Long-term analysis of Irukandji stings in Far North Queensland

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Abstract

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Introduction: We reviewed the occurrence, trends, definition and severity of the Irukandji syndrome for the Cairns region of North Queensland, Australia.

Methods: A retrospective analysis of patient files from two sources was conducted: historic accounts kept by Dr Jack Barnes for the period 1942 to 1967, and records from the Emergency Unit in Cairns Base Hospital for 1995 to 2007.

Results: There has been a significant increase in the length of the Irukandji season since it was first reliably recorded (15 days in 1961; 151 days in 2002); however, annual numbers of envenomations were highly variable. Traditionally, greater frequencies of Irukandji stings were reported at onshore as opposed to offshore locations. However, in recent years this trend has reversed, potentially because of increased safety protocols for beach regions. Mean Troponin I levels were higher in offshore reef envenomations compared to those from islands or coastal regions. In terms of morphine-equivalent doses, patients given fentanyl received significantly greater opioid doses compared to those given morphine or pethidine. Opioid dosage was indicative of syndrome severity and correlated with other physiological parameters measured. Five major symptoms were associated with Irukandji syndrome: pain, nausea/vomiting, diaphoresis, headache and shortness of breath. Pain was the overwhelming symptom, followed closely by nausea/vomiting.

Conclusions: The duration of the Irukandji season appears to be increasing. Conversely the number of envenomings appears to be decreasing, possibly because of improved beach management in recent years. Offshore envenomings appear to have a higher potential for more severe envenomings with five associated major symptoms.

Key words

Marine animals, jellyfish, envenomation, medical database, pain, treatment, epidemiology

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Introduction

Irukandji syndrome is a set of debilitating symptoms, first described from around Cairns, North Queensland, Australia, arising from envenomation by particular species of box jellyfish.[1–3] Initial envenomation is typically recorded as insignificant; however, after a delay of generally 20 to 60 minutes, systemic symptoms including headache, backache, nausea, vomiting, abdominal cramps, hypertension, tachycardia and feelings of impending doom develop.[3–5] Although numerous case reports occur annually from this area, great disparity still exists not only in the reporting of the syndrome but also its seasonal occurrence.[1,3]

The Irukandji season in Australia has previously been reported to start as early as October and run as late as May; however, envenomations occur in all months bar July and August.[6–9] The peak time for Irukandji envenomations in the Cairns region has been declared around December/January; however, these observations were made over a single season with no long-term analyses being documented.[9,10] There is some suggestion of a potential correlation between sting incidence and the ecology of the animals responsible, but this may only reflect conditions in which people opt to utilize the beaches with higher frequency.[11,12] For example, Christmas Day has one of the greatest recorded incidences of sting occurrence, potentially reflecting increased beach usage.[6]

While the syndrome was originally described as only affecting bathers utilising the sandy coastal beaches and not on the reef, envenomations from the outer reef and island regions are now commonly reported, with some of the serious cases documented from these offshore locations.[5,12,13] Anecdotal reports have suggested that there may be a pattern in the timing of the more severe envenomations that present to hospital, with the general consensus being that the more serious Irukandji stings present later in the season.[4] However, as with the sting-severity hypothesis, no empirical data currently exist to support this premise.

Presently, no detailed studies on the ecology of Irukandji jellyfish exist, so the only avenue available to uncover patterns in Irukandji syndrome envenomations is the retrospective analysis of patient files. To this end, data from Irukandji syndrome envenomations in the Cairns region, covering a period of 65 years, were analysed to investigate trends in sting occurrence in the region. Additionally, trends in sting severity and treatment success were sought for potential insight into improving clinical management. Finally, we investigated the frequency and range of symptoms.

Materials and methods

PATIENT RECORDS

Patients who suffer from Irukandji stings are typically coded as either “marine sting”, “Irukandji sting”, or “sting from venomous jellyfish or starfish”, and these patients were extracted from the Cairns Base Hospital database for potential inclusion into this study. Patients included in the trial were those who had contact with seawater pre-60 minutes of symptoms developing, a delay in symptoms from an initial sting and at least one of the defined systemic clinical symptoms, which included headache, nausea, anxiety, vomiting, sweating, restlessness, muscle cramps in all four limbs, abdomen and chest or severe lower back pain.[14] Any stings that were deemed to have resulted from contact with a large Chirodropid jellyfish (i.e., *Chironex fleckeri* or *Chiropsella bronzie*) or those from the hydrozoan *Physalia* sp., (noted by the visible and/or substantial welts with an absence of systemic symptoms) were excluded. A total of 347 envenomations covering the years from 1995 to 2007 were included and accessed under Cairns Base Hospital Ethics Committee approval number 287. In several cases, not all categories of data were able to be extracted from the medical records (e.g., geographic location or total amount of opioids administered due to treatment at other locations before transfer to Cairns Base Hospital, admittance into a randomized controlled trial using magnesium), and these cases were excluded from specific analyses if the relevant data were missing.

