Infiltration and Topical and Anesthesia

On occasion, anesthesia providers will place field blocks either as supplementation for a marginal regional anesthetic block or as the sole form of anesthesia. In addition, anesthesia providers should be knowledgeable about this form of anesthesia/analgesia for our surgeon and patient's sake. It is not uncommon to be asked by the surgeon, "How much can I inject?" As the 'expert' in local anesthetics, the anesthesia provider may be called upon to share their knowledge with surgical colleagues.

It is essential to know maximum local anesthetic dosages for plain and epinephrine containing local anesthetic solutions. Knowledge of the local anesthetic concentration/dose and the patients' weight will allow for rapid calculation of the maximum dose and volume of local anesthetic that can be safely administered. In addition to the maximum dose based on mg/kg, there is a total maximum dose regardless of weight. Avoidance of toxic dosages is essential. Maximum doses are also important to know for any peripheral nerve block that is placed.

Basic facts about infiltration:

- Almost any local anesthetic can be used for infiltration anesthesia.
- Onset is almost immediate for intradermal and subcutaneous administration.
- Epinephrine will prolong the duration of action of all local anesthetics, but is most pronounced with lidocaine.
- The conscious patient will experience some discomfort during infiltration due to the acidic nature of these solutions.
- Epinephrine containing local anesthetics should never be injected into end organs such as ears, nose, penis, fingers, or toes. Epinephrine may cause vasoconstriction and subsequent necrosis of tissue.

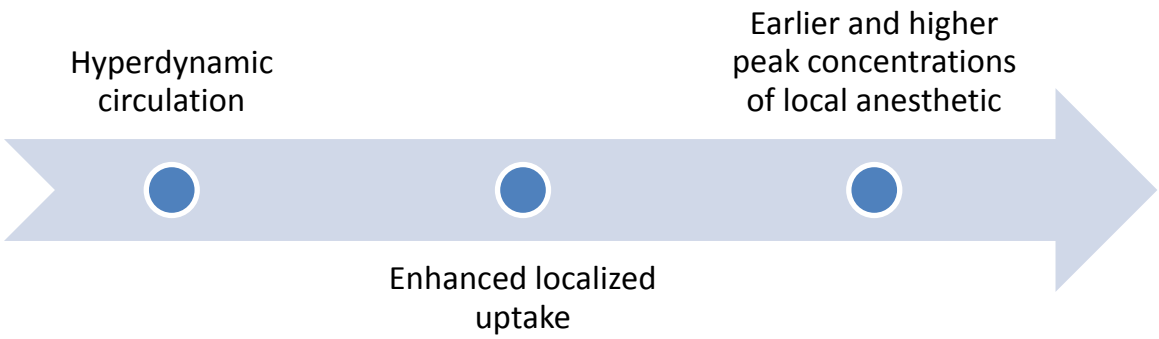
Maximum Doses for Local Anesthetics

Maximum doses for local anesthetics are not based on available evidence but on manufacturer recommendations, animal studies, and case reports. Manufacturers vary in recommended doses from country to country.

Local Anesthetic	Finland	Sweden	United States
Bupivacaine plain	175 mg	150 mg	175 mg
Lidocaine plain	200 mg	200 mg	300 mg
Mepivacaine with epinephrine	None listed	350 mg	550 mg
Ropivacaine	225 mg	200 mg	225 mg

Adopted from Rosenberg, et al., 2004.

Animal studies are often used to identify a quantal dose-effect curve regarding median effective dose (ED50) and median toxic dose (TD50). Therapeutic index is derived as a ratio of TD50 and ED50. Animal studies do not replicate the complexities found within human populations. Site of administration, use of vasoconstrictors, and disease processes all impact eventual plasma concentrations. Site of administration directly impacts subsequent plasma concentrations. Epinephrine generally decreases local anesthetic absorption. Vasoconstrictor effect and subsequent plasma levels depend on the specific local anesthetic used and site of administration. Specific disease processes and medication interactions impact plasma concentrations of local anesthetics. For example, hyperdynamic circulation is noted in the late stages of pregnancy and uremia. Increased circulation results in enhanced absorption that causes higher and earlier peak concentrations of local anesthetics.



