoming. Multiple factors probably contribute to the severity of envenoming,<sup>6</sup> including possible differences in jellyfish species or stage of maturity.<sup>35</sup> Our Northern Territory data showed that sting lesions generally resembled previous descriptions for Irukandji syndrome,<sup>6,11,28</sup> but there were exceptions, including multiple linear lesions. Lesions consistent with both tentacle contact and contact with the jellyfish bell were observed (Figure 3). Unlike most multi-tentacled box jellyfish (Chirodroids) such as *C fleckeri*, *C barnesi* and other 4-tentacled box jellyfish (Carybdeids) usually have

batteries of nematocysts on their bells, as well as on their tentacles.

This study confirms that the majority of Irukandji syndrome cases are not life threatening. Clinically important cardiotoxicity was unusual, although cardiac marker testing was infrequently performed and the 5 cases of oxygen desaturation to less than 95% on pulse oximetry might suggest transient acute pulmonary edema that resolved before further investigation. ECG abnormalities were common in the Northern Territory cases but of uncertain significance. Nevertheless, the risk of severe cardiovascular sequelae in patients with unremitting pain, as noted in this study and others,<sup>1,8,10-12,23,28</sup> may require management in an appropriate setting and timely transfer from remote areas. The high admission rates of Northern Territory patients to the hospital probably reflect the remoteness of many patients from treatment centers, which makes early discharge impractical. The single case of re-presentation after treatment should remind clinicians to be cautious when considering the discharge of patients with systemic symptoms.

Treatment of Irukandji syndrome is currently based on anecdotal evidence,<sup>36</sup> and variance is likely in remote locations where health workers may have minimal experience in its management.<sup>37</sup> The lack of response in the case in which *C fleckeri* antivenom was given was consistent with previous reports of its ineffectiveness in Irukandji syndrome.<sup>38</sup> Vinegar is widely recommended as first aid because it inactivates the undischarged nematocysts of box jellyfish,<sup>39</sup> although application of vinegar in Irukandji syndrome may be delayed and ineffective in many cases because the initial sting can be innocuous. Given that 99% of *C fleckeri* stings in the Northern Territory are treated with vinegar,<sup>29</sup> public health measures are needed to increase the rates of vinegar use for Irukandji stings.

Mean opioid requirements were lower in the Northern Territory than in Broome<sup>11</sup> or Cairns<sup>23</sup>; this may reflect incomplete data, outliers in the other studies, delayed presentations with partial resolution of symptoms, differences in the use of adjunctive treatments, difficulties in assessing pain levels in indigenous Australians because of cultural differences, and the possible underestimation of morphine equivalents required for pain relief because the meperidine to morphine parenteral equivalence is variably reported as 75 to 100 mg to 10 mg.<sup>31</sup> The relative efficacy of different opioids<sup>3,28</sup> and antiemetics<sup>28</sup> for the treatment of Irukandji syndrome is uncertain. Similarly, despite initial encouraging anecdotes,<sup>40,41</sup> magnesium sulfate remains an unproven therapeutic option for Irukandji syndrome refractory to conventional management.<sup>42</sup>

Although Irukandji syndrome is infrequent, awareness of it must be heightened among health professionals and the general public across northern Australia. The challenge now is to accurately determine and describe exactly which jellyfish species cause Irukandji syndrome and why, which will enable a more accurate assessment of the global distribution of Irukandji syndrome and its public health importance. First, we need a better understanding of the pathophysiology. The specific

toxin(s) responsible for putative endogenous catecholamine excess remains undefined, and there are no specific diagnostic laboratory tests available. More rigorous clinical evaluation of patients presenting to the emergency department after jellyfish stings may enable better distinction between Irukandji syndrome and "Irukandji-like" cases. We also encourage clinicians around the world to investigate the epidemiologic and clinical features of their own local jellyfish envenomings to improve our understanding of the global distribution, clinical syndromes, and effect of jellyfish envenoming worldwide.

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**Editor's Capsule Summary:** *What question this study addressed:*

This case series examines findings in likely cases of Irukandji syndrome to understand potential preventive measures and treatments. *What this study adds to our knowledge:* The study confirms characteristics of pain and signs of catecholaminergic excess. Irukandji syndrome is most common when prevailing winds are offshore. This series includes cases of priapism and pancreatitis, conditions that not been previously reported in association with Irukandji syndrome.