ADDITIONAL HISTORIC DATA INCLUSION

A historic sting database exists from Dr Jack Barnes' comprehensive records of sting cases from 1942 to 1967.[15] These cases were all from Irukandji syndrome stings from the Cairns region and were all seen and documented by Barnes.[15] The dates of Irukandji syndrome stings from this report were added into this retrospective study for analysis into the occurrence of Irukandji syndrome stings with time.

DATA COLLECTED

Information extracted from patient files covered the three main areas of patient demographics, sting occurrence and symptoms/treatment progression. Some files were incomplete, so not all areas could be comprehensively recorded for all stings. The following factors of envenomed patients were recorded:

- Total opioid requirements in morphine-equivalent doses. Three opioids – pethidine, morphine and fentanyl – were used and dosages were calculated in terms of morphine-equivalent doses to allow for direct comparison; 1 mg morphine = 10 mg pethidine = 10 µg fentanyl.[5]
- The observed peak percentage blood pressure (BP) increase, measured as both the maximum mean arterial pressure (MAP, approximated using the equation: MAP = (2 x diastolic pressure + systolic pressure)/3), and peak systolic pressure from regular observations. BP just prior to discharge was deemed indicative of the patient's 'normal' level. The peak recorded BP was calculated as a percentage increase above this 'normal' reading.
- The observed peak percentage heart rate (HR) increase: the maximum HR recorded during regular observations while in hospital care was calculated as a percentage increase to the HR recorded at discharge.
- Troponin I level (cTnI, normal < 0.7 g L^{-1}).
- Length of stay (hours) from first admission for each patient was assumed to indicate the level of care needed for the syndrome to subside.

Additional to the physiological information gathered, logistical information on sting events was recorded including, where possible, the geographic location of stings. To distinguish between geographical regions, three categories were selected (these are thought to reflect the different habitats Irukandji jellyfish may inhabit). Any stings occurring from the coastal beaches were defined as 'onshore'; stings originating from water activities around the coastal islands were classified as 'islands'; and stings that occurred from the outer reef regions were classed as 'reef' stings. All the documented symptoms were recorded, with those that appeared in at least 5% of the cases marked into categories. These symptoms recorded throughout all the cases examined were found to fall into five categories: pain (limb pain, back pain, abdominal pain and chest pain), headache, nausea and vomiting, diaphoresis and shortness of breath, so these and troponin levels were used for analysis.

DATA ANALYSIS

For several of the analyses, data were non-normally distributed and residuals were heteroscedastic. In these cases, data were transformed to normalize the distribution and produce homoscedastic residuals to avoid violation of assumptions for a general linear model analysis. A general linear model (ANOVA) was used to investigate the effect of year (1995/6 to 2006/7) and/or geographic location (onshore, reef or island) on the length of the Irukandji season. Post hoc analysis (LSD) was performed on significant effects to determine which treatment means were different. Only stings from 1995/6 onwards were used for this analysis as this information was lacking from many records in Barnes' published database. Similarly an ANOVA was used to elucidate any effects location and/or year had on the level of Troponin I leakage seen in envenomed victims.

Regression analysis was used to determine the relationship between the length of the Irukandji season and time (from 1956 to 2007). Chi squared analysis was used to compare the ratio of stings seen onshore versus offshore locations with each year from 1995 to 2007. Bivariate correlations were performed to determine the significance of correlations between morphine-equivalent dosage and length of stay, percentage MAP and systolic BP changes or Troponin I level.

Finally, to determine if mean morphine-equivalent dosage varied with the number of symptoms recorded (pain, headache, nausea/vomiting, diaphoresis, shortness of breath) or Troponin I leakage, data were analysed using ANOVA and LSD post hoc to determine within-treatment differences.