Based on these observations the use generic maximum doses have been called into question. An attempt to make broad recommendations based on age, renal, hepatic, cardiac diseases, and pregnancy has been attempted. Due to the poor quality of data available (case series, cohort studies) specific recommendations cannot be made at this time. In the future research should identify an evidence based approach to maximum local anesthetic dose calculations based on individual patient characteristics. Until then medicolegal issues consign the anesthesia provider to follow established practices.

Commonly Administered Local Anesthetics for Infiltration as well as other Regional Techniques

Plain local anesthetics (maximum doses based on 70 kg)

Local Anesthetic	Type	Concentration %	Max dose	Max dose mg/kg	Duration
Lidocaine	amide	0.5-1.0	300	4.5	30-60 minutes moderate duration
Mepivacaine	amide	0.5-1.0	300	4.5	45-90 minutes moderate duration
Bupivacaine	amide	0.25-0.5	175	2.5-3	120-240 minutes long duration
Ropivacaine	amide	0.1-1	200	3	120-360 minutes long duration

Local anesthetics with epinephrine (1:200,000) for infiltration

Local Anesthetic	Type	Concentration %	Max dose	Max dose mg/kg	Duration
Lidocaine	amide	0.5-1.0	500	7	120-360 minutes moderate duration
Mepivacaine	amide	0.5-1.0	500	7	120-360 minutes moderate duration
Bupivacaine	amide	0.25-0.5	225	3	180-420 minutes long duration

Topical Anesthesia

Several local anesthetics can be used for topical anesthesia. The most common local anesthetics include:

- Lidocaine
- Dibucaine
- Tetracaine
- Benzocaine
- EMLA (eutectic mixture of local anesthetic)

Topical local anesthetics provide effective, short term analgesia when applied to mucous membranes and abraded skin. Lidocaine and tetracaine sprays can be used for endotracheal anesthesia prior to intubation. EMLA is a preparation used to provide cutaneous anesthesia through intact skin. EMLA is a mixture of 2.5% lidocaine and 2.5% prilocaine. The risk of methemoglobinemia is very rare. EMLA is effective in anesthetizing the skin in preparation for the placement of intravenous needles and skin grafting procedures. To be effective, EMLA must be placed under an occlusive dressing for 45-60 minutes.

Topical anesthesia is used in the emergency room for repairing lacerations. TAC is a mixture of 0.5% tetracaine, 1:200,000 epinephrine, and 10-11.8% cocaine. It is safe to use on skin, but should not be used on mucous membranes since rapid absorption may lead to toxicity. The maximum dose for adults is 3-4 ml. For the pediatric population, a dose of 0.05 ml/kg is considered safe. Concerns about cocaine toxicity, abuse, or diversion has led to the creation of an equally effective preparation, LET. LET is a preparation of lidocaine, epinephrine, and tetracaine. In the past ENT surgeons used cocaine for vasoconstriction and anesthesia; however this practice is rapidly being replaced by the use of oxymetazoline or phenylephrine in combination with a local anesthetic, such as 2-4% lidocaine. Dilute solutions should be used in children. Of concern to the anesthesia provider is the systemic absorption of phenylephrine, which can result in hypertension and reflex bradycardia. Oxymetazoline has a larger margin of safety and is absorbed less systemically.

