Please refer to the following pages for the emergency management of the Irukandji Syndrome that has been developed through the Prevention and Response Working Group of the Irukandji Taskforce.

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They have been approved by the Prevention and Response Working Group of the Queensland Irukandji Taskforce and were endorsed by the Taskforce on 29 January 2007.
Irukandji Taskforce Guidelines for the Emergency Management of Irukandji Syndrome

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Irukandji syndrome is described as a tropical marine sting (usually minimal discomfort) followed in 15-40 mins by significant systemic symptoms of pain, agitation, restlessness, and clinically associated with signs of catecholamine excess. A small number go on to develop cardiac failure. There have been two fatalities in patients who have presented with Irukandji syndrome, both of whom succumbed from intracerebral bleeds.

Where a patient is suspected to be experiencing Irukandji syndrome the following guidelines may be found useful.

Over the phone advice may be sought through the Poisons Information Centre, Phone: 131 126.
Management Guidelines for Irukandji Syndrome

1) Resuscitation
   • Application of vinegar, if not already administered
   • Attention to airway, breathing and circulation
   • Cardiac arrest managed as per standard protocols

2) Stabilisation
   • Apply high flow oxygen
   • Establish monitoring (ECG, SpO2)
   • Check blood pressure
   • Establish IV access

   a) Analgesia
      Options available:
      • IV opiates, titrate to effect
        a. Morphine (0.05 mg/kg), or fentanyl (0.5mcg/kg), repeated every 5 min until adequate analgesia or 4 doses.
        b. Opiate infusions should be considered
      • Recent experience shows good response to MgSO4 infusions (see Appendix 1)
        a. initial bolus over 15 min of 0.15mmol/kg,
        b. repeat if necessary
        c. then add infusion of 0.1 - 0.15mmol/kg/hr

      Adjuncts to analgesia include:
      a. Chlorpromazine 0.3 mg/kg IV
      b. Promethazine 0.3 mg/kg IV
      c. Midazolam 25mcg/kg IV up to 4 doses

   b) Hypertension
      • Control of hypertension may be life saving given that both Irukandji related deaths succumbed to intracerebral haemorrhages.
      • Nitrates should be used as first line antihypertensives for severe hypertension (see Appendix 2)
        - contraindicated in patients on selective phosphodiesterase inhibitor (Viagra, Levitra etc.)
        - GTN spray initially,
        - followed by a GTN IV infusion, using standard cardiac dilutions and doses.
      • MgSO4 infusion may be commenced early where GTN is contraindicated
      • IV phentolamine has been used successfully (see appendix 3) and may influence pain as an additional effect.

      NOTE: If patient is unstable or unresponsive to treatment, ring the Poisons Information Centre on 131126 for further advice.

3) Investigations
   • If available, all suspected Irukandji syndromes should have:
     On arrival:
     Pathology: FBC, UEC, Mg, cTnI
     12 lead ECG
     CXR
   • An echocardiogram may be required if there is clinical or radiographic evidence of cardiovascular instability
4) Maintenance
- Infusions can be reduced or ceased after 4 hours and recommenced if there is recurrence of symptoms or signs (See appendix 4)
- Monitoring is required if there is an abnormal initial cTnI or continuing severe symptoms.

5) Disposition
- Many patients settle after initial boluses of opiates and can be discharged home after 4 hours (even if they are experiencing mild symptoms), with simple analgesia provided their symptoms are resolving and investigations are normal.
- If they require narcotic or magnesium infusions they should be admitted for observation and management. Management in hospital for at least 6 hours after the cessation of infusions is mandated and may require admission. If no opiate or magnesium have been required for 6 hours, and symptoms have resolved, the patient may be discharged
- For any patients with ongoing severe pain, or cardiac abnormalities on ECG, CXR or raised Troponin, there is a risk they may deteriorate further and warrant high dependency monitoring with serial ECGs, CXR and cTnI.

- For overt cardiac failure or the need for phentolamine infusions, or if there is evidence of neurological dysfunction the patient should be admitted/transferred to an ICU for aggressive management.
Magnesium Sulphate (MgSO₄)

- Peripheral inhibitor of catecholamine release and effect

Setup:
Option 1: neat Magnesium Sulfate for Injection (2mmol/ml) 50 ml in syringe driver. Requires side-line fluid to ensure MgSO₄ is flushed in and to reduce injection pain.

