

# Local Anesthetic Systemic Toxicity: Management

## Site Applicability

PHC: Acute Care

BC Cancer: Surgical Suites

## Practice Level:

Specialized: RN in critical care specialty area, High Acuity Unit, Surgical Suites and Anesthesia Assistants

## Need to Know

Local Anesthetic Systemic Toxicity (LAST) is a rare but life threatening complication of regional anesthesia. Local anesthetics such as Bupivacaine, lidocaine or Ropivacaine may have harmful central nervous system and cardiac effects if inadvertently administered into the intravascular space at high doses.

**Note:** LAST can also occur in patients receiving lidocaine infusions intravenously or subcutaneously therefore it is important to monitor closely for mild symptoms of local anesthetic toxicity.

Regional techniques of local anesthesia include neuraxial blocks (spinal and epidural) and peripheral nerve blocks. These techniques are used to create sensory anesthesia, skeletal muscle paralysis and autonomic nerve block for the operative site. Local anesthetics are typically injected near the nerve where it will then penetrate the nerve shaft by the process of diffusion. Local anesthetics act by interfering with normal sodium and potassium activity within cells. This results in blocking the sensory and motor function of the nerve, by preventing depolarization of the nerve cells.

Local anesthetics are classified as esters or amides. Esters, such as benzocaine, have short acting properties due to the breakdown by plasma cholinesterase and are therefore limited to short procedures or allergy to amides. Amides, such as Ropivacaine or Bupivacaine, are metabolized by the liver and are considered more long acting in block efficacy. Bupivacaine and Ropivacaine have slower onset of action and a longer duration of effect and are more desirable when regional anesthesia is needed for a longer period of time. Bupivacaine is more cardiotoxic and should be used with caution in patients with a cardiac history. For a list of commonly used local anesthetics, please see [Appendix A](#).

Local anesthetics are amphiphilic and have an affinity for both lipid and water environments. This allows the local anesthetic to enter many cellular compartments including heart, brain and skeletal muscle tissue. In certain body tissues, such as the brain and heart, an interruption in normal cellular function can result in greater consequences. Listed below are signs and symptoms of toxicity.

## Signs and Symptoms of Local Anesthetic Toxicity

Mild	Moderate	Severe
<ul style="list-style-type: none"> <li>• Perioral numbness and tingling</li> <li>• Metallic taste in mouth</li> <li>• Ringing in the ears</li> <li>• Lightheadedness</li> <li>• Dizziness</li> <li>• Visual disturbances</li> <li>• Confusion</li> </ul>	<ul style="list-style-type: none"> <li>• Nausea and vomiting</li> <li>• Severe dizziness</li> <li>• Decreased hearing</li> <li>• Tremors</li> <li>• Changes in heart rate and blood pressure (hypo/hypertension)</li> <li>• Confusion</li> </ul>	<ul style="list-style-type: none"> <li>• Drowsiness</li> <li>• Confusion</li> <li>• Muscle twitching</li> <li>• Convulsions</li> <li>• Loss of consciousness</li> <li>• Cardiac arrhythmias</li> <li>• Cardiac arrest</li> </ul>

Several approaches to safe administration of regional anesthetics are implemented such as judicious needle placement using ultrasound for peripheral nerve blocks, fractionated dosing with frequent aspiration and upper dose limits. In addition frequent blood pressure, heart rate, heart rhythm and oxygen saturation monitoring allow for early warning of possible inadvertent intravascular injection. However, despite these safety techniques the need for a plan for managing this complication is highly recommended. The *American Society of Regional Anesthesia and Pain Medicine* developed guidelines for the treatment of LAST ([Appendix B.](#))

## Equipment and Supplies:

1. \*Lipid Emulsion 20% 250mL bag
2. Alaris infusion pump and IV tubing
3. Two (2) 60 mL luer lock syringe
4. Two (2) 18 GA blunt fill needle
5. Emergency resuscitation equipment
6. Crash cart

\*Lipid Emulsion 20% (Intralipid™) can be found in the Omnicell(s) in PACU and in the anesthesia regional block cart.(and in the Omnicell on the surgical units (10A,B & C at SPH)

## Guideline

### Local Anesthetic Systemic Toxicity (LAST) Treatment

The recommended treatment for the management of local anesthetic systemic toxicity is lipid emulsion (INTRALIPID 20%) therapy. This is in addition to advanced cardiac life support guidelines with some modifications.