Figure 1
Scatter plot of total length of stinger season annually in days based on stings recorded (R^2 linear = 0.427)

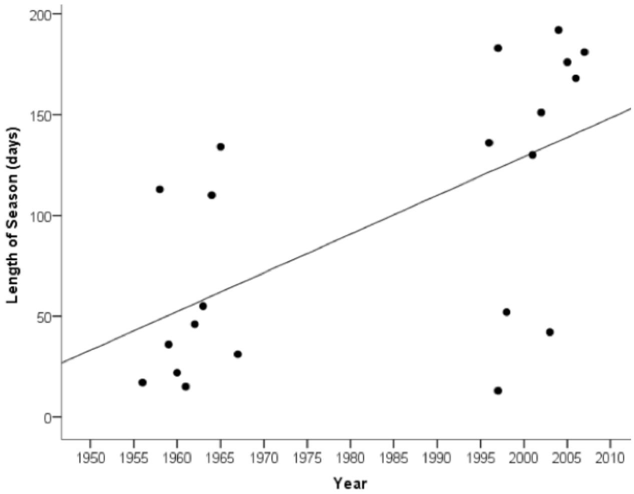
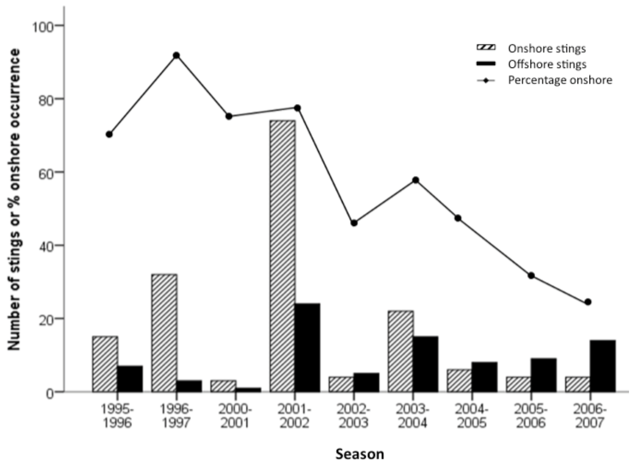


Figure 2
Frequency of recorded Irukandji stings from both offshore and onshore locations in the Cairns region and percentage of those stings that occur onshore



Results

DISTRIBUTION OF ENVENOMINGS

Patients in this study consisted of 55% males and 45% females. Patients ranged in age from 1 to 77 years old with a mean of 24 years. Children (defined in Queensland as age 16 years and under) comprised 25% of the sample population.

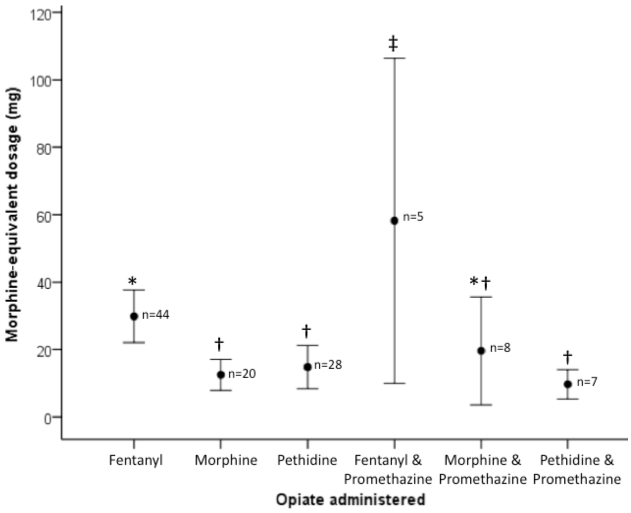
There was a significant positive correlation ($F_{(1x19)}$ = 10.822, $P < 0.005$) between year and the length of the Irukandji syndrome season, with a minimum of 15 days in 1961 to a maximum of 151 days in 2002 (Figure 1). For stings recorded from 1995 to 2007, significantly more stings occurred onshore than offshore in the earlier years; however, this trend reversed with more stings occurring offshore ($\chi^2_{(8)}$ = 32.9, $P < 0.001$) in later years (Figure 2). There was a significant negative correlation ($F_{(9x1)}$ = 22.03, $P < 0.05$) between percentage of stings onshore and season with a high of 93% in 1996–1997 and a low of 26% in 2006–2007.

