Tumescent Lidocaine

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Tumescent Lidocaine

Introduction

- Tumescent local anesthesia is a form of local anesthesia
- Tumescent anesthesia describes the practice of injecting a dilute solution of local anesthetic combined with epinephrine and sodium bicarbonate into subcutaneous tissue until it becomes firm and tense (tumescent)
- Local anesthesia :
  - Conventional dosage of lidocaine is up to 4.5 mg/kg, with adrenaline is up to 7 mg/kg

J Cutan Aesthet Surg. 2020 Oct-Dec; 13(4): 275–282.

Tumescent anesthesia

Introduction

- Frequently combined :
  - Sedation
  - Regional anesthesia blocks
  - General anesthesia
- Excellent hemostasis achieved and prolonged analgesia
- This mode of anesthesia allows high volume surgical centres to manage a significant caseload on a day-care basis including in both hospital and office-based environments

Tumescent anesthesia

History and definitions

- The tumescent anesthetic technique was initially used to perform **liposuction** under local anesthesia
- 1986 in Philadelphia at the Second World Congress on Liposuction, and first published in a peer reviewed journal in 1987
- Aspirate volumes using these techniques occasionally exceeded 4 L in one session under sedation or general anesthesia
- Liposuction using tumescent anesthesia
  - Recommended maximum dose of lidocaine with adrenaline is up to 55 mg/kg**

Dermatol Surg. 2006;32:709–16

Tumescent anesthesia

History and definitions

- Associated with excessive blood loss of up to 10% of the aspirated volume
- Tumescent liposuction the infiltration solution volume is often up to 4 times the volume of the aspirated fat
- **Avoidance of excessive flow rates makes infiltration more comfortable for patients**

: Speed between 30 mL/h and 1500 mL/h depending on the location

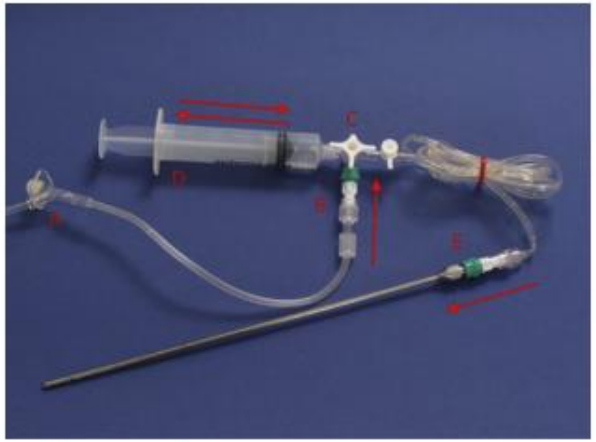
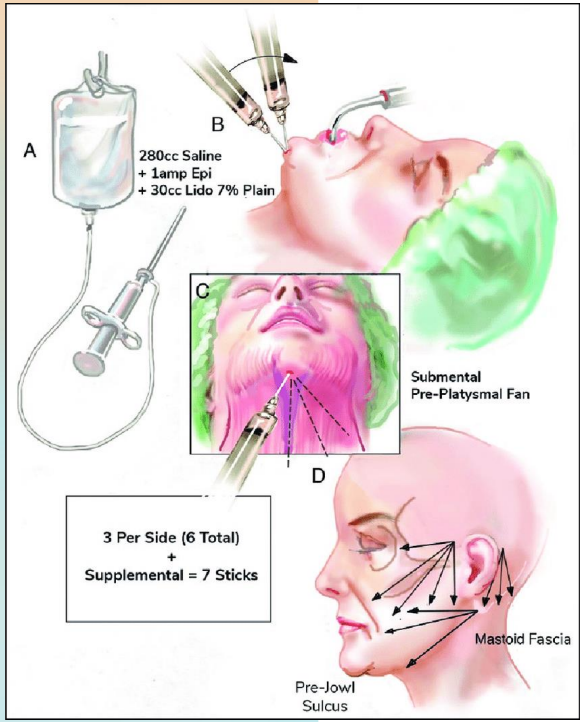


Fig. 1 – Example of three-way stopcock system for the administration of tumescent anaesthesia.[15]