Steps	Rationale								
1. Immediately <b>stop</b> the infiltration of local anesthetic.									
2. Treat and stabilize actual and potential life threatening conditions using basic and advanced cardiac life support guidelines. <b>Call</b> a CODE BLUE for immediate assistance. Call for Lipid Rescue kit (Regional anesthesia cart). Keep crash cart at bedside. <ul style="list-style-type: none"> <li>• Maintain patent <b>airway</b>, ventilate with 100% oxygen as necessary.</li> <li>• <b>Monitor</b> ECG, oxygen saturation and blood pressure closely. <b>Treat</b> hypotension and bradycardia – <b>if pulseless, start CPR.</b></li> <li>• Assist with advanced airway placement if needed.</li> <li>• <b>The Pharmacological Treatment of LAST is Different from Other Cardiac Arrest Scenarios</b> <ul style="list-style-type: none"> <li>○ <b>Reduce</b> individual <b>epinephrine</b> boluses to 1 mcg/kg or less.</li> <li>○ <b>Avoid</b> vasopressin, calcium channel blockers, beta blockers or other local anesthetics.</li> <li>○ Consider amiodarone for ventricular arrhythmias.</li> </ul> </li> <li>• For <b>seizure</b> suppression treat with benzodiazepines.</li> </ul>	<p>Hypoxia can lead to further progression of cardiovascular symptoms of local anesthetic toxicity.</p> <p>Standard dose epinephrine (1 mg) can impair resuscitation from LAST and reduce the efficacy of lipid rescue.</p> <p><b>Avoid</b> large doses of <b>proPOFol</b>, especially in hemodynamically unstable patients.</p>								
3. Using 60 mL syringes and 18 gauge blunt fill needle draw up appropriate amount of lipid emulsion INTRALIPID 20% for bolus administration. Bolus dose is given rapidly into a patent running IV.	Program INTRALIPID 20% at 0.05 gram/kg/min								
<table border="1"> <thead> <tr> <th colspan="2">Lipid Emulsion 20% (Precise volume and flow rate are not crucial)</th></tr> <tr> <th>Greater than 70 kg patient</th><th>Less than 70 kg patient</th></tr> </thead> <tbody> <tr> <td> <b>Bolus 100 mL Lipid Emulsion 20%</b> rapidly over 2 to 3 minutes                             <ul style="list-style-type: none"> <li>• Lipid emulsion infusion 200 to 250 mL over 15 to 20 minutes</li> </ul> </td><td> <b>Bolus 1.5 mL/kg Lipid Emulsion 20%</b> rapidly over 2 to 3 minutes                             <ul style="list-style-type: none"> <li>• Lipid emulsion infusion 0.25 mL/kg/min (ideal body weight)</li> </ul> </td></tr> <tr> <td colspan="2"> <b>If patient remains unstable:</b> <ul style="list-style-type: none"> <li>• Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (12 mL/kg)</li> <li>• Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g. more than 30 minutes)</li> </ul> </td></tr> </tbody> </table>	Lipid Emulsion 20% (Precise volume and flow rate are not crucial)		Greater than 70 kg patient	Less than 70 kg patient	<b>Bolus 100 mL Lipid Emulsion 20%</b> rapidly over 2 to 3 minutes <ul style="list-style-type: none"> <li>• Lipid emulsion infusion 200 to 250 mL over 15 to 20 minutes</li> </ul>	<b>Bolus 1.5 mL/kg Lipid Emulsion 20%</b> rapidly over 2 to 3 minutes <ul style="list-style-type: none"> <li>• Lipid emulsion infusion 0.25 mL/kg/min (ideal body weight)</li> </ul>	<b>If patient remains unstable:</b> <ul style="list-style-type: none"> <li>• Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (12 mL/kg)</li> <li>• Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g. more than 30 minutes)</li> </ul>		<p>Lipid formulation of proPOFol is only 10%, due to the amount of drug required to create similar effect of lipid emulsion 20%, cardiovascular collapse will likely ensue following administration of proPOFol.</p> <p><b>Note: proPOFol is NOT a suitable substitute for lipid emulsion 20%.</b></p>
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4. Prime Alaris IV tubing with lipid emulsion 20%.									