OPIOIDS FOR PAIN RELIEF

The majority of patients given opioids for pain relief received fentanyl (26%) or a mixture of opioids (20.2%). Fewer patients were given pethidine (16.2%) or morphine (11.6%) alone or various combinations of all three opioids. Envenomed patients treated with a fentanyl/promethazine combination required significantly higher ($F_{(106x5)}$ = 6.230, $P < 0.001$) mean morphine-equivalent doses (mean = 59 mg) than those treated with any other opioid combination (Figure 3). Those treated with fentanyl alone required significantly higher morphine-equivalent doses than those treated with morphine, pethidine or pethidine/promethazine (Figure 3).

There was a significant positive correlation (Pearson's correlation 0.499) between opioids and symptoms experienced, with patients receiving significantly higher amounts of opioids as more symptoms developed (Figure 4).

Figure 3
Mean total morphine-equivalent doses for different opioids (means followed by same symbol are not statistically different at the 0.05 level by LSD post hoc analysis) (n = 143)



Approximately 31% of patients diagnosed as suffering from Irukandji syndrome showed only one of the five major symptoms, with 43% recording two symptoms (Figure 5). Notably, only one patient showed all five symptoms. For patients experiencing only one symptom, over 80% of these were pain of some description (chest, back, limb pain). The second most predominant symptom was nausea/vomiting with troponin rises being displayed only in patients who showed three or more clinical symptoms (Figure 6).

Morphine-equivalent dosage was shown to have a strong positive correlation with all variables examined but was more

Figure 4
Mean morphine-equivalent dose received (mg) for number of symptoms reported

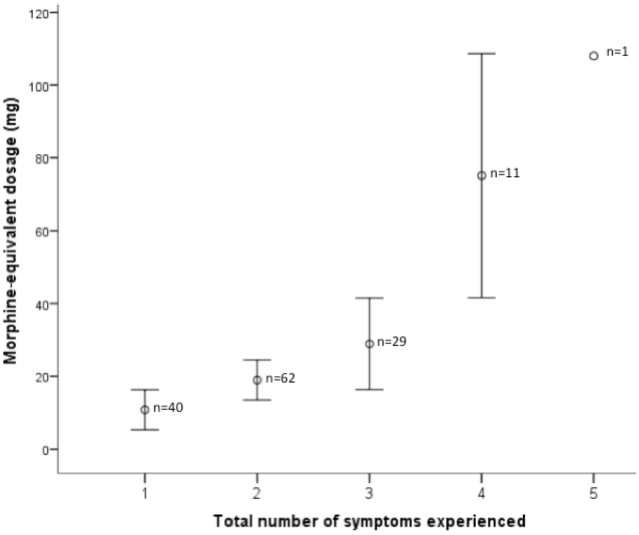


Figure 5
Mean percentage of cases presenting with the number of symptoms experienced (n = 143)

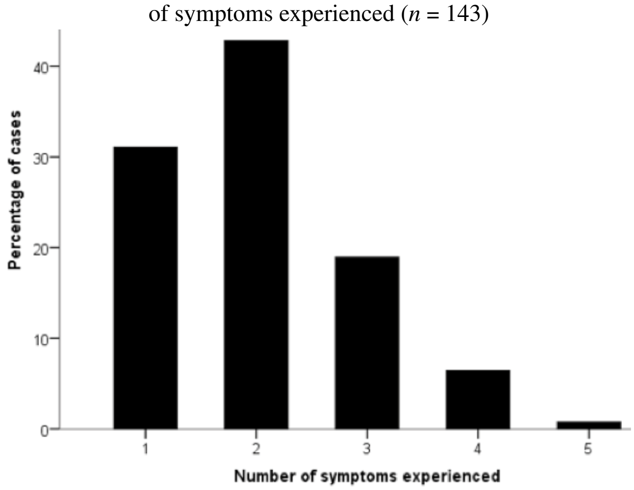
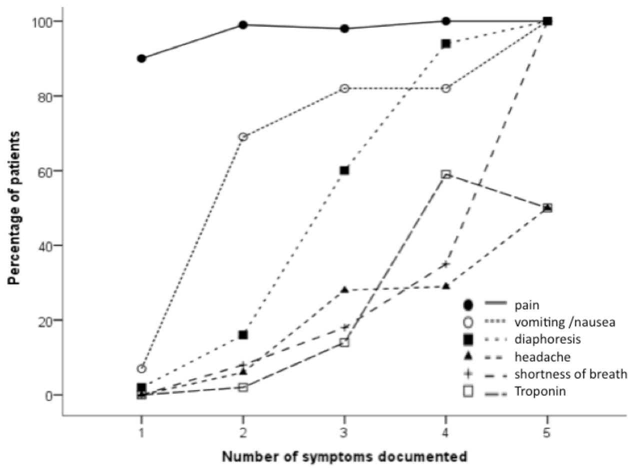


