ARE YOUR PATIENTS GETTING COMFORTABLY NUMB?
LOCAL ANESTHESIA PHARMACOLOGY UPDATE

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Patients rate “painless injections” as the most important criteria in evaluating their dentist or dental hygienist.

90% of all patients report being anxious about going to the dentist or dental hygienist and receiving a shot.

Physiology of Anesthetic Agents

How do we assess anesthesia?
- Question the patient
- Probe the area
- Electric pulp tester
- Cold test

How is anesthetic success defined in studies?
- Ideal: 2 consecutive 80/80 readings with EPT within 15 minutes of injection (and sustained for 60 mins)

Cold Test:
- Spray some Endo Ice (or use an ice stick) on to a cotton swab and place it on the dried buccal surface of the tooth/teeth you need to work on

Onset of anesthesia:
1. Dependent upon anesthetic agent
   - Concentration
   - Diffusion to the site
   - Lipid solubility

Protein binding to receptor sites

<table>
<thead>
<tr>
<th>Agent</th>
<th>Lipid Solubility</th>
<th>Protein Binding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>2.9</td>
<td>65%</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>1</td>
<td>75%</td>
</tr>
<tr>
<td>Prilocaine</td>
<td>1.5</td>
<td>55%</td>
</tr>
<tr>
<td>Articaine</td>
<td>49.5</td>
<td>95%</td>
</tr>
</tbody>
</table>
**Physiology of Anesthetic Agents**

- **Onset of anesthesia:**
  1. Dependent upon anesthetic agent
     - Concentration
     - Diffusion to the site
     - Lipid solubility
     - Protein binding to receptor sites
  2. Dependent upon technique, block versus infiltration
     - Infiltration has faster onset
     - Block has longer duration

- **Blocks versus Infiltrations**

  - **Advantages of infiltrations**
    1. Faster onset
    2. Simple
    3. Safe
    4. Good hemostasis (with vasoconstrictor)
  - **Disadvantages of infiltrations**
    1. Multiple injections for multiple teeth
    2. Shorter duration of anesthesia, especially with children due to their higher metabolic rate

**Blocks versus Infiltrations**

- Dental anesthetic agents: all amides
  1. Lidocaine – (plain or) with vasoconstrictor
  2. Mepivacaine – plain or with vasoconstrictor
  3. Prilocaine – plain or with vasoconstrictor
  4. Articaine – with vasoconstrictor
  5. Bupivacaine – with vasoconstrictor
- Amide anesthetics have replaced ester anesthetics because of their very low risk of allergic reaction

**Blocks versus Infiltrations**

- **Duration of anesthesia and onset:**
  1. Dependent upon anesthetic agent
     - Concentration
     - Diffusion to/from the site
     - Lipid solubility
     - Protein binding to receptor sites
  2. Dependent upon technique, block versus infiltration
  3. Dependent upon vasoconstrictor presence, but **NOT** vasoconstrictor concentration*

Jastak, Yagiela, Donaldson, Local Anesthesia of the Oral Cavity, WB Saunders Co, 1995
Physiology of Anesthetic Agents

1. Overall diameter (size) of the nerve bundle
2. Amount of myelin (lipid) sheath present
   - Time for entire nerve bundle to be penetrated
   - Central Core Theory:
     - Peripheral fibers anesthetized first
     - To most proximal structures (molars)
     - Central fibers anesthetized last
     - To most distal structures (incisors)

DeJong RH, Physiology and Pharmacology of Local Anesthesia, 1970

Jastak, Yagiela, Donaldson, Local Anesthesia of the Oral Cavity, WB Saunders Co, 1995

Physiology of Anesthetic Agents

- Critical length = 3 nodes minimum (5 – 8 mm)
- Tissue space & density → Anesthetic volume

Node of Ranvier

Evers & Haegerstam, Introduction to Dental Local Anesthesia, MBD, 1980

Physiology of Anesthetic Agents

- The “right” volume depends on many variables
  - For infiltration injections, ½ to ¾ cartridge is generally ideal for adults; ½ for kids
  - For an inferior alveolar nerve block,
    - Less than ½ cartridge tends to be ineffective
    - ½ – 1 cartridge is ideal for adults; ½ for kids
    - An additional cartridge may increase profundity & decrease onset time*

Nusstein et al. Anesthetic efficacy of different volumes of lidocaine with epinephrine for inferior alveolar nerve blocks, Gen Dent, Vol 50, 2002

Physiology of Anesthetic Agents

- How do local anesthetics work?
  - BH⁺ = acidic, ionized form:
    - Can’t pass through nerve membrane (water soluble)
  - B = basic, unionized form:
    - Can pass through nerve membrane (lipid soluble)

Physiology of Anesthetic Agents

- How do we assess anesthesia?
  - Question the patient
  - Probe the area
  - Electric pulp tester
  - Cold test

Soft tissue only
Pulpal tissue

- Delayed pulpal onset: occurs in the mandible of 19 – 27% of patients (even though soft tissue is numb)
- Delayed over 30 minutes in 8%


Physiology of Anesthetic Agents

- Reasons for delayed or failed onset
  - Disassociation rate, transport/perfusion rate, re-association rate, binding rate

BH⁺ = acidic, ionized form:
Can’t pass through nerve membrane (water soluble)
B = basic, unionized form:
Can pass through nerve membrane (lipid soluble)
Troubleshooting Local Anesthesia

Is this failed anesthesia?
Frequency dependent conduction phenomenon

Wait!
I Still Feel That!