Common Topical Preparations

Anesthetic	Concentration %	Form	Area of use
Benzocaine	1.5 20 20	Cream Ointment Aerosol	Skin and mucous membrane Skin and mucous membrane Skin and mucous membrane
Cocaine	4.0	solution	Ear, nose, throat
Dibucaine	0.25-1.0 0.25-1.0 0.25-1.0 0.25 2.5	Cream Ointment Aerosol Solution suppositories	Skin Skin Skin Ear Rectum
Lidocaine	2-4 2 2.5-5 2 10 10	Solution Jelly Ointment Viscous Suppositories aerosol	Oropharynx, trachea, nose Urethra Skin, mucous membranes Oropharynx Rectum Gingival mucosa
Tetracaine	0.5-1.0 0.5-1.0 0.25-1.0	Ointment Cream solution	Skin, rectum, mucous membranes Skin, rectum, mucous membranes Nose, tracheobronchial tree
EMLA	Lidocaine 2.5 Prilocaine 2.5	cream	Intact skin
TAC	Tetracaine 0.5 Epinephrine 1:200,000 Cocaine 11.8	solution	Cut skin
LET	Lidocaine 4 Epinephrine 1:200,000 Tetracaine 0.5	solution	Cut skin

Methemoglobinemia

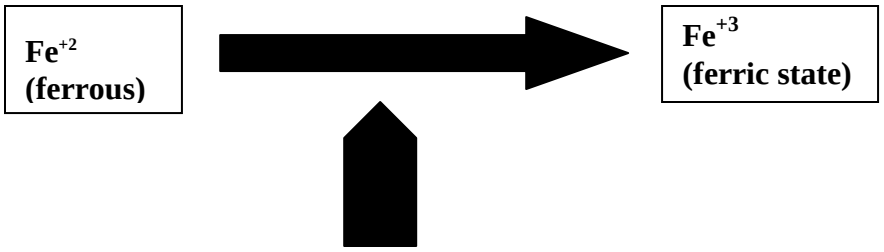
Benzocaine administration to the mucous membranes can result in the relatively uncommon but potentially fatal complication of methemoglobinemia. The anesthesia provider may encounter methemoglobinemia by assisting in airway management in another department (i.e. endoscopy suite), or in the OR when using this local anesthetic to anesthetize the upper airway. Other local anesthetics may cause methemoglobinemia. Prilocaine is one of the most likely candidates. Prilocaine is metabolized in the liver (since it is an amide). One of its metabolites is O-toluidine which oxidizes hemoglobin. Since prilocaine is rarely used clinically (with the exception of EMLA cream) it is unlikely that this cause will be seen. Benzocaine, on the other hand, is still being used as a spray clinically and available over the counter.

Benzocaine made its debut into clinical use in 1900. It is used solely as a topical anesthetic. Benzocaine is the most commonly implicated local anesthetic associated with methemoglobinemia. The incidence of methemoglobinemia has been reported as high as 1 in 7,000 exposures. Up to 35% of topical benzocaine, when applied to mucous membranes, can be absorbed systemically. Inflamed areas of the mucous membranes absorb benzocaine at a higher rate. One of the problems with the administration of topical benzocaine sprays is estimating how much local anesthetic has been delivered. Application of topical benzocaine to mucous membranes should be limited to 1 second. Clinicians often fail to realize the significant absorption rate of benzocaine. In addition, clinicians may use multiple sprays or spray for longer than 1 second. In a review of benzocaine induced methemoglobinemia it was found that 46.4% of the cases reported had more than 1 spray of benzocaine.

Methemoglobinemia

Hemoglobin contains four heme groups (Fe+2) located on the surface of the molecule. Heme has the ability to reversibly bind with oxygen. Methemoglobin (MHb) is a form of hemoglobin that is unable to bind with oxygen. The ferrous irons (Fe+2) of the heme are oxidized to a ferric iron (Fe+3). The ferric heme is unable to bind with oxygen, resulting in a diminished ability to deliver oxygen to tissue.