<p>I. For patients <b>greater than 66 kg</b> recommended dose rate is greater than 999 mL/hr and will need to run to gravity.</p> <p>II. For patients <b>66 kg or less</b>:</p> <ol style="list-style-type: none"> <li>Program the infusion pump.</li> <li>In the critical care drug library, <b>select INTRALIPID 20%</b> (67 kg and under) and enter the patient's weight.</li> <li>BC Cancer: Basic Infusion (Alaris Pump)</li> <li>The desired dose is 0.05 gram/kg/min or 0.25 mL/kg/min.</li> <li>Confirm volume to be infused with physician and enter volume.</li> </ol>	
<p>5. <b>If patient remains unstable</b></p> <ol style="list-style-type: none"> <li><b>re-bolus</b> once or twice at the same dose and double the infusion rate (0.1 gram/kg/min). When the infusion rate is <b>greater than 999 mL/hr run by gravity</b>.</li> </ol> <p>Be aware of dosing limit (12 mL/kg) or (2.4 g/kg). Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (more than 30 minutes). If failure to respond to lipid emulsion, consider initiation of cardio-pulmonary bypass or ECMO.</p>	<p>Dose limit is particularly important in the small adult or child. – Much smaller doses are typically needed for LAST treatment –</p>
<p>6. Continue monitoring (continuous ECG, O<sub>2</sub> saturation, airway and frequent blood pressure) for at least 4 to 6 hours after a cardiovascular event or for at least 2 hours after a limited CNS event.</p>	
<p>7. Report events of local anesthetic systemic toxicity to <a href="http://www.lipidrescue.org">www.lipidrescue.org</a></p>	<p>Professional development of care standards.</p>

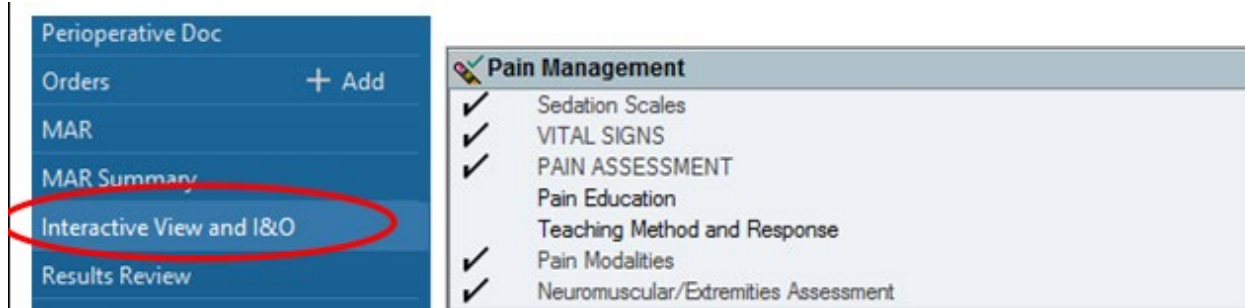
## Documentation

Document all arrests on the *Cardio-Pulmonary Resuscitation Record*.

Documentation of peripheral nerve blocks, epidural and spinal anesthesia can be found on the *Anesthesia Record* and *Anesthesiology Peripheral Nerve Block Consultation Record*.

All local anesthetic agents administered by nursing will be documented on the *Medication Administration Record*

Please note: all related assessments in Cerner PowerChart will be found in the Pain Management band within the **Interactive View and I & O**.



BC Cancer Regional Brachytherapy PARR Clinical Record

BC Cancer Regional Brachytherapy Intra-Operative Record

BC Cancer Anesthesia Record

## Patient and Family Education

Patient health and education materials can be found [here](#).

## Related Documents

1. [B-00-13-10003](#) Epidural Analgesia
2. [B-00-13-10128](#) Lidocaine Infusion for Patients in Palliative Care Unit
3. [B-00-13-10171](#) Lidocaine Intravenous Low Dose infusion Orders: Post-Operative Pain Management
4. [B-00-13-10084](#) Lidocaine (Intravenous ) Long Term Infusion
5. [B-00-13-10064](#) Lidocaine (Intravenous) Short Term Infusion – Intermediate Dose
6. [B-00-13-10098](#) Lidocaine Subcutaneous Infusion for Neuropathic Pain
7. [B-00-13-10129](#) Lidocaine (Subcutaneous): Set Up for Home Infusion
8. [B-00-13-10070](#) Nerve Blocks (Trigger Point Injections, Sympathetic Blocks, Epidural Steroids)
9. [B-00-13-10116](#) Perineural Anaesthesia: Patient Controlled Analgesia (PCPA)

BC Cancer:

1. [NPR \(Nursing Practice Reference\) – Assisting with General and Regional Anaesthesia](#)
2. [NPR \(Nursing Practice Reference\) – Caring for Patients Undergoing Local Anaesthesia in Surgical Suite/Procedure Room](#)

## References

1. Clark, M.K. (2008). Lipid Emulsion as Rescue for Local Anesthetic-Related Cardiotoxicity. *Journal of PeriAnesthesia Nursing*, 23(2), 111-121.
2. Neal, J.M., et al. (2018). The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity: Executive Summary 2017. *Regional Anesthesia and Pain Medicine*, 43(2), 113-123.