Physiology of Anesthetic Agents

- Frequency dependent conduction phenomenon

If we stimulate the nerve at sub-threshold levels, we can increase the number of open binding sites available to the anesthetic, increasing our anesthetic success.

Use of Distraction Techniques

- Surface vibration
  - Creates a mucosal surface distraction
  - Ultrasonic surface vibration enhances mucosal penetration of topical anesthetics
- Devices that create deep tissue vibration via ultrasonics
  - Produce low-level sensory nerve stimulation, allowing greater anesthetic access to receptor sites to produce better anesthesia
  - By activating the Frequency Dependent Conduction phenomenon

Anesthesia Delivery Assistance Devices

- Devices that create ultrasonic vibration activate the Frequency Dependent Conduction phenomenon
- Based on the Gate Control Theory of Pain

Anesthesia Delivery Assistance Devices

- The Gate Control Theory of Pain
  - Upon injection of anesthetic solution:
    - Nociceptors send most of the pain messaging to the brain via slow conducting, thin C nerve fibers
    - By contrast, vibration stimuli of the oral mucosa are transmitted by rapid conducting, large A-beta fibers
  - By applying the vibrations before starting the injection, the vibration sensations reach the brain first and cause release from inhibitory interneurons, blocking the C fiber pain stimulation by "closing the pain gate"

Reasons for Anesthetic Failures

1. Anatomical/physiological variations
2. Technical errors of administration
3. Patient anxiety
4. Inflammation and infection
5. Defective/expired solutions


Reasons for Anesthetic Failures

4. Inflammation and infection
   - Causes increased tissue acidity (decreased pH)
   - Less anesthetic solution is available to enter into the nerve due to unfavorable dissociation equilibrium
   - Result is decreased anesthetic effect

Inflammation or infection pH = 5.0 to 3.0
- pH 5.0 = 0.13% (1/20 of 7.4 pH)
- pH 4.0 = 0.013% (1/200 of 7.4 pH)
- pH 3.0 = 0.0013% (1/2000 of 7.4 pH)

Troubleshooting Anesthesia

- The "Hot" Tooth / "Hot" Gum
  - Includes:
    1. Infected teeth with irreversible pulptits
    2. Severe periodontal infections
    3. Hypoplastic teeth with severe sensitivity
    4. Teeth with hypersensitivity due to recession, occlusal trauma/bruxing, etc.

  All of these may be highly problematic to anesthetize

### Infiltration Anesthesia

- **Works well for the maxilla...**
  - Work fairly well for anterior and bicuspids
  - More variable predictability for molars
  - Greater success using articaine & faster onset
    - Lidocaine 45% - 67% articaine 75% - 92%
    - Lidocaine 6.1 - 11.1 minutes, articaine 4.2 - 4.7 minutes

**Facial**


**Mandibular, Practical Dental Local Anesthesia, Quintessence, 2003**

### Troubleshooting Anesthesia

- **The “Hot” Tooth / “Hot” Gum**
- **First, give a block injection**
  - The Gow-Gates mandibular division block has a significantly higher success rate than all other techniques
  - Gow-Gates 52%
  - Vaziri-Akinosi 41%
  - Conventional IA 36%
  - Buccal-plus-lingual infiltration 27%

**No technique was fully acceptable by itself**


### Pharmacology of Anesthetic Agents

- **A Practical Armamentarium:**
- From a meta-analysis of 13 clinical trials:
  - Evidence strongly supported articaine’s superiority over lidocaine for infiltration anesthesia
  - Evidence was weak for any significant difference between lidocaine and articaine for block anesthesia
  - Articaine was 4 times more effective, with greater duration, than lidocaine as an infiltration injection when used for teeth diagnosed with irreversible pulps

Troubleshooting Anesthesia

- The “Hot” Tooth / “Hot” Gum
  - Why is the “hot” tooth so hard to anesthetize?
    - Inflammation may cause an increase in anesthetic-resistant sodium channels that exist in pain neurons.
    - Inflammation may cause an increase in the number and in the receptive field of pain neurons.
    - The barrage of pain impulses to the CNS produces “central sensitization”: an exaggerated CNS response to even gentle peripheral stimuli.
    - Apprehensive patients have a reduced pain threshold.

  *Hot teeth are tough to treat!*


- There is no contraindication for combining any of the amide anesthetic agents
- Using plain anesthetics for “pre-injection”, then using anesthetic with vasoconstrictor
  - Anesthetic with vasoconstrictor: pH ~3.5, highly acidic
  - Plain anesthetic: pH ~6.5, significantly less acidic
  - Therefore, plain anesthetics have less “burning” sensation
- Using a plain anesthetic first may be more comfortable for the patient,
- But it may also mildly increase the cardiovascular side-effects of vasoconstrictor in the second injection

Troubleshooting Anesthesia

- The “Hot” Tooth / “Hot” Gum
  - Ongoing research: Acupuncture
  - For teeth with irreversible pulpitis:
    - IA block alone: 20% success
    - IA block + LI4 Hegu acupoint: 60% success


WHAT’S NEW IN DENTAL LOCAL ANESTHESIA?