Aesthetic Plast Surg 2011;35:601-2

Tumescent anesthesia

Applications of tumescent anesthesia



- Liposuction
- Dermatologic surgery: dermabrasion, CO2 laser resurfacing, chemical peels, facelift, Moh's micrographic surgical excisions (using the dermal tumescent technique with injection into the dermis as opposed to the subcutaneous tissue layer)
- Hair transplantation
- Mastectomy, breast reduction surgery
- Burn excision and grafting
- Anesthesia for Zoster dermatitis
- Skin grafts/flap procedures, abdominoplasty
- Varicose vein surgery
- Thyroidectomy
- Cervical lymph node dissection

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Tumescent anesthesia

Applications of tumescent anesthesia

Indications and use of TLA	
Dermatologic surgery	Benign skin lesions, skin cancer, sentinel-node- biopsy, lymph node dissection, phlebectomy
Gynecological surgery	(total) mastectomy
Plastic surgery	Liposuction, burn surgery
General surgery	Inguinal hernia repair
Cardiothoracic surgery	Pacemaker implantation
Hand surgery	Tendon repair, tenolysis, tendon transfer, carpal tunnel
Pediatric surgery	Dermatologic surgery, pediatric burn patients, genital surgery e.g. circumcision

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Tumescent anesthesia

Local anesthetic pharmacology

- Local anesthetics act by slowing depolarization of the cell membrane through reversible blockade of the fast voltage gated sodium channels

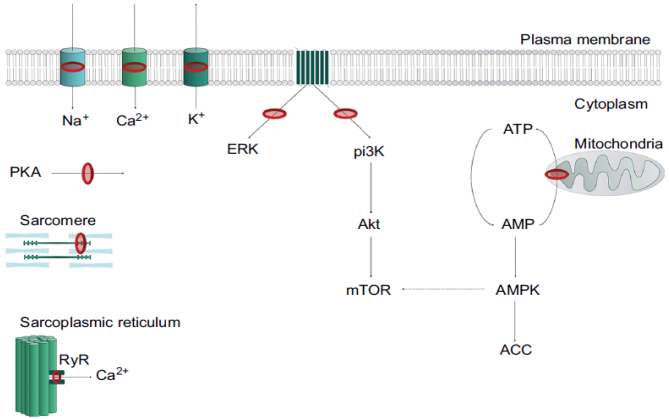

Figure 2 Representation of key LA cellular targets contributing to local anesthetic systemic toxicity.
Notes: In the plasma membrane, LAs block the Na_v channel (Na^+), potassium (K^+) and calcium channels (Ca^{2+}). Inhibition of second messenger systems on metabotropic transmembrane G-protein-coupled receptors leads to inhibition of ERK and pi3K. This leads to dysregulation of downstream kinase pathways, including a reduction in Akt and, thus, mTOR. Mitochondrial phosphorylation of AMP to ATP is inhibited, leading to an increase in the inhibitory, energy-sensing kinase AMPK, which in turn further mitigates mTOR. Other inhibitory targets include PKA, calcium-dependent contractility inhibition at the sarcomere, and modulation of the RyR. Red rings represent sites of action of LAs. Dotted lines represent inhibitory actions.
Abbreviations: AMP, adenosine monophosphate; ATP, adenosine triphosphate; LA, local anesthetic; RyR, ryanodine receptor.

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Tumescent anesthesia

Local anesthetic pharmacology

- Local anesthetics may be divided in to **esters and amides** on the basis of the bridge separating the hydrophobic aromatic ring and the hydrophilic tertiary amine group
- Esters are generally short acting and the more toxic of the two groups - they are metabolized by plasma cholinesterase
- Amides are metabolized in the liver by the CYP450

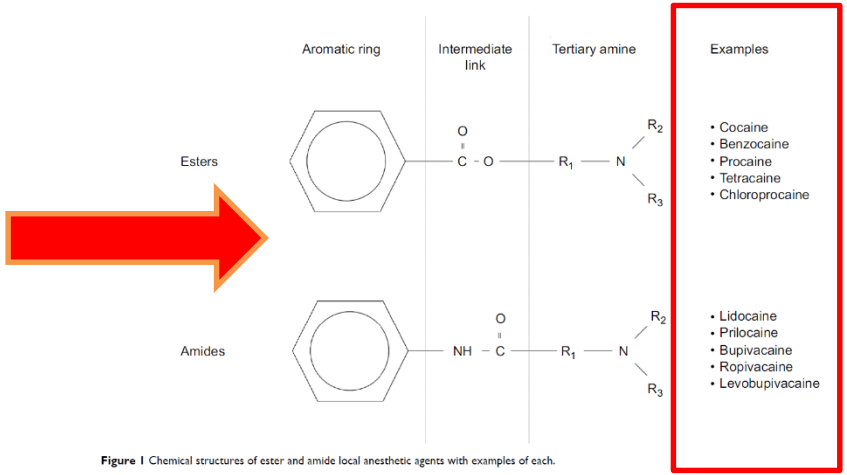

Figure 1 Chemical structures of ester and amide local anesthetic agents with examples of each.