Figure 6
Percentage of patients presenting with the number and type of symptoms reported (n = 143)



strongly positively correlated with length of hospital stay (Pearson corr. (r) = 0.665), than with cTnI levels (r = 0.509), percentage BP change (r = 0.441), % MAP (r = 0.328) or percentage HR change (r = 0.195). The mean, minimum, maximum and median data for morphine-equivalent dosage, peak BP, peak MAP, peak HR, cTnI level and length of stay are presented in Table 1.

TROPONIN 1

Envenomed patients from reef locations had significantly higher levels of cTnI (mean = 3.78 µg L^{-1}) than those from either the island (mean = 0.99 µg L^{-1}) or onshore locations (mean = 1.06 µg L^{-1}) ($F_{(2x152)}$ = 7.577, P = 0.001; Figure 7).

Discussion

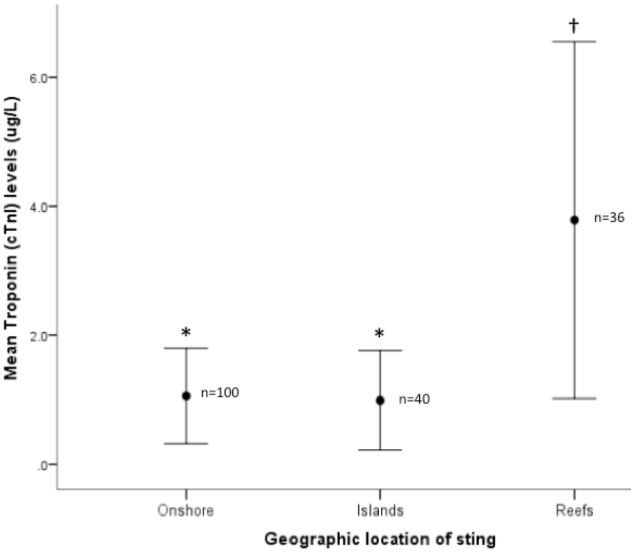
Irukandji syndrome, while difficult to determine, has most recently been defined as requiring at least three systemic clinical symptoms, including nausea, vomiting, headache, sweating, anxiety, restlessness, muscle cramps in all four limbs, the abdomen and chest or severe low back pain.[14] Investigation of the Cairns records shows that the use of this definition would in fact exclude 74% of Irukandji sting cases, with 31% of patients examined displaying only one symptom. As such, we suggest that a new variation of the definition for the syndrome be:

- recent contact with seawater;
- a delay of 5 to 60 minutes between a relatively mild sting and the onset of constitutional symptoms and
- one or more of the following five symptoms: pain,

Table 1
Range of physiological parameters recorded for envenomed patients documented

	n	Mean	Median	Mode	Range	Minimum	Maximum	25th percentile	75th percentile
Morphine-equivalent dose (mg)	264	25	13	0	255	0	255	1.2	35
Peak blood pressure (mmHg)	251	141	140	130	140	90	230	125	155
Peak MAP (mmHg)	249	105	105	100	115	68	183	93	116
Peak heart rate (bpm)	204	95	93	80	156	47	203	80	107
Troponin score (ug L^{-1})	189	1.5	0	0	34	0	34	0	0.1
Length of stay (h)	265	16	12	3	167	1	167	3.9	21

Figure 7
Mean detected Troponin I (cTnI) levels in patients stung from different geographical locations (means followed by same symbol are not statistically different at the 0.05 level by LSD post hoc analysis) (n = 176)



headache, nausea and vomiting, diaphoresis and shortness of breath, +/- cTnI leak.

To date, this is the largest data set of Irukandji envenomings analysed, spanning 65 years, with the majority of previous studies focusing on only a single season's records. These findings give insight into the seasonal occurrence of the syndrome, symptoms that are displayed and the treatment and management of this disease.