- Buffered Anesthetics
- Inhalation Local Anesthesia
- Iontophoretic Anesthesia
- Anesthetic Reversal Agent

Buffering of Local Anesthetics

- Buffer with sodium bicarbonate immediately before delivery
  - Increases dissociation of anesthetic agent for rapid uptake into the nerve
    - Potentially faster onset
    - Potentially more comfortable
    - Potentially more profound
    - Potentially higher success rate
Buffering of Local Anesthetics

% of Effective Anesthetic (Lidocaine)

Buffering of Local Anesthetics

Buffering of Local Anesthetics

Buffering of Local Anesthetics

Buffering of Local Anesthetics

Buffering of Local Anesthetics

Buffering of Local Anesthetics

Buffering of Local Anesthetics
New Technology: Buffering

- Improve patient satisfaction
  - More comfortable injections
  - More predictable anesthesia
  - More profound anesthesia
- Decrease appointment times
  - Less waiting for anesthetic onset (1 – 2 minutes)
  - See more patients
    - Emergency patients
    - Hygiene patients

New Product: Kovanaze

- Intranasal spray delivery
  - Utilizing the BD ACCUSPRAY® technology currently used in the Flumist® nasal product
  - 3% tetracaine HCl plus 0.05% oxymetazoline vasoconstrictor
  - Produces a regional block enabling invasive quadrant dentistry on maxillary teeth #4 – 13 and A – J in children ≥ 40 kg/88 lb.

New Product: Kovanaze

- “Sniff” administration
  - No needle
  - Non-invasive, painless
  - Easy to administer
  - Anesthetic enters the trigeminal neural pathway within the nasal cavity
    - Adult dosage: 2 sprays; 1st spray, wait 4 minutes; 2nd spray, wait 10 minutes
    - Start work: about 15 minutes from 1st spray

New Product: Kovanaze

- Phase 3 clinical trial results:
  1. 88% success for restorative procedures for 1st premolar, canine, and incisors (compared to 93% success with infiltration injection of 2% lidocaine with 1:100,000 epi)
  2. 60 – 66% success for 2nd premolar
  3. Side effects:
     a. Runny nose 57%
     b. Nasal congestion 26%
- FDA approved June 2016

New Product: Kovanaze

- Safety profile
  - Tetracaine is an ester anesthetic; metabolism begins as soon as it enters the bloodstream
    - Less burden on the liver
    - No lip/face anesthesia
  - Shorter duration of post-operative anesthesia
    - Safer for children?
    - More comfortable for adults?
  - Minor side effects: stuffy nose, sneezing, runny nose
    - Side effects same as for common OTC nasal decongestant products

New Product: Kovanaze

- Instructions for use:
  - The sprays must be administered into the nasal cavity on the same side (ipsilateral) as the planned dental procedure.
  3. The first spray must be horizontal at approximately a 30° angle to the face; wait 4 minutes.
New Product: Kovanaze

Instructions for use:

After 4 minutes:

4. The second spray must be at approximately a 45° angle up; wait 10 minutes.

5. Before starting the dental procedure *wait 10 minutes*.

**Important:**

To ensure efficacy, please wait the ENTIRE 10 minute period before doing the test drill.

Then Do Test Drill

WAIT 10 Minutes

6. Optional 3rd spray (adults only)

   - For adults ≥ 18 years: If the anesthesia is insufficient, you will need to administer a third spray (repeat Step 5). Wait an additional 10 minutes after the third spray.

   - **DO NOT ADMINISTER A THIRD SPRAY TO CHILDREN UNDER 18 YEARS OLD.**

New Research: Iontophoresis

- Uses a low-density electric current to introduce ionic drugs into the body through the skin or mucosa
- Over 100 years of research in medical settings
- In early stages of dental efficacy research
- Needle-free anesthetic delivery
- Faster onset and prolonged duration likely


New Research: Light-Reactive Anesthetics

- Anesthetic is clinically inactive when injected
- Activated by exposure to a particular wavelength of *violet light*
- At end of the procedure, anesthetic is inactivated by exposure to a particular wavelength of *green light*

The ultimate on-off switch!
Electronic Anesthesia

- The ultimate on/off switch?
- TENS units
- H - wave machine
- 3M machine
- Cedeta

Cell Demodulated
Electronic Targeted
Anesthesia

None of these devices are currently being marketed.

OraVerse Reversal Agent

Indicated for reversal of soft-tissue anesthesia,
- i.e., anesthesia of the lip and tongue, and the associated functional deficits resulting from an intraoral submucosal injection of local anesthetics containing a vasoconstrictor

Restores normal sensation twice as fast*
- Accelerates the return to normal function so patients can speak, smile and drink normally

* Versus control group in clinical trials

OraVerse Reversal Agent

Pulpal anesthesia wears off in 45-60 minutes
Soft tissue numbness can last 3-5 hours

<table>
<thead>
<tr>
<th>Local Anesthetics with Vasoconstrictors</th>
<th>Expected Duration (minutes)</th>
<th>Pulp Anesthesia</th>
<th>Soft Tissue Anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine 4% + epinephrine 1:100,000</td>
<td>45-60</td>
<td>180-300</td>
<td></td>
</tr>
<tr>
<td>Lidocaine 2% + epinephrine 1:100,000</td>
<td>60</td>
<td>180-300</td>
<td></td>
</tr>
<tr>
<td>Mepivacaine 2% + neosynephrine 1:20,000</td>
<td>60</td>
<td>180-300</td>
<td></td>
</tr>
<tr>
<td>Prilocaine 4% + epinephrine 1:200,000</td>
<td>60-90</td>
<td>180-480</td>
<td></td>
</tr>
</tbody>
</table>

