LOCAL ANAESTHETIC SYSTEMIC TOXICITY (LAST) IN CHILDREN

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Background

- Local Anaesthetics (LA) are used to provide regional anaesthesia and analgesia for children of all ages. The safety record of LA use is very good and its administration within safe guidelines should be encouraged.
- Local Anaesthetic Systemic Toxicity (LAST) occurs following either inadvertent intravascular injection (symptoms then occur within a few minutes) or absorption from tissue depot (symptoms delayed by many minutes, or even hours). Adequate knowledge of LA pharmacology and LAST prevention, detection and treatment is important to all clinicians who work in areas where LA is administered.
- Children are more at risk of LAST because of pharmacodynamic and pharmacokinetic immaturity.
- This document focuses on the cardiovascular and neurological systemic toxicity of LA and does not include methaemoglobinaemia or allergic reactions.

Precautions before and during injection of local anaesthetic

- Identify factors that increase risk of LAST. Neonates and infants < 6months, reduce LA dose by 50%. Reduce the LA dose by 10-20% if renal dysfunction, liver dysfunction and cardiac failure, and if patient taking medications that strongly inhibit cytochrome P450 enzymes (CYP) e.g. itraconazole, cimetidine and fluvoxamine.
- Use the lowest effective dose of LA. Importantly, different sites exhibit varied systemic absorption rates: more vascular areas may present a greater risk of systemic toxicity.

Table 1. Recommended maximum dose of commonly used LA for infiltration:

Commonly Used Agents	No Added Adrenaline	With Adrenaline 1:200'000
Lignocaine	3mg/kg	5mg/kg
Bupivacaine	2.5mg/kg	2.5mg/kg
Levobupivacaine	2.5mg/kg	2.5mg/kg
Ropivacaine	3mg/kg	3mg/kg

(**NOTE:** LAST may occur at doses lower than the recommended maximum dose)

- For caudal or epidural, check for free-flow of blood or CSF without aspiration, and then gently aspirate needle or catheter before each injection observing for blood or CSF. Aspiration has >2% false negative rate for identifying intravascular injection.
- Inject small volumes incrementally, pausing one circulation time of 30-60 seconds and observing for signs and symptoms of toxicity between each injection. Hold needle or catheter firmly to the patient to prevent displacement.
- Use a test dose to detect intravascular injection. Adrenaline 0.5mcg/kg to1mcg/kg produces ≥10 beats per minute increase in heart rate and ≥15mmHg increase in systolic blood pressure. Sensitivity increases with increasing adrenaline dose. One method is to use LA premixed with adrenaline 1:200,000 solution, or make a fresh 1:200,000 adrenaline solution by adding 5mcg/ml of adrenaline to the total dose of LA and give 1ml/10kg as test dose. Another method is to draw up the total dose of LA in a syringe, then decant ¼ of the volume into another syringe. To this 1/4 does syringe add 1mcg/kg adrenaline, and use as the test dose.
- Ultrasound guided blocks may reduce the frequency of intravascular injection.

Recognition of LAST

- The importance of vigilance cannot be over stated. The use of electrocardiogram (ECG), blood pressure and oxygen saturation are recommended during and after any regional blockade where potential toxic doses of LA are used. See Australian and New Zealand College of Anaesthetists (ANZCA) Recommendations on Monitoring During Anaesthesia.
- If patient is awake, frequently check the level of consciousness and communicate with the patient to monitor for symptoms of toxicity.
- The timing of onset of LAST can be widely variable from a few seconds (suggesting intravascular injection) to a few hours. Onset may occur at any time during LA infusions.
- The initial presentation of LAST may be either Neurological or Cardiovascular. Neurological toxicity is usually only seen in the awake or lightly sedated patient. It may require seizure treatment and support of the unconscious patient. Cardiovascular toxicity and ensuing compromise requires resuscitation according to standard protocols, with the addition of lipid emulsion (see treatment).

CNS signs (will be masked by sedation or anaesthesia)
• Excitation (agitation, confusion, muscle twitching, seizure) • Depression (drowsiness, reduced consciousness coma, apnea) • Nonspecific (metallic taste, circum-oral numbness, diplopia, tinnitus, dizziness)

Cardiovascular signs (often the only presentation especially under general anaesthesia)
• Tachycardia, ventricular arrhythmias, hypotension, conduction block, bradycardia, or asystole. • ECG changes preceding CVS collapse may include, increased T wave amplitude, widened QRS complex, conduction block and bradycardia, premature ventricular ectopics. • Rapid progression to ventricular tachycardia, torsades de pointe, ventricular fibrillation may occur.

Treatment of LAST (click here to see RCH LAST management protocol)

- Stop local anaesthetic (LA) injection or infusion.
- Call for help and for the nearest lipid kit.
- **A.** Maintain airway, if necessary, secure with tracheal tube.
- **B.** Ventilate with 100% oxygen to avoid hypoxia and acidosis - both can worsen LAST.
- **C.** Confirm or establish intravenous access. Consider drawing blood for analysis but do not delay treatment. Treat hypotension early with small incremental doses of adrenalin 1mcg/kg. Start standard cardiopulmonary resuscitation (CPR) protocol if circulatory arrest occurs.
- **D.** Treat seizures immediately with benzodiazepines: midazolam 0.15 mg/kg IV/IO/IM, 0.3 mg/kg (max 10mg) buccal or intranasal. Avoid propofol or thiopentone if there is cardiovascular compromise. Muscle relaxants can be used to control excessive muscle activity despite adequate benzodiazepine to minimise acidosis and hypoxia. See afebrile seizures guideline. Don't forget to check glucose and correct hypoglycaemia. See hypoglycaemia guideline.
- **Give lipid emulsion therapy** during continued standard CPR. Give lipid emulsion 20% 1.5ml/kg intravenous bolus, repeat 5 minutely and start infusion at 0.25ml/kg/minute (15ml/kg/hour). Consider early use of lipid at the first signs of suspected LAST before progression to circulatory arrest e.g. during treatment of severe hypotension. This is supported by latest case reports. Maximum total dose is approximately 10ml/kg in the first 30 minutes.
- Prolonged monitoring >24 hours is recommended after any signs of cardiac toxicity because cardiovascular depression due to LA can persist or recur after treatment.

Departmental preparations

- Establish and maintain a lipid emulsion therapy box in areas where local anaesthetics are frequently administered.
- RCH Melbourne operation theatres lipid box is kept on the bottom self of theatre pharmacy store: 20% Intraipid 500 ml bottle x2, 20ml syringe x2, 50ml Syringe x2, and needless access devices x2. See Figure 1.
- Attach a simple and clear treatment protocol to the lipid kit. Click here to see RCH LAST management protocol.

Figure 1

References and further reading

1. Association of Anaesthetists of Great Britain and Ireland (AAGBI) Safety Guidline – Management of Severe Local Anaesthetic Toxicity
2. American Society of Regional Anesthesia and Pain Medicine (ASRA) Practice Advisory on Local Anesthetic Systemic Toxicity and its treatment.
3. LipidRescue™ website for further local anaesthetic toxicity, particularly prevention, identification, diagnosis, mechanisms, and treatment and registry for case reports.
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Paediatric Case Reports of Intralipid Use

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