These data suggest the length of the Irukandji season in the Cairns area appears to be increasing with time. With the global rise in seawater temperatures, a prolonged state of optimal temperature conditions may exist, which in turn may allow medusae to survive until later in the year then they have in the past.[16] Certainly there has been a trend in other cnidarian species to increase in numbers due to sea temperature increases, eutrophication and possible over-fishing.[17] The northern Queensland data, while not conclusive, may support this hypothesis. This has direct consequences to physicians who may be under the impression that this syndrome only occurs over a few months of the year.

These data also show that recently there has been a change in the ratio of onshore to offshore stings, with onshore sting numbers decreasing. Although impossible to test, a potential for this reversal in trend is the increase in beach safety protocols that have been instigated in recent years. In 2001, there was a change in the Irukandji sting protocols of Surf Lifesaving Queensland for onshore beach locations, to include a 24-hr mandatory closure if a positive Irukandji sting occurred, and the addition of daily drags conducted by surf lifesavers to check for the presence of carybdeids on a routine basis (SLSQ Stinger protocol). The sting data that coincide with this new management strategy are supportive of this increased safety approach for beachgoers in decreasing the sting incidence. No such strategy has been initiated for offshore reef and island regions and, with increasing numbers visiting these regions, there is great potential for sting numbers to increase. A preventative strategy and risk management system is essential in these regions if occurrence of this syndrome is to be controlled.

Of additional concern for the reef envenomings is the higher levels of cTnI measured in patients from this region. While cTnI levels are used as an indicator of myocardial damage and the link to Irukandji syndrome patients experiencing myocardial dysfunction has been reported previously, there is uncertainty as to the relationship of these levels and their association with cardiac dysfunction.[5] Patients with elevated cTnI levels have been flagged as potentially developing cardiac complications and, as patients originating from reef regions show higher mean levels, origin of sting would seem a potential tool for severity diagnosis in Irukandji syndrome presentation. Further evidence for this comes from the only recorded Irukandji syndrome-related death in this region that occurred from an offshore reef location, with this patient also displaying vastly elevated cTnI levels.[5,18]

Additional to geographical origin for sting severity prediction would be the number of symptoms experienced, with patients who display three or more of the defined symptoms, increasing their propensity for cTnI presence. This suggests that a combination of sting origin, opioid requirements and number of symptoms displayed could be used as a risk assessment technique for patient severity prediction, assuming that those with an elevated cTnI are at higher risk.

Effective pain relief is the key to managing Irukanji syndrome. Opioid requirements varied and, with its substantially shorter half-life than that of either morphine or pethidine, higher total doses of fentanyl were required for pain relief; the shorter duration of action requiring more frequent doses to maintain effective blood concentrations.[19,20] Morphine has been reported to be more likely to induce vomiting in Irukandji syndrome patients, whilst pethidine in large doses may possibly cause seizures and cardiac depression, worsening myocardial function of patients with Irukandji syndrome.[3,9] Therefore, pethidine is not recommended in Irukandji syndrome.[9] Fentanyl would appear to be the opioid of choice because of its relatively low toxicity and good tolerance profile reported in other studies.[9,21] However, individual patient responses vary and each case must be assessed with patient safety considerations foremost.[21] There is no reported experience with the newer fast-acting opioids such as remifentanyl.

Promethazine has previously been suggested as improving the outcome of patients with this syndrome by lowering the amount of opioid required and because of its antiemetic, antihistaminic and sedative effects.[9] However, our data appear contrary to this view, with no significant decrease in morphine or pethidine dosages and a higher average dosage of fentanyl in patients receiving promethazine. While promethazine may provide some favourable effects for the patient, there is no evidence in this series to suggest it affects opioid dosage advantageously.

Ecological data on the types of carybdeids giving rise to Irukandji syndrome are still lacking and such fundamental questions as which species are involved and how these animals vary both geographically and seasonally are needed urgently. Control measures for onshore coastal locations appear to have reduced the number of envenomings in the short term; however, a broader, proactive warning system for all regions would be highly valuable, and this cannot be accomplished without further widespread investigations. Irukandji syndrome represents a significant health problem in the North Australian region, but there is also evidence for its increased reporting from other global locations.[12,22–24] With evidence for the season increasing in length, medical practitioners are now facing exposure to patients presenting with this syndrome for approximately six months of the year so further clarification of protocols and treatment strategies is paramount to ensure optimal patient treatment.