OraVerse Reversal Agent

Loss of Function can result in
- Difficulty with speaking
- Difficulty in smiling
- Difficulty with eating
- Difficulty with drinking
- Uncontrolled drooling
- Biting of lip or cheek
- Patient’s perceived sense of altered appearance

OraVerse (Phentolamine Mesylate)

Phentolamine mesylate (alpha adrenergic antagonist) is a vasodilator originally developed in 1952 to treat hypertension

Administered by injection
- With standard dental syringe, same injection site, and identical technique used for delivery of the original local anesthetic agent(s)

Dilates blood vessels at the anesthetic site, speeding up vascular removal of the anesthetic

Reverses the effect of vasoconstrictors

OraVerse Reversal Agent

Recovery time:
- Median time to recovery of normal lip sensation
- Lower lip:
  - 70 minutes for OraVerse group vs. 155 minutes for control group (121% faster)
  - Reduced median time to normal sensation by 85 minutes
  - After 1 hour: 41% OraVerse patients normal vs. 7% of controls
- Upper lip:
  - 50 minutes for OraVerse group vs. 133 minutes for control group (166% faster)
  - Reduced median time to normal sensation by 83 minutes
  - After 1 hour: 59% OraVerse patients normal vs. 12% of controls

OraVerse Reversal Agent

- **Recovery time:**
  - Median time to recovery of normal sensation
  - 110 minutes for OraVerse group vs. 180 minutes for control group
  - Reduced median time to normal sensation by 70 minutes
  - Median time to recovery of normal function
  - 111 minutes for OraVerse group vs. 190 minutes for control group
  - Reduced median time to normal function by 79 minutes
  - At any point, the OraVerse patients had a 2.94-fold higher chance of recovery to normal function versus control patients


- **Safety Profile**
  - Across all studies:
    - No contraindications
    - No evident toxicity
    - No known drug interactions with OraVerse
    - No difference in adverse events versus control
    - Only 1% difference in transient injection site pain for OraVerse group (5%) versus the Control group (4%)
    - All adverse events were mild and resolved within 48 hours


- **When to use:**
  - Patients who have received anesthetic with a vasoconstrictor
  - Procedures where post-procedural pain is not anticipated:
    - Cavity preparations
    - Crown preparations
    - Crown placements
    - Inlays
    - Onlays
    - Veneers
    - Non-surgical periodontal scaling and root planning
  - Patients who may not be able to control post-op tendency to bite themselves


- **Case Selection:**
  - Special needs patients
  - Children going back to school or to after-school activities
  - People that want to get back to work, to their day
    - "As a busy executive, not allowing me the option to pay for this product is a complete disservice... In this economy I can't afford to lose work; not giving me the option to purchase this product is just wrong!!" Patient blog
  - People who dislike being numb

OraVerse Reversal Agent

- **A patient service that may distinguish your practice from others**
  - This is a service, an option, to be able to offer your patients
  - It’s the thought that counts!
PHARMACOLOGY OF ANESTHETIC AGENTS

Pharmacologic Factors for Success and Safety

Pharmacology of Anesthetic Agents

- Dental anesthetic agents: all amides
  1. Esters: high incidence of allergic reaction
     - Frequent cross-reactivity
     - No longer available in U.S. in dental cartridges
     - Available in multidose bottles
  2. Amides: <1% incidence of allergic reaction
     - True allergy very rare
     - Sensitive patients usually not reactive to other amide agents
     - Recommend patch testing by allergist
     - Note: This is not entirely reliable

Baluga JC et al, Allergy to local anesthetics in dentistry: Myth or reality? Allergol Imunopathol, 30(1), 2002

- Common usage:
  (Expected duration of pulpal anesthesia)
  - Short procedures: less than 1 hour
    1. Mepivacaine 3% plain (as infiltrate or block)
  - Routine procedures: 1 to 2 hours
    1. Lidocaine 2% with vasoconstrictor
    2. Mepivacaine 2% with vasoconstrictor
    3. Articaine 4% with vasoconstrictor
    4. Prilocaine 4% with vasoconstrictor

- Difficult to anesthetize patients:
  1. Prilocaine 4% with vasoconstrictor
  2. Articaine 4% with vasoconstrictor

A Practical Armamentarium:
- 2% Lidocaine with 1:100,000 epinephrine
  - For one to two hour procedures and most block injections
- 3% Mepivacaine plain
  - For short duration procedures or the rare “no vasoconstrictor” patient
- 4% Articaine with 1:200,000 epinephrine
  - For infiltrations and “hard to anesthetize” patients
- 0.5% Bupivacaine with 1:200,000 epinephrine
  - For prolonged pain control and long duration procedures
- And some buffering agent and OraVerse anesthetic reversal agent
Pharmacology of Anesthetic Agents

- Adverse reactions to anesthetic agents:
  1. Psychogenic reactions
     - Syncope the most common reaction
  2. Allergic reactions - uncommon
  3. Toxic reactions - uncommon
  4. Idiosyncratic reactions
     - Emotional factors may play a key role in producing unusual symptoms that cannot be related to pharmacology or anatomy