Option 2: MgSO₄ 8% solution. 500ml bag contains 162mmol (40g). See below.

Ampoules of Calcium gluconate 20mls need to be kept near the patient if on a magnesium infusion

Precautions and troubleshooting:
- Renal failure, neuromuscular disorders mandate extreme care.
- Monitoring of tendon reflexes is important for avoiding toxicity. Loss of tendon reflexes should prompt cessation of the infusion and clinical reassessment with a view to recommencement at a lower rate.
- ECG monitoring is highly recommended for all patients with Irukandji syndrome and should be continued throughout the infusion.
- Hypotension due to vasodilation may occur. This is more common in patients who are dehydrated and/or on antihypertensive medications. Hypotension may be treated by discontinuing the infusion, administering a fluid bolus (Hartmanns 10ml/kg) then once the blood pressure has settled recommencing at the maintenance rate without a further bolus. Calcium gluconate will reverse cardiovascular and neuromuscular effects of MgSO₄ and should be available whenever MgSO₄ is used for any indication.
- Injection pain may be reduced by slowing the loading dose or further diluting the MgSO₄.

Initiation:
Bolus dose 0.15mmol/kg over 15min, then commence infusion at 0.1-0.15mmol/kg/hr.

MgSO₄ 8% solution

Premixed 500ml bags of 8% MgSO₄ are now available. These should when possible be used for infusions in place of drawing up multiple ampoules.

<table>
<thead>
<tr>
<th>Volume (ml)</th>
<th>MgSO₄ mass (g)</th>
<th>MgSO₄ mass (mmol)</th>
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<tr>
<td>500</td>
<td>40</td>
<td>162</td>
</tr>
<tr>
<td>50</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>31</td>
<td>2.5</td>
<td>10</td>
</tr>
<tr>
<td>12.5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>1</td>
<td>0.08</td>
<td>0.32</td>
</tr>
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Regimen - adult | MgSO₄ 8%
Load 10mmol     | 31ml over 10min
Repeat load if required | 31ml over 10min
Infusion 10mmol/hr | 31ml/hr
See Irukandji Guidelines for weaning
Regimen- paediatric  
<table>
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<tr>
<td>Load 0.15mmol/kg</td>
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**Monitoring:**
Clinical response.
- There is little role in monitoring serum levels.
- If tendon reflexes are preserved then titration to clinical endpoints is appropriate.
- ECG monitoring should be maintained.
- Reflexes should be assessed hourly and prior to any bolus MgSO4 administration

**Weaning:**
- Once symptoms are controlled for 4 to 6 hours the infusion is reduced by 1-2 mmol/hr/hr.
- If breakthrough symptoms occur, a 0.04mmol/kg (adult 2.5-3mmol) dose is given as a bolus, the infusion recommenced at the previous rate and weaning recommenced 4 hours later.
**Glyceryl Trinitrate (GTN)**

- Indicated for severe hypertension: SBP > 200mmHg, DBP > 120mmHg

**Setup:** 50mg Glyceryl Trinitrate in 500mls N/Saline or 5% Dextrose = 100mcg/ml
Exclude recent use of a selective phosphodiesterase inhibitor (e.g. Viagra, Levitra etc.)

**Initiation:**
- **Puffer:** 2 x GTN puffs every 5 mins while infusion is being set up.
- **IV:** Commence at 3 ml/hr (5mcg/min)
- Double rate every 5 min until SBP less than 160mmHg and DBP less than 100mmHg

**Monitoring:**
- NIBP every 5 min
- Aim for SBP 100 to 160 mmHg, and DBP 50 to 100 mmHg

**Weaning:**
- After BP and pain is controlled for 4 hours
- Halve GTN rate every 20 mins if BP remains within target range
- Cease if BP controlled on 3ml/hr

**Precautions and troubleshooting:**
Patients on a selective phosphodiesterase inhibitor (e.g. Viagra, Levitra etc.) will experience a life threatening hypotensive episode if GTN is administered.