3. Neal, J.M., Woodward, C.M., & Harrison, T.K. (2018). The American Society of Regional Anesthesia and Pain Medicine Checklist for Managing Local Anesthetic Systemic Toxicity. *Regional Anesthesia and Pain Medicine*, 43(2), 150-153.
4. Sandlin-Leming, D.C. (2010). Resuscitation of Local Anesthesia-Induced Cardiac Arrest: Lipids to the Rescue. *Journal of PeriAnesthesia Nursing*, 25(6), 418-420.
5. Weinberg, G.L. (2012). Lipid Emulsion Infusion: Resuscitation for Local Anesthetic and Other Drug Overdose. *Anesthesiology*, 117(1), 180-187.

### **Persons/Groups Consulted:**

Regional anesthesia lead

CNS Acute Pain Services

Pharmacy – Parenteral Services

Nurse Educator - Surgical Services MSJ

Practice leads BC Cancer

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	Professional Practice Standards Committee	PHSA BC Cancer Leadership
<b>Owners:</b>	PHC	PHSA
	PACU	BC Cancer Surgical Suites

## Appendix A: Local Anesthetics Commonly Used

Infiltration Anesthetic	Concentration (percent)	Pharmacokinetics		Maximum allowable dose		Maximum total dose
		Onset of action (min)	Duration (min)	mg/kg	mL/kg	mg  equivalent solution volume
Esters						
benzocaine	20	Rapid	30 to 60	N/A	N/A	Maximum of 5 sprays per use
Amides						
lidocaine (Xylocaine)	1	2 to 5	50 to 120	4 to 5	0.4 to 0.5	300  30 mL of 1 percent
lidocaine with epinephrine	1	2 to 5	60 to 180	5 to 7	0.5 to 0.7	500  50 mL of 1 percent
BUpivacaine (Marcaine)	0.25	5 to 10	240 to 480	2	0.8	175  70 mL of 0.25 percent
BUpivacaine with epinephrine	0.25	5 to 10	240 to 480	3	1.2	225  90 mL of 0.25 percent
ROpivacaine (Naropin)	0.5	1 to 5	120 to 600	5	1	250  50 mL of 0.5 percent

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## Appendix B: Checklist for Treatment of Local Anesthetic Systemic Toxicity (LAST)

(Used with permission from the American Society of Regional Anesthesia and Pain Medicine)

*AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE*

### CHECKLIST FOR TREATMENT OF LOCAL ANESTHETIC SYSTEMIC TOXICITY (LAST)

#### The Pharmacologic Treatment of LAST is Different from Other Cardiac Arrest Scenarios

- ❖ **Reduce** individual **epinephrine** boluses to  $\leq 1$  mcg/kg
- ❖ **Avoid** vasopressin, calcium channel blockers, beta blockers, or other local anesthetics
- Stop injecting local anesthetic
- Get help
  - Consider lipid emulsion therapy at the first sign of a serious LAST event
  - Call for the LAST Rescue Kit
  - Alert the nearest cardiopulmonary bypass team - resuscitation may be prolonged
- Airway management
  - Ventilate with 100% oxygen / avoid hyperventilation / advanced airway device if necessary
- Control seizures
  - Benzodiazepines preferred
  - **Avoid** large doses of **propofol**, especially in hemodynamically unstable patients
- Treat hypotension and bradycardia – **If pulseless, start CPR**

Lipid Emulsion 20%	
(Precise volume and flow rate are not crucial)	
Greater than 70 kg patient	Less than 70 kg patient
<b>Bolus 100 mL Lipid Emulsion 20%</b> rapidly over 2-3 minutes	<b>Bolus 1.5 mL/kg Lipid Emulsion 20%</b> rapidly over 2-3 minutes
<ul style="list-style-type: none"> <li>Lipid emulsion infusion 200-250 mL over 15-20 minutes</li> </ul>	<ul style="list-style-type: none"> <li>Lipid emulsion infusion ~0.25 mL/kg/min (ideal body weight)</li> </ul>
<b>If patient remains unstable:</b> <ul style="list-style-type: none"> <li>Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (12mL/kg)</li> <li>Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g., &gt; 30 minutes)</li> </ul>	