- Psychogenic reactions
  - Syncope the most common reaction
  - 76% of medical emergencies in the dental office are related to stress and anxiety
  - Low blood sugar, lack of sleep, and/or dehydration may also cause syncope
  - To avoid syncope:
    - Give injections with the patient lying supine, then slowly sit the patient upright

- Allergic reactions
  - Question the patient carefully
  - Get a full history of the incident
  - Was it really an allergic reaction?
  - Allergy to an amide anesthetic is very rare

- Toxic reactions
  - Uncommon

- Idiosyncratic reactions
  - Emotional factors may play a key role in producing unusual symptoms that cannot be related to pharmacology or anatomy

- Management of syncope:
  - Lay patient supine with legs above head
  - Maintain airway; may administer O₂
  - Monitor pulse, blood pressure & breathing
  - Loosen tight collar; keep patient warm
  - Calmly reassure the patient

- Allergic reactions
  - Mild
    - Rash, skin itches, runny nose and eyes (leaky capillaries)
    - Majority of allergic responses are contact dermatitis
  - Moderate
    - Swelling of tongue or throat
    - Asthmatic wheezing (respiratory constriction)
  - Severe
    - Anaphylaxis: may develop within minutes
    - CV system relaxes, BP drops, shock, failure

- Anaphylaxis
  - Initial signs and symptoms:
    - Warm moist skin, apprehension, diffuse erythema/hives, itching, angioedema
  - Subsequent signs:
    - Abdominal cramps, vomiting, wheezing, dyspnea, difficulty talking
  - Progressive signs and symptoms develop very quickly!

Most adverse drug reactions develop during the injection or within 5 to 10 minutes post-injection.
Pharmacology of Anesthetic Agents

- Adverse reactions to anesthetic agents:
  - Allergic reactions: mild to moderate
    | Reactions         | Treatment                          |
    | Urticaria         | Diphenhydramine (Benadryl)         |
    | Angioneurotic edema | 25 to 50 mg orally if no respiratory or circulatory compromise |
    | Mucous membrane congestion | Continue every 6 hours for 2 to 3 days |
    |                   | Bronchodilator: Albuterol or Alupent inhaler |

- Adverse reactions to anesthetic agents:
  - Allergic reactions: severe
    | Reactions         | Treatment                          |
    | Anaphylaxis       | Have front desk call 911          |
    | Airway restriction | Give positive pressure O₂         |
    | Hypotension       | Epinephrine 1:1000 (Epi pen)      |
    | “something wrong” | 0.3 – 0.5 cc subcutaneously, repeat every 10 – 15 mins if needed |
    | “sick feeling”    | Diphenhydramine 2 mg/kg IV or IM |

- Adverse reactions to anesthetic agents:
  - Allergic reactions: primary reasons for allergic reactions to dental local anesthetics:
    - The preservative for the anesthetic: Methyl paraben
      FDA ordered removed from all U.S. dental cartridges in 1984
    - Ester anesthetics: high allergic incidence; cross-reactive
      Replaced with amide anesthetics in mid 1990’s
    - Latex in cartridge stopper and diaphragm: molecules leached into the anesthetic solution
      Replaced with silicone in early 2000’s
    - The antioxidant for the vasoconstrictor: Sodium or potassium metabisulfite (0.50 mg/ml)

- Adverse reactions to anesthetic agents:
  - Allergic reactions to a cartridge of 2% lidocaine with 1:100,000 epinephrine:
    - Lidocaine HCl 2% concentration
    - Epinephrine (as the bitartrate dilution)
    - Distilled water
    - Sodium chloride 10.2 mg
    - (Citric acid 0.34 mg)
    - Sodium or potassium metabisulfite 0.85 mg

- Adverse reactions to anesthetic agents:
  - Allergic reactions: amide anesthetic is suspected:
    - Have patient patch tested (skin “prick” test followed by intradermal injection) for all amides and for at least one ester anesthetic (send dental cartridges with patient)
    - A challenge test to duplicate symptoms can be used if there is no response to skin testing; this is more reliable
    - May use 1% diphenhydramine (Benadryl) with 1:100,000 epinephrine as an alternative anesthetic
      Short duration (infiltrant), may require multiple injections
Pharmacology of Anesthetic Agents

- Adverse reactions to anesthetic agents:
  3. Toxic reactions: Uncommon
  Signs:
  - Low: sedation, analgesia
  - Intermediate: lightheadedness, slurred speech, drowsiness, euphoria/dysphoria, diplopia, muscle twitching
  - High: disorientation, tremors, respiratory depression, tonic/clonic seizures
  - Lethal: coma, respiratory arrest, cardiovascular collapse
  Progression may be very rapid with local anesthetics

Pharmacology of Anesthetic Agents

- Toxic reactions: Contributing factors
  - Type of anesthetic
    - Plain anesthetics have rapid systemic absorption
  - Dosage of anesthetic
  - Route of administration
  - Rate of administration
  - Patient's physical condition and health
  - Includes previous exposure
  - Drug interactions
  - Psychological response

Chen AH, Toxicity and allergy to local anesthesia, J Calif Dent Assoc, Vol 26 No 9, 1998

Pharmacology of Anesthetic Agents

- Local anesthetic dosage
  - Calculating dosage:
    150 lb. adult
    2% lidocaine with epinephrine
    150 lb. x 3.2 mg/lb. = 480 mg
    500 mg is the maximum for any patient
    480 mg
    \[ \frac{36 \text{ mg/cartridge}}{500 \text{ mg}} = 13.33 \text{ cartridges} \]
    14 cartridges is the maximum for any patient ≥ 156 lb.