- b) Early recognition and aggressive management is required
- c) Cessation of infusion
- d) IV volume loading
- e) Adrenaline boluses

Other hypotension
- f) Responds to cessation of infusion, and fluid loading.
Phentolamine

- Alpha-1 receptor antagonist.
- Phentolamine decreases peripheral sensitivity to the catecholamines released in Irukandji Syndrome. It is also used in Pain Medicine as a peripheral modulator of nociception and has been described as reducing pain in Irukandji Syndrome,
- In vitro, it reduces the direct effects of related jellyfish venoms on cardiac and vascular smooth muscle and may confer some benefit via this mechanism.

**Setup:** Initial boluses of 30-80 mcg/kg (adult dose 2-5 mg) over 2 minutes may be given to control severe hypertension. Half life is 19 min. If multiple boluses are required consider infusion.

Infusion: 30mg phentolamine to 50ml 5%%dextrose and infuse at an initial rate of 2-10ml/hr with titration to effect

**Precautions and troubleshooting:**
- Hypovolaemia, allergy to sulpha.
- If GTN is already in use the hypotensive effect may be exaggerated.
- Blood pressure should be monitored closely.
- The half life is 19 minutes (prolonged in renal failure) so effects may wear off quickly from bolus administration.

If hypotension occurs discontinue infusions, elevate legs and give 20ml/kg IV Hartmanns solution if required. If rebound hypertension occurs after this then recommence infusion at 50% of original rate.

**Initiation:**
- Bolus dose 2-5mg (adult) as above.
- If repeated doses are required commence infusion:
  - add 30mg phentolamine to 50ml 5% dextrose and infuse at an initial rate of 2-10ml/hr with titration to effect.
  - Target systolic blood pressure 100-150 (adult) or within 95% normal range in children.

**Monitoring:**
BP closely monitored- every 5min for at least 1 hr then every 15min subsequently until stable. ECG should be monitored.

**Weaning:**
After BP controlled for 4 hours reduce infusion by 25% each 40 minutes.

ANY patient requiring this level of cardiovascular intervention needs to be admitted/transferred to an Intensive Care Unit.
Dx Irukandje Syndrome

First

Apply high flow oxygen
Establish monitoring (ECG, SpO2)
Check blood pressure
Establish IV access

Then

1. Opiate analgesia: Fentanyl 0.5mcg/kg q5min, up to 4 doses
   Morphine 0.05mg/kg q5min, up to 4 doses
2. GTN spray: 2 puffs q5min until infusion started
   (contraindicated in patient on Viagra/Levitra etc.)
3. Mg SO\textsubscript{4}: 0.15mmol/kg over 15min
   then infusion (for analgesia and hypertension)
Adjuncts:
   − Midazolam: 25mcg/kg q5min up to 4 doses or,
   − Chlorpromazine or promethazine 0.3mg/kg IV over 10 minutes

Observe q30min for 4hr
If symptoms and signs have been controlled on simple analgesics then may be discharged home for LMO F/U.
If initial cTnI is raised then admit for monitoring O/N

Seek assistance (RING PIC 131126 or/and your regional ICU)
Readminister analgesic
And commence infusion. See appendices
Patient will require admission and can be discharged when symptom free for 6 hours.

If on opiates: commence opiate infusion
add Mg SO\textsubscript{4} bolus and infusion
If on MgSO\textsubscript{4}: readminister MgSO\textsubscript{4} bolus,
add opiate & opiate infusion if necessary
For BP control: commence GTN infusion unless contraindicated,
Discuss with PIC regarding:
   a) MgSO\textsubscript{4} infusion,
   b) Phentolamine infusion

POISONS Info Centre: 131126

Opiate side effects and precautions
   Respiratory depression
   Reduced level of consciousness
   Increased nausea
   Itch
   Urinary retention

MgSO\textsubscript{4} side effects and precautions:
   Flushing and mild to moderate injection site pain are common
   Hypotension may occur especially if the pt is dehydrated or on antihypertensive drugs
   If significant hypotension occurs: Stop infusion
   Give 10ml/kg Hartmanns solution stat
   Consider calcium gluconate

Hypotension from GTN
May be related to unsuspected use of a selective phosphodiesterase inhibitor (Viagra/Levitra). If BP doesn’t improve with cessation of GTN, aggressive IV fluids and adrenaline will be required.

Cardiac toxicity has not been reported in humans without antecedent disturbance of neuromuscular function. Serum level is not a useful guide to either therapy or toxicity. Dose limits are determined by maintenance of reflexes and clinical effect.