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Tumescent anesthesia

Local anesthetic pharmacology

- Lidocaine is the most popular local anesthetic used in tumescent anesthesia → Rapid onset and a clinically useful duration of action particularly when combined with epinephrine

Physico-chemical properties

- **Lipophilicity**
- Lidocaine is highly soluble in fat resulting in a prolonged elution into the systemic circulation
- **Dissociation constants, pKa, pH and commercial preparations of lidocaine**
- Lidocaine pKa = 7.9
- This more lipophilic moiety crosses the lipid bilayer of the neuron to exert its physiological effect

Tumescent anesthesia

Local anesthetic pharmacology

- **Plasma protein binding**
- Alpha I acid glycoprotein is an acute phase reactant and a major binding protein for lidocaine; overall 65-75% of lidocaine in plasma is bound
- Anti-inflammatory and antibacterial effects
- Many local anesthetics have well described anti-inflammatory properties
- Amide local anesthetics disrupt microbial cell membrane permeability and, at high enough concentrations, result in cell lysis

Table 1 – Local anaesthetics used in tumescent anaesthesia.

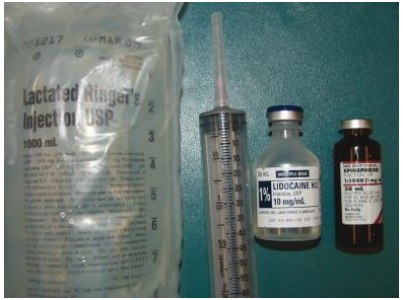
Class	Agent	pKa	Hepatic extraction ration	Protein binding (%)	Relative potency	Relative duration of lidocaine	t ½ (min)
Esters	Procaine	8.9	–	6	1	0.75	7.7
	Chloroprocaine	8.7	–	7	4	0.75	6
Amides	Lidocaine	7.9	0.72	65	1	1	96
	Prilocaine	8.0	–	55	1	1.5	96
	Etidocaine	7.7	0.74	94–97	4	2–4	162
	Bupivacaine	8.1	0.4	90–97	4	2.4	162
	Levobupivacaine	8.1	0.47	95	4	2–4	162
	Ropivicaine	8.1	0.4	94	4	2–4	108

Tumescent anesthesia

Additives for tumescent anesthesia

Crystalloid
Epinephrine
Sodium bicarbonate
Hyaluronidase

→ Klein's solution : 50-cc bottle of plain 1% lidocaine and 1 cc vial of 1:1000 epinephrine to a standard 1-L bag of sodium chloride solution, 10 mEq of sodium bicarbonate is added to 1L of tumescent solution

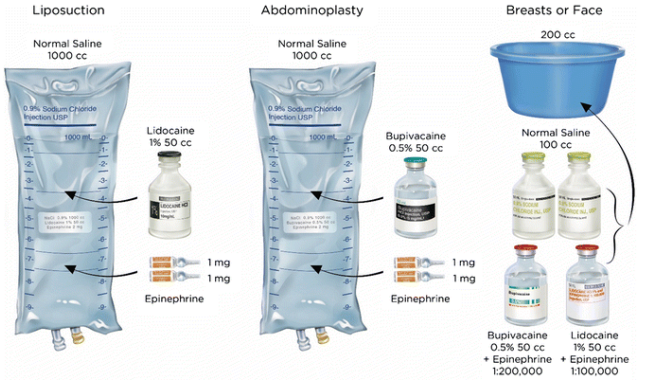


Crystalloid

- **The choice of crystalloid used to dilute local anesthetic solutions for tumescent anesthesia is between either normal saline or compound sodium lactate**

Epinephrine

- **Prolongs the local anesthetic effect**
- **Plain lidocaine injected subcutaneously reaches a maximal plasma concentration (Tmax) at 3.4 h → combined with epinephrine this Tmax is reached in 11 h**
- **Induces vasoconstriction and blood loss is thus significantly reduced**