Schematic diagram demonstrating the formation of methemoglobinemia

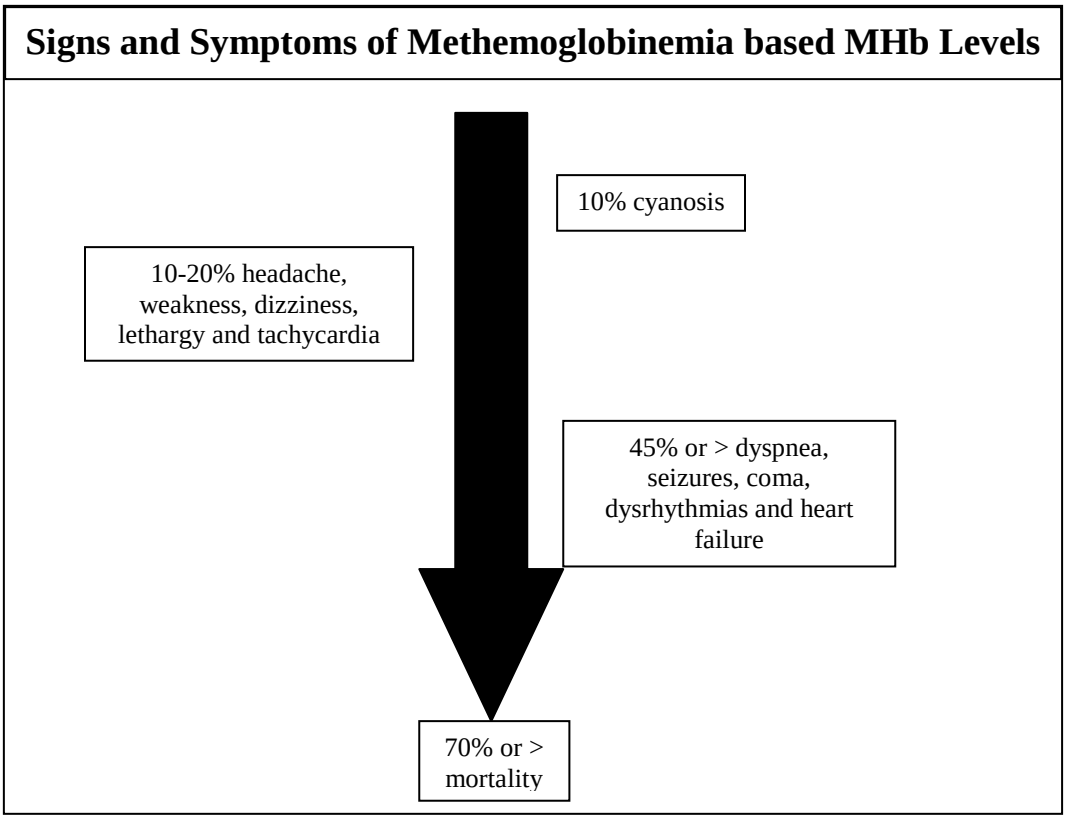


Oxidization occurs directly or due to metabolism

Illustration from Methemoglobinemia and Benzocaine. DD Moos, JD Cuddeford. Gastroenterology Nursing. 2007:30:5

Signs and Symptoms of Methemoglobinemia

Signs and symptoms are dependent on the levels of MHb. Patients with anemia and cardiopulmonary disorders may exhibit signs and symptoms earlier. When levels of MHb reach 10% or greater, the patient may appear cyanotic. MHb levels of 15% or greater may demonstrate: cyanosis, headache, weakness, dizziness, lethargy, and tachycardia. Levels between 10-20% are usually well tolerated. At levels of 45% or greater, signs and symptoms may include dyspnea, cyanosis, seizures, coma, dysrhythmias, and heart failure. At levels 70% or greater, mortality can occur.



Reprinted with permission: Moos DD, Cuddeford JD. Methemoglobinemia and Benzocaine. Gastroenterology Nursing. Volume 30, Number 5, 2007.