*Within a 24 hour timeframe

Pharmacology of Anesthetic Agents

- Local anesthetic dosage
  - FDA approved max. dosage
  1. 2% lidocaine w/epi 3.2 mg/lb
  4% articaine w/epi
    (500 mg max. for any patient)
  3. 3% mepivacaine plain 3.0 mg/lb
  2% mepivacaine w/levo
    (400 mg max. for any patient)
  4. 4% prilocaine plain or w/epi 4.0 mg/lb
    (600 mg max. for any patient)
  5. 0.5% bupivacaine w/epi 0.6 mg/lb
    (90 mg max. for any patient)

*Within a 24 hour timeframe
Local anesthetic dosage (FDA approved max. dosage)

Calculating dosage: 70 lb. child

2% lidocaine with epinephrine

70 lb. x 3.2 mg/lb. = 224 mg

224 mg

36 mg/cartridge = 6.22 cartridges

For 50 lb. child = 2.77 cartridges

2% lidocaine with epinephrine

70 lb. x 2.0 mg/lb. = 140 mg

140 mg

36 mg/cartridge = 3.88 cartridges

For 50 lb. child = 2.77 cartridges

3% mepivacaine plain

150 lb. x 3.0 mg/lb. = 450 mg

But... 400 mg is maximum for any patient!

400 mg

54 mg/cartridge = 7.40 cartridges

7 cartridges is the maximum for any patient ≥ 135 lb.
### Pharmacology of Anesthetic Agents

**Local anesthetic dosage (FDA approved max. dosage)**

- **Calculating dosage: 150 lb. adult**

  - 2% mepivacaine with levonordefrin
    - $150 \text{ lb.} \times 3.0 \text{ mg/lb.} = 450 \text{ mg}$
    - But...400 mg is maximum for any patient!

  \[
  \frac{400 \text{ mg}}{36 \text{ mg/cartridge}} = 11.11 \text{ cartridges}
  \]

  - 11 cartridges is the maximum for any patient $\geq 135 \text{ lb.}$

- **4% prilocaine plain or with epinephrine**
  - $150 \text{ lb.} \times 4.0 \text{ mg/lb.} = 600 \text{ mg}$
  - 600 mg is maximum for any patient!

  \[
  \frac{600 \text{ mg}}{72 \text{ mg/cartridge}} = 8.33 \text{ cartridges}
  \]

  - 8 cartridges is the maximum for any patient $\geq 150 \text{ lb.}$

- **0.5% bupivacaine with epinephrine**
  - $150 \text{ lb.} \times 0.6 \text{ mg/lb.} = 90 \text{ mg}$
  - 90 mg is the maximum for any patient!

  \[
  \frac{90 \text{ mg}}{9 \text{ mg/cartridge}} = 10 \text{ cartridges}
  \]

  - 10 cartridges is the maximum for any patient $\geq 150 \text{ lb.}$

- **2% mepivacaine with levonordefrin**
  - $70 \text{ lb.} \times 2.0 \text{ mg/lb.} = 140 \text{ mg}$
  - 140 mg is maximum for any patient!

  \[
  \frac{140 \text{ mg}}{36 \text{ mg/cartridge}} = 3.88 \text{ cartridges}
  \]

- **4% articaine with epinephrine**
  - $150 \text{ lb.} \times 3.2 \text{ mg/lb.} = 480 \text{ mg}$
  - 500 mg is the maximum for any patient!

  \[
  \frac{480 \text{ mg}}{72 \text{ mg/cartridge}} = 6.66 \text{ cartridges}
  \]

  - 7 cartridges is the maximum for any patient $\geq 156 \text{ lb.}$

- **4% prilocaine plain or with epinephrine or articaine with epinephrine**
  - I do not recommend using this anesthetic in children.

- **Calculating dosage: 70 lb. child**

  - 4% prilocaine plain or with epinephrine or articaine with epinephrine
    - $70 \text{ lb.} \times 2.0 \text{ mg/lb.} = 140 \text{ mg}$

  \[
  \frac{140 \text{ mg}}{72 \text{ mg/cartridge}} = 1.94 \text{ cartridges}
  \]
Pharmacology of Anesthetic Agents

- Local anesthetic dosage
  - Factors to keep in mind:
    1. The time interval of injections is important
       - The half-life of lidocaine in the bloodstream is 90 minutes; for articaine the half-life is <30 minutes
       - Half-life is a serum phenomenon related to potential toxicity; it is not related to anesthetic duration
    2. Ultimately, the total dosage given is the important toxicity factor, but the timeframe of administration affects duration
       - Small amounts given over time provide better duration and are safer than large amounts given quickly

- Vasoconstrictors in local anesthetics
  - Are they safe to use?
    1. Review patient’s health history
    2. Is the patient medically stable?
    3. OK to use unless physician consult says “No!”
    4. Always aspirate
    5. Inject slowly
    6. Minimize volume injected

- Absolute contraindications:
  - Unstable angina
  - Myocardial infarction within 6 months
  - Coronary artery bypass surgery within 3 months
  - Refractory arrhythmias
  - Untreated or uncontrolled hypertension
  - Untreated or congestive heart disease
  - Uncontrolled diabetes or other endocrine diseases
  - *The timeframe is variable; a physician consult is recommended

- Vasoconstrictors in local anesthetics
  - All anesthetic agents are vasodilators
  - Vasoconstrictors
    1. Slow the rate of uptake into the bloodstream
    2. Lidocaine plain reaches a maximum blood level at 10 minutes after injection
    3. Lidocaine with epinephrine reach maximum blood level at 60 minutes and at a lower concentration
    4. Therefore, vasoconstrictors reduce the risk of toxicity
    5. Increase the duration of anesthesia
    6. Induce localized hemostasis

- Vasoconstrictors in local anesthetics
  - Local anesthetics, with or without vasoconstrictors, are remarkably safe at therapeutic doses.
  - Two basic concerns when treating medically complex patients
    1. Existing systemic diseases that may be exacerbated by the agent, and
    2. Medications that may have an adverse interaction with the agent

- Patients with stabilized hypertension or other cardiovascular diseases
  - The results of a number of studies indicate that the use of 1 or 2 cartridges of vasoconstrictor-containing anesthetic is of little clinical significance for most patients with stabilized hypertension or other CV diseases.
  - The benefits of maintaining adequate anesthesia for the duration of the procedure should not be underestimated.
  - The important issue: the patient’s tolerance of stress.
Pharmacology of Anesthetic Agents

- **Vasoconstrictors in local anesthetics**
  - Patients with stabilized hypertension or other cardiovascular diseases
  - Maximum dosage of epinephrine:
    - Healthy patients: up to 0.2 mg equals 11 cartridges
    - Cardiac patients: up to 0.04 mg equals 2.2 cartridges (1:100,000)
  - 1:100,000 epinephrine = 0.018 mg/cartridge
  - 1:200,000 epinephrine = 0.009 mg/cartridge

American Heart Association and American Dental Association, 1964

- **Epinephrine has its primary effect on the alpha 1 receptors**
  - Produces localized vasoconstriction
  - Increases peripheral blood pressure as it enters the bloodstream (minimal if over time)
  - Caution to prevent intravascular injection
  - Requires caution with hypertensive patients
  - Check blood pressure before injecting
  - Are they controlled?

- **Levonorefrin (Neo-Cobefrin)**
  - Similar to epinephrine, but a little less beta effect on heart rate
  - Has a moderate effect on blood pressure
  - 1/5 the potency, therefore in 5x the concentration:
    - 1:20,000
  - Contraindicated in the same patients as epinephrine


- **Relative contraindications:**
  - Patients taking tricyclic antidepressants (Elavil, Triptil, Aventyl)
  - No interactions with serotonin re-uptake inhibitors (Paxil, Zoloft, Prozac)
  - Patients taking phenothiazine antipsychotics (Thorazine, Compazine, Haldol)
  - Patients taking nonselective beta blockers (propranolol & timolol); fewer problems with atenolol & Topressor

*ADA/PDR Guide to Dental Therapeutics, 5th Ed, 2009
Pharmacology of Anesthetic Agents

- Vasoconstrictors in local anesthetics
  - Patients taking tricyclic antidepressants (Elavil, Triptil, Aventyl)
  - Uses: treatment of depression, neuropathic pain, chronic pain, obsessive compulsive disorder, anxiety, and panic disorder.
  - Other possible uses may include migraine prophylaxis, treatment of attention-deficit/hyperactivity disorder (ADHD), and nocturnal enuresis, and as adjunctive therapy for smoking cessation.
  - Can carefully use epinephrine, but monitor for possible sympathomimetic side-effects, i.e. increased blood pressure and heart rate
  - Use of levonordefrin is NOT recommended due to greater tendency to produce sympathomimetic side-effects than seen with epinephrine

- Metabolism of local anesthetics
  - Amide agents primarily biotransformed in the liver by P-450 cytochrome enzymes
  - Due to decreased liver function
  - Plasma levels of anesthetic stay elevated longer
  - Additional doses are additive: possible toxicity
  - Reduce maximum safe dosage figures for patients
    1. With liver impairment due to cirrhosis, hepatitis, etc., or
    2. Taking medications metabolized by the P-450 liver enzymes, which includes many, many medications

- Other local anesthetic complications
  - Excessive doses have been associated with drug-induced methemoglobinemia
    - Small amounts are normal in everyone
    - Systemic methemoglobinemia a rare disease
    - Risk factors for anesthetic-induced disease:
      1. Extremes of age
      2. Anemia
      3. Respiratory disease
      4. Certain hereditary enzyme deficiencies

---

Pharmacology of Anesthetic Agents

- Vasoconstrictors in local anesthetics
  1. Slow the rate of uptake into the bloodstream, reducing the risk of toxicity
  2. Increase the duration of anesthesia
  3. Induce localized hemostasis

Vasoconstrictors increase safety

- Metabolism of local anesthetics
  - Articaine begins rapid biotransformation in the bloodstream due to its ester moiety, then completed in the liver
  - 90–95% metabolized in the bloodstream; 5–10% metabolized in the liver
  - Articaine may be a better local anesthetic agent for patients with impaired liver function

- Other local anesthetic complications
  - Excessive doses (injectable or topical) have been associated with drug-induced methemoglobinemia
  - Risk may be increased in presence of oxidizing drugs such as acetaminophen, nitroglycerin, or sulfonamides.
  - Particular caution recommended with use of prilocaine (Citanest) in patients at risk
  - Respiratory obstruction: COPD, emphysema
  - Anemia
  - Pregnancy
Pharmacology of Anesthetic Agents

- Safest local anesthetics during pregnancy and breastfeeding:
  - Lidocaine and prilocaine are FDA Category B
  - All others are Category C

- Risk of methemoglobinemia with topicals (especially esters: benzocaine, tetracaine) and injectable prilocaine
  - Epinephrine is OK!
  - 2% lidocaine with 1:100,000 epinephrine is the safest anesthetic to use during pregnancy
  - Always use only as much as is truly necessary

**U.S. Food and Drug Administration pregnancy risk factor definitions.**

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>The results of controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of risk in later trimesters), and the possibility of fetal harm appears remote</td>
</tr>
<tr>
<td>B</td>
<td>Either the results of animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women or the results of animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester and there is no evidence of risk in later trimesters</td>
</tr>
<tr>
<td>C</td>
<td>Either the results of studies in animals have revealed adverse effects (teratogenic, embryocidal, or other) on the fetus and there are no controlled studies in women or results of studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus</td>
</tr>
<tr>
<td>D</td>
<td>There is positive evidence of human fetal risk, but the benefits of use in pregnant women may be acceptable despite the risk (for example, if the drug is needed in a life-threatening situation or if the risk of the use of the drug in pregnant women clearly outweighs any possible benefits, or if the drug is contraindicated in women who are or may become pregnant)</td>
</tr>
<tr>
<td>X</td>
<td>Results of studies in animals or humans have demonstrated fetal abnormalities or evidence of fetal risk based on human experience, or both, and the risk of use of the drug in pregnant women clearly outweighs any possible benefits, or use of the drug is contraindicated in women who are or may become pregnant</td>
</tr>
</tbody>
</table>

**Treating medically complex patients**

- Local anesthetics, with or without vasoconstrictors, may be safely used in most medically complex patients.
- Observance of simple safety guidelines for administration of local anesthetics should be universally applied to all patients.

**Safety Guidelines for local anesthesia**

1. Aspirate carefully before injecting to reduce the risk of unintentional intravascular injection.
2. Inject slowly! A maximum rate of 1 minute per cartridge.
   - For safety, efficacy, and comfort!
3. Monitor the patient for unusual reactions both during and after the injection.

**Safety Guidelines for local anesthesia (contd.)**

4. Select the anesthetic agent and whether to use it with or without a vasoconstrictor based upon the duration of anesthesia needed for the planned procedure.
5. Use the minimum amount of anesthetic solution that is needed to achieve adequate anesthesia to keep the patient comfortable throughout the procedure.
Pharmacology of Anesthetic Agents

- **Safety Guidelines for local anesthesia**
  6. An additional guideline useful for the majority of medically complex patients is to reduce the amount of vasoconstrictor containing anesthetic to no more than 2 cartridges if possible.
  - If additional volume of anesthetic solution is required, consider switching to a plain, non-vasoconstrictor containing agent.

Troubleshooting Anesthesia

- The tooth is only partially numb!
- Or the tooth is numb, but duration is short and/or anesthesia is not profound
- Solution: give a second injection in the same site with a different anesthetic agent
  - Increases the volume at a correct site
  - Addresses patient sensitivity variations to anesthetic agents
  - There is no contraindication for combining any of the amide anesthetic agents
  - If a different anesthetic, or combination of anesthetics, is found to work better for a patient, record that fact and start with that anesthetic at the next appointment

Troubleshooting Anesthesia

- There is no contraindication for combining any of the amide anesthetic agents
  - However, all of the amide anesthetics are additive in dosage,
  - Therefore, you should not exceed the maximum safe dosage for the agent with the highest concentration.

Pharmacology of Anesthetic Agents

- Troubleshooting
  - Summation of the amide anesthetics increases the risk of toxicity
  - Keep count!

Pharmacology of Anesthetic Agents

- Local anesthetic dosage
  - Calculating dosage: For adults
    - 150 lb. adult (FDA approved max. dosage):
      - 2% lidocaine w/epi = 13 cartridges maximum
      - 4% prilocaine = 8 cartridges maximum
      - Lidocaine & prilocaine together = 8 cartridges maximum
      - 4% articaine = 7 cartridges maximum
      - Lidocaine & articaine together = 7 cartridges maximum
      - For 70 lb. child, lidocaine & articaine together = 1.94 max

Use of nitrous oxide/oxygen analgesia/anxiolysis does not require reduction of local anesthesia dosage

Pharmacology of Anesthetic Agents

- Treating local anesthetic complications
  - One more suggestion:
    In severely immunocompromised patients, an antiseptic rinse such as chlorhexidine prior to injection can reduce the risk of infection from the injection – a risk that is normally very low.

  It's the thought that counts!
**ARE 4% ANESTHETIC SOLUTIONS SAFE?**

The Controversy Surrounding Articaine and Prilocaine

---

### 4% Dental Anesthetic Agents

- **Articaine (Septocaine, Zorcaine, Articadent)**
  - Released in the U.S. in 2000
  - Released in Europe in 1975 (Germany), and in Canada in 1983

- **Prilocaine (Citanest & Citanest forte)**
  - Released in the U.S. in 1965
  - Released in Europe in 1960, Canada shortly thereafter

---

**Articaine is a unique “hybrid” amide