- Continue monitoring
  - At least 4-6 hours after a cardiovascular event
  - Or, at least 2 hours after a limited CNS event
- Do not exceed 12 mL/kg lipid emulsion (particularly important in the small adult or child)
  - Much smaller doses are typically needed for LAST treatment
- See reverse side of this checklist for further details



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### Risk Reduction (Be sensible)

- Use the least dose of local anesthetic necessary to achieve the desired extent and duration of block.
- Local anesthetic blood levels are influenced by site of injection and dose. It is important to identify patients at increased risk of LAST prior to using local anesthetics, e.g., infants <6 months old, small patient size, advanced age and frailty, heart failure, ischemic heart disease, conduction abnormalities, or rhythm disorders, metabolic (e.g., mitochondrial) disease, liver disease, low plasma protein concentration, acidosis, and medications that inhibit sodium channels. Patients with very low ejection fraction are more sensitive to LAST and may be especially prone to elevated local anesthetic levels associated with 'stacked' injections.
- Consider using a pharmacologic marker and/or test dose, e.g. epinephrine 2.5 to 5 mcg/mL (total 10-15 mcg). Know the expected response, onset, duration, and limitations of a "test dose" in identifying intravascular injection.
- Aspirate the syringe prior to each injection while observing for blood in the syringe or tubing
- Inject incrementally, while observing for signs and inquiring for symptoms of toxicity between each injection.
- Consider discussing local anesthetic dose as part of the pre-procedural or pre-surgical pause ("time out").

### Detection (Be vigilant)

- Monitor the patient during and after completing injection. Clinical toxicity can be delayed 30 minutes or longer.
- Use standard American Society of Anesthesiologists (ASA) monitors.
- Communicate frequently with the patient to query for symptoms of toxicity.
- Consider LAST in any patient with altered mental status, neurological symptoms or signs of cardiovascular instability after a regional anesthetic (e.g., change in HR, BP, ECG). Consider LAST even when the local anesthetic doses is 1) small (susceptible patient), 2) atypically administered (subcutaneous, mucosal, topical), 3) administered by the surgeon, or 4) after recent tourniquet deflation.
- Central nervous system signs (may be subtle, atypical, or absent)
  - o Excitation (agitation, confusion, vocalization, muscle twitching, seizure)
  - o Depression (drowsiness, obtundation, coma, or apnea)
- Non-specific (metallic taste, circumoral numbness, diplopia, tinnitus, dizziness)

- Cardiovascular signs (occasionally the only manifestation of severe LAST)
  - o Initially may be hyperdynamic (hypertension, tachycardia, ventricular arrhythmias), then
  - o Progressive hypotension
  - o Conduction block, bradycardia or asystole
  - o Ventricular arrhythmia (ventricular tachycardia, Torsades de Pointes, ventricular fibrillation or asystole)
- Sedation may abolish the patient's ability to recognize or report LAST-related symptoms.

### Treatment

#### Suggested components of a "LAST Rescue Kit"

- 1 L (total) lipid emulsion 20%
- Several large syringes and needles for administration
- Standard IV tubing
- ASRA LAST Checklist

- Administer lipid emulsion at the first sign of a serious LAST event.
- Lipid emulsion can be used to treat LAST caused by any local anesthetic.
- Standard dose epinephrine (1 mg) can impair resuscitation from LAST and reduce the efficacy of lipid rescue. Use smaller doses than typical for ACLS, e.g.,  $\leq 1$  mcg/kg boluses, or for treating hypotension.
- Propofol should not be used when there are signs of cardiovascular instability.
- Prolonged monitoring (2-6 hours) is recommended after any signs of LAST, since cardiovascular depression due to local anesthetics can persist or recur after treatment.
  - o If LAST event is short-lived and without signs of cardiovascular instability, one may consider proceeding with surgery after an uneventful ~30 minute interval of monitoring.

Please report LAST events to [www.lipidrescue.org](http://www.lipidrescue.org)

The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity. Executive Summary 2017. Reg Anesth Pain Med 2018;43:113-123

The ASRA LAST™ smart phone app can be purchased from The Apple App Store or Google Play



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