Diagnosis

Methemoglobinemia should be considered in any patient who develops cyanosis after the use of topical pharyngeal anesthesia. Pulse oximetry readings will be inaccurate and not reflect the degree of hypoxia the patient is experiencing. Readings may range from 80-85% regardless of the severity of methemoglobinemia. A MHb level greater than 10% will result in an oximetry reading that is unreliable. Co-oximetry is able to differentiate between oxyhemoglobin, deoxyhemoglobin, carboxyhemoglobin, and MHb. The gold standard for confirming a diagnosis of methemoglobinemia is co-oximetry. This is available with most, but not all, ABG determinations. It is important to request co-oximetry when sending blood samples to the laboratory.

Treatment

Patients who become cyanotic or hypoxic after the application of benzocaine should have supplemental oxygen placed. If their condition improves, then further evaluation for cardiopulmonary problems should be considered. If their condition does not improve and methemoglobinemia is suspected, then an arterial blood gas (ABG) with co-oximetry should be sent for evaluation. Methylene blue administration is not recommended until the presence of MHb is confirmed by co-oximetry, if available. Methylene blue, 1-2 mg/kg, is the treatment of choice for methemoglobinemia and should be administered over 5 minutes. Methylene blue accelerates the capacity of NADPH MHb reductase to reduce MHb. Reported side effects of methylene blue include: dizziness, confusion, restlessness, headache, abdominal pain, nausea and vomiting, dyspnea, hyper/hypotension, and diaphoresis. If the patient's condition improves after the administration of

methylene blue, the patient should be monitored for the reoccurrence of symptoms. Methylene blue will not improve methemoglobinemia related to G-6-deficiency, NADPH methemoglobinemia, and cytochrome b5 reductase deficiency. Patients with a G-6-deficiency require transfusion or dialysis for treatment and methylene blue administration should be avoided. Patients with NADPH deficiency may acquire hemolytic anemia with the administration of methylene blue. For patients with no contraindications, repeated doses of methylene blue may be required. A second dose may be repeated in an hour. The total dose should not exceed 7 mg/kg since excessive methylene blue administration can result in methemoglobinemia. After initial treatment, the patient should be transferred to the intensive care unit for monitoring. Additional MHb levels should be measured at hours 2 and 8 after the initial dose of methylene blue to monitor the patient for rebound methemoglobinemia.

Summary of Common Local Anesthetics

Local Anesthetic	Type	Onset of Action	Duration	Clinical Use
Procaine	Ester	Slow	Short	Spinal
Bupivacaine	Amide	Moderate	Long	Peripheral Nerve Blocks Infiltration Spinal Epidural
Ropivacaine	Amide	Moderate	Long	Peripheral Nerve Blocks Epidural
Chloroprocaine	Ester	Fast	Short	Peripheral Nerve Blocks Epidural
Etidocaine	Amide	Fast	Long	Peripheral Nerve Blocks Infiltration Epidural
Lidocaine	Amide	Fast	Moderate	Peripheral Nerve Blocks Infiltration Spinal Epidural Bier Block
Mepivacaine	Amide	Fast	Moderate	Peripheral Nerve Blocks Infiltration
Prilocaine	Amide	Fast	Moderate	Peripheral Nerve Blocks Infiltration Bier Block

Practical Application

A.) The surgeon wishes to use 1% plain lidocaine to infiltrate along the incision in a 4 kg pediatric patient. How much can he use?

- What about 0.5% plain lidocaine?
- What about 0.5% lidocaine with epinephrine?
- What about 0.5% plain bupivacaine?
- What about 0.5% bupivacaine with epinephrine?

B.) The surgeon wishes to use 1% plain lidocaine to infiltrate the wound in a 55 kg adult patient. How much can he inject?

- What about 0.5% plain lidocaine?
- What about 0.5% lidocaine with epinephrine?
- What about 0.5% plain bupivacaine?
- What about 0.5% bupivacaine with epinephrine?

C.) You are in the ENT room. The surgeon is having problems with visualization due to bleeding during a nasal endoscopy. Your patient's blood pressure continues to trend upwards but the heart rate is slowing. What may be one of the causes?

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