Tumescent anesthesia

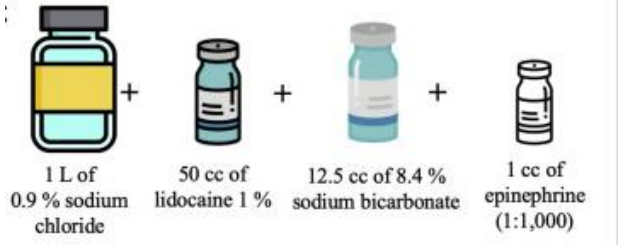
Additives for tumescent anesthesia

Sodium bicarbonate

- Alkalinization of local anesthetic or "anesthetic buffering" prior to injection using a bicarbonate solution will not only reduce pain on injection but also hasten the onset of the block
- Formulations of tumescent lidocaine and epinephrine typically include 10 mEq $NaHCO_3$/L of solution : **Alkalinization however, may decrease amine solubility and result in local anesthetic precipitation which in turn may be harmful to local tissues**

Hyaluronidase

- The addition of hyaluronidase is well recognized part of retro and peri-bulbar blocks for ophthalmic surgery



Tumescent anesthesia

Pharmacokinetics of tumescent anesthesia

Absorption, redistribution and elimination

- Peak plasma concentrations of local anesthetics are directly related to tissue vascularity and site of injection
- Intravenous > intra-tracheal > intercostal > paracervical > lumbar epidural > brachial > spinal > subcutaneous
- Peak plasma concentrations of lidocaine: 8 and 18 h
- Subcutaneous tissues and adipose tissues be have as a sink for tumescent solutions; the lipophilic local anesthetic with its high Vd
- Vasoconstrictive effects of epinephrine further ensure a delayed release of local anesthetic into the central compartment

Tumescent anesthesia

Pharmacokinetics of tumescent anesthesia

Absorption, redistribution and elimination

- Important to remember that although toxic local anesthetic plasma levels might not be achieved by high doses patients can still experience symptoms**
    - Slight to moderate side effects were observed in 12.9%
    - Hot flushes to mild myoclonus though in most cases prilocaine
- Recommended that the maximum allowable dose should be reduced by about 10% for males
- Lidocaine is metabolized by the cytochrome P450 enzyme group
- Lidocaine undergoes oxidative N-deethylation to monoethylglycinexylidide (MEGX)

Rudlof K, Ru¨ffert H, Wehner M, Wetzig T, Eichhorn K, Olthoff D. Tumescent anaesthesia for dermatological surgery. Plasma concentrations of lidocaine and prilocaine. Anaesthesist 2007;56:785e9.

Tumescent anesthesia

Pharmacokinetics of tumescent anesthesia

Table 2 – Examples of substrates, inhibitors and inducers of CYP3A4 (isoenzyme responsible for lidocaine metabolism).[37]

Drug class	Substrates	Inhibitors	Inducers
Sedatives/Anticonvulsants	Midazolam Alprazolam Carbamazepine		Phenytoin Phenobarbital Carbamazepine
Anti-microbials	Erythromycin	Erythromycin Clarithromycin HIV protease inhibitors Ketoconazole Voriconazole	Rifampicin
Immunosuppressants	Dexamethasone Cyclosporine		Dexamethasone
Anti-hypertensives	Diltiazem Nifedipine	Diltiazem	

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Tumescent anesthesia

Choice of local anesthetic agent for tumescent anesthesia

Prilocaine

- Prilocaine displays similar pharmacokinetics to lidocaine, and is also licensed for use in intrave nous regional anesthesia (e.g. Bier's block of the upper or lower limbs)

Ropivicaine

- This agent is less cardiotoxic and neurotoxic than bupivacaine
- Use of ropivacaine for tumescent anesthesia has been reported at total doses of up to 300 mg with no major or minor local anesthetic related complications

Bupivacaine

- Bupivacaine : caution due to the severity of potential side effects and slow elimination rate of bupivacaine
- use of bupivacaine in cosmetic surgery in doses up to 550 mg (up to 9.2 mg/kg)

Anesthetic mixtures: compounding

Tumescent anesthesia

Local anesthetic dose and toxicity

Lidocaine dose

- Maximum dose of commercial 1 or 2% preparations of lidocaine with epinephrine is 7 mg/kg (or 500 mg, whichever is the lower)
- Recommended that 35 mg/kg of dilute tumescent lidocaine be the maximum safe dose for local anesthesia with liposuction
- One small study has asserted that a total lidocaine dose of up to 55 mg/kg is safe for use in liposuction