Conclusions

This retrospective study indicates that the season for Irukandji stings is increasing. The percentage of these stings originating from the offshore reef areas is also increasing and these stings have shown an increased potential for cardiac complications as indicated by higher levels of cTnI in these patients. Opioid dosage appears to correlate with the severity of the syndrome. Although total dosage (in morphine equivalents) is greater with fentanyl, it is probably the opioid of choice, as it appears to have fewer adverse reactions than, for instance, pethidine, which may increase complications in Irukandji syndrome. Finally, we believe that a new definition for the syndrome should be made, mainly marine envenomation with a delay in the onset of one or more of five major systemic symptoms.

Acknowledgements

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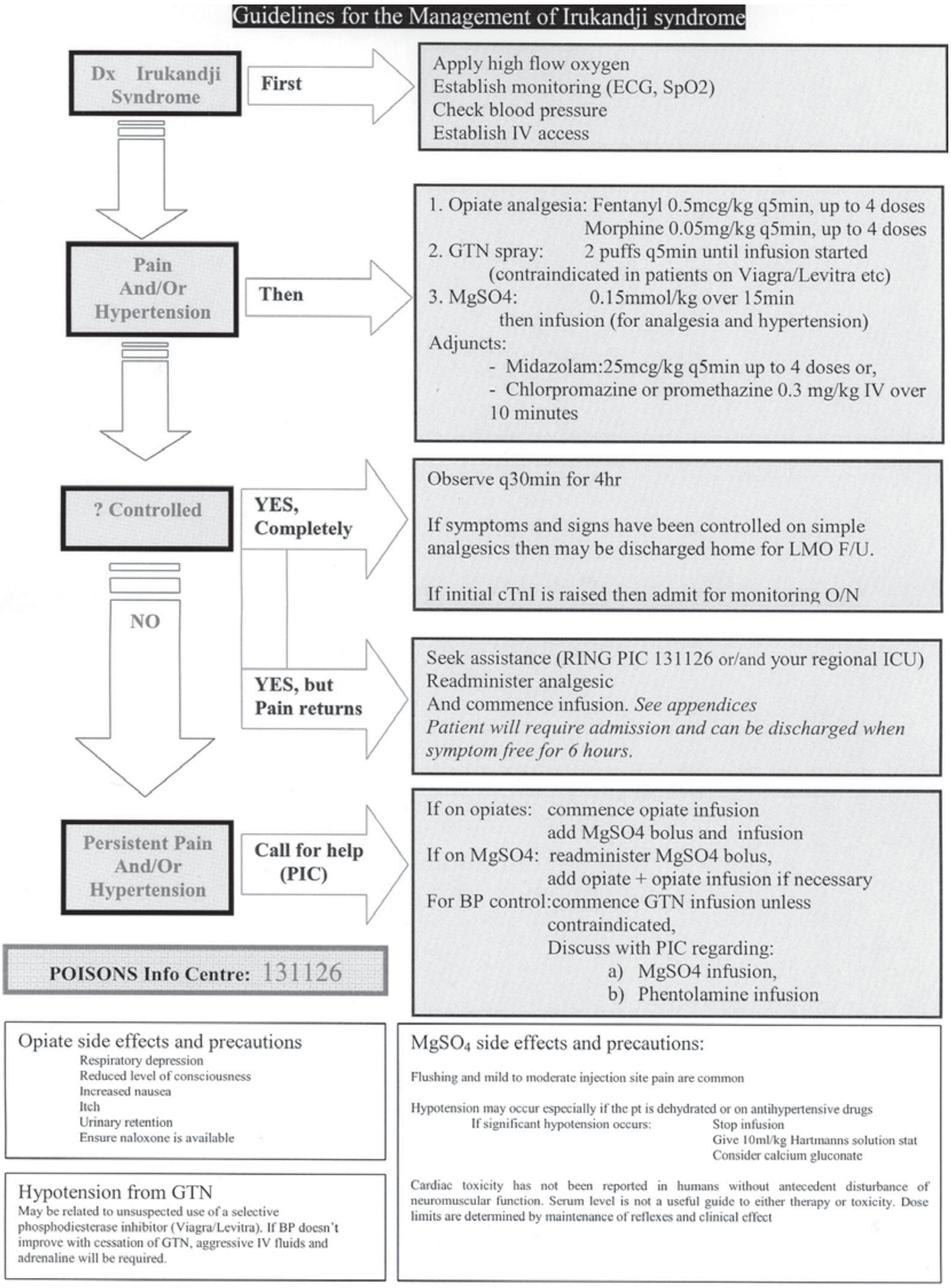

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