Lidocaine toxicity

- Lidocaine : Narrow therapeutic range (therapeutic blood concentration, 1-5 mcg/ml)

Tumescent Lidocaine

Local anesthetic systemic toxicity

Table 1 Suggested dosing recommendations for commonly used local anesthetic agents

Local anesthetic	Plain		With epinephrine	
	Maximum dose	Maximum dose	Maximum dose	Maximum dose
Bupivacaine	2 mg·kg^{-1}	175 mg	3 mg·kg^{-1}	225 mg
Levobupivacaine	2 mg·kg^{-1}	200 mg	3 mg·kg^{-1}	225 mg
Lidocaine	5 mg·kg^{-1}	350 mg	7 mg·kg^{-1}	500 mg
Mepivacaine	5 mg·kg^{-1}	350 mg	7 mg·kg^{-1}	500 mg
Ropivacaine	3 mg·kg^{-1}	200 mg	3 mg·kg^{-1}	250 mg
Prilocaine	6 mg·kg^{-1}	400 mg	8 mg·kg^{-1}	600 mg

Notes: Data from Berde and Strichartz.[92] Dadure C, Sola C, Dalens B, Capdevila X. Regional anesthesia in children. In: Miller RD (Ed.). *Miller's Anesthesia*, eighth ed. Philadelphia: Elsevier; 2015:2718.[93] American Academy of Pediatrics; American Academy of Pediatric Dentistry, Cote CJ, Wilson S; Work Group on Sedation. Guidelines for monitoring and management of pediatric patients during and after sedation for diagnostic and therapeutic procedures: an update. *Pediatrics* 2006;118:2587–2602.[94]

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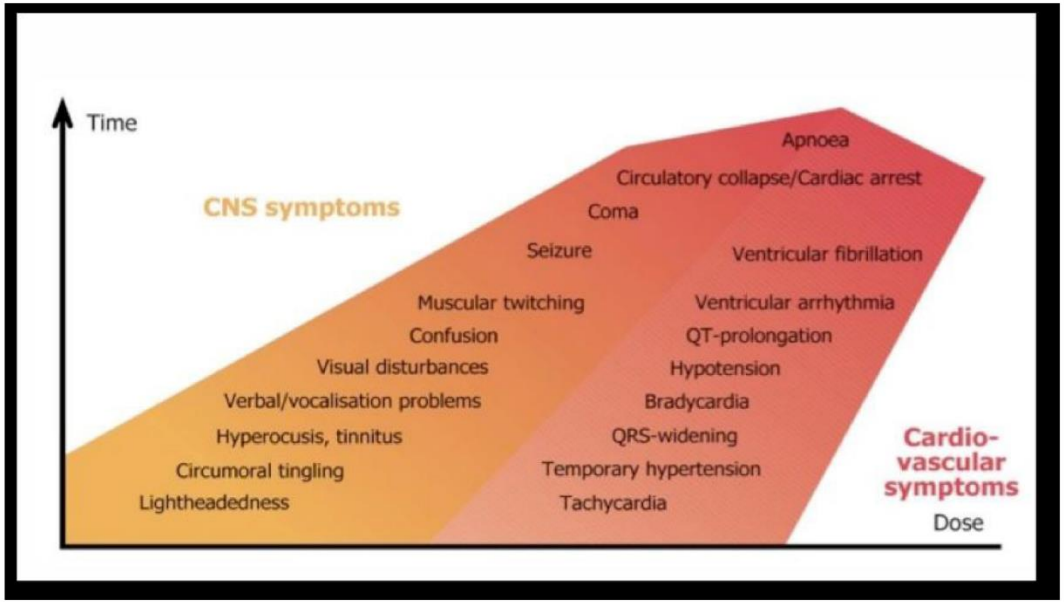

Dr John Vassiliadis MBBS FACEM, 2008

Tumescent Lidocaine

Local anesthetic systemic toxicity

Table 3 – Studies measuring serial plasma lidocaine levels from the time of tumescent infiltration into the postoperative period.

Study	Surgery	*n*	Lidocaine concentration (%)	Total dose given (mg/kg)	Time to peak plasma concentration (Tmax) (h)	Peak plasma concentration (Cmax) (mcg/ml)
Klein[35]	Liposuction	14	0.05–0.1	11.9–34.1	11–15	0.75
Samdal et al.[60]	Liposuction	12	0.1	10.5–34.4	6–12	0.9–3.6
Ostad et al.[62]	Liposuction	10	0.05–0.1	47.2–67.7	4–8	3.6
Kenkel et al.[59]	Liposuction	5	0.29	19.9–27.6	8–28	2.2–2.7
Nordstrom and Stange[56]	Liposuction	8	0.08	30–35	5–17	1.67–2.93
Ramon et al.[2]	Facelift	6	0.33	17.5–26.3	8–11	1.01–1.81
Swanson[57]	Liposuction/ Abdominoplasty	51	0.5	37.7 maximum	8–18	2.44 maximum

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Tumescent anesthesia

Estimated Maximal Safe Dosages of Tumescent Lidocaine

BACKGROUND: Tumescent lidocaine anesthesia consists of subcutan
tively large volumes (up to 4 L or more) of dilute lidocaine (≤1 g/L) and e
Although tumescent lidocaine anesthesia is used for an increasing var
dures, the maximum safe dosage is unknown. Our primary aim in this
serum lidocaine concentrations after subcutaneous administration of tu
and without liposuction. Our hypotheses were that even with large dos
serum lidocaine concentrations would be below levels associated with mi
concentration-time profile would be lower after liposuction than without li
METHODS: Volunteers participated in 1 to 2 infiltration studies without lip
study with tumescent liposuction totally by local anesthesia. Serum lid
were measured at 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, and 24 hours after eac
infiltration. Area under the curve (AUC∞) of the serum lidocaine concentr
peak serum lidocaine concentrations (Cmax) were determined with and w
any given milligram per kilogram dosage, the probability that Cmax >6 µg
mild lidocaine toxicity was estimated using tolerance interval analysis.
RESULTS: In 41 tumescent infiltration procedures among 14 volunteer
lidocaine dosages ranged from 19.2 to 52 mg/kg. Measured serum lidocaine concentrations were all <6 µg/mL over the 24-hour study period. AUC∞s with liposuction were significantly less than those without liposuction ($P = 0.001$). The estimated risk of lidocaine toxicity without liposuction at a dose of 28 mg/kg and with liposuction at a dose of 45 mg/kg was ≤1 per 2000.
CONCLUSIONS: Preliminary estimates for maximum safe dosages of tumescent lidocaine are 28 mg/kg without liposuction and 45 mg/kg with liposuction. As a result of delayed systemic absorption, these dosages yield serum lidocaine concentrations below levels associated with mild toxicity and are a nonsignificant risk of harm to patients. (Anesth Analg 2016;122:1350–9)

Maximum safe dosages of tumescent lidocaine :
28 mg/kg without liposuction
45 mg/kg with liposuction

(Anesth Analg 2016;122:1350–9)

Tumescent Lidocaine

Local anesthetic systemic toxicity

Table 2 Precautionary and emergency measures.

Side Effects	Precautionary and emergency measures
Local anesthesia systemic toxicity (LAST)	Discontinue application of TLA Oxygenation, seizure management (benzodiazepines), advanced cardiac life support, administration of 20 % lipid emulsion, continuous monitoring of vital signs
Neurologic symptoms (convulsions, loss of consciousness, agitation)	Discontinue application of TLA Oxygenation, airway management, seizure management (benzodiazepines), consider EEG, ECG monitoring
Apnea following cerebral toxicity	Discontinue application of TLA Oxygenation, advanced cardiac life support, continuous monitoring of vital signs
Cardiovascular symptoms (bradycardia, hypotension, cardiac arrhythmias)	Discontinue application of TLA Oxygenation, ECG monitoring, epinephrine and/or atropine for bradycardia, consider cardiac pacing for severe bradycardia, i.v.-fluids for hypotension, advanced cardiac life support in case of cardiac arrest, specific treatment according to ECG findings
Methemoglobinemia	Discontinue application of TLA Oxygenation, administer methylene blue in symptomatic acute toxicity (or ascorbic acid in individuals with G6PD deficiency or on serotonergic medication), seizure management (benzodiazepines) if needed, consider blood transfusions in anemic patients
Allergic reactions	Discontinue application of TLA ECG monitoring, i.v.-fluids, H1-receptor antagonist, consider corticosteroids (i.v.) and epinephrine (i.m. or i.v.) in severe cases, advanced cardiac life support in case of bradycardia

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ASRA practice advisory on treatment of local anesthetic systemic toxicity

Emergency management of local anesthetic toxicity is outlined in practice guidelines of the American Society of Regional Anesthesia and Pain Medicine

For Patients Experiencing Signs or Symptoms of Local Anesthetic Systemic Toxicity (LAST)

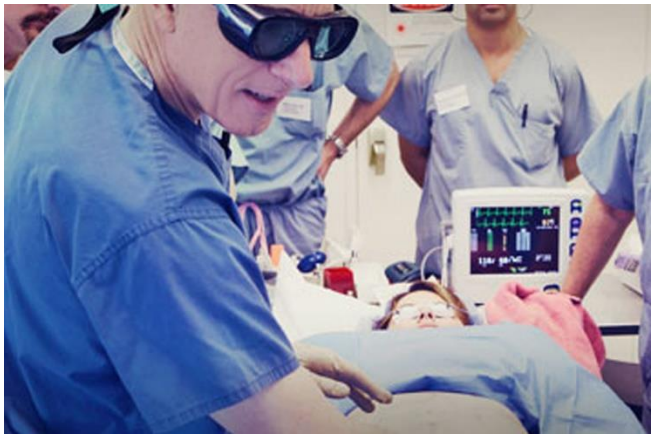
- **Get Help**
- **Initial Focus**
  - o ***Airway management:*** ventilate with 100% oxygen
  - o ***Seizure suppression:*** benzodiazepines are preferred
  - o ***Basic and Advanced Cardiac Life Support (BLS/ACLS)*** may require prolonged effort
- **Infuse 20% Lipid Emulsion (values in parenthesis are for a 70 kg patient)**
  - o ***Bolus 1.5 mL/kg*** (lean body mass) intravenously over 1 min (~100 mL)
  - o ***Continuous infusion at 0.25 mL/kg/min*** (~18 mL/min; adjust by roller clamp)
  - o Repeat bolus once or twice for persistent cardiovascular collapse
  - o Double the infusion rate to 0.5 mL/kg per minute if blood pressure remains low
  - o ***Continue infusion*** for at least 10 mins after attaining circulatory stability
  - o Recommended upper limit: approximately 10 mL/kg lipid emulsion over the first 30 mins
- **Avoid** vasopressin, calcium channel blockers, β-blockers, or local anesthetic
- **Alert** the nearest facility having cardiopulmonary bypass capability
- **Avoid propofol** in patients having signs of cardiovascular instability
- **Post LAST events** at www.lipidrescue.org and report use of lipid to www.lipidregistry.org

Reg Anesth Pain Med 2012;37:16-8.

Tumescent Lidocaine

Safety of tumescent anesthesia

- **Tumescent anesthesia and sedation:** Goals of conscious sedation are anxiolysis, amnesia, sedation and analgesia
  - Hypoxemia, Hypercarbia, Aspiration
- **Tumescent anesthesia and general anesthesia**
  - American Society of Plastic Surgeons recommends that consideration be given to not using tumescent lidocaine when general or regional anesthesia is utilized
- **Patient monitoring following tumescent anesthesia**
  - Recommends that the patient be monitored for **'several hours or possibly overnight'**



Conclusion

Tumescent anesthesia practice points

- Focused history and physical to determine presence of hepatic or renal disease
- Obtain a thorough medication history to detect Cytochrome P450 inducers or inhibitors
- Do not use bupivacaine for tumescent infiltration, it is six times more toxic than lidocaine and precipitates with sodium bicarbonate
- Adopt the appropriate recommended level of perioperative monitoring
- Resuscitation equipment and rescue medications for the emergency management of local anesthetic toxicity as per ASRA guidelines should be immediately available

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Conclusion

Tumescent anesthesia practice points

- Calculate the maximum allowable dose of local anesthetic in milligrams
- Intravascular diffusion of the infiltrated tumescent fluid may result in circulatory overload in patients with poor physiological reserve
- Calculate the maximum allowable volume of diluted local anesthetic concentration for infiltration
- Warming the local anesthetic to 37-40 C prior to injection reduces the pain of local infiltration and the likelihood of hypothermia
- Exercise great caution when administering additional local anesthetics for at least 12-18 hours after tumescent anesthesia

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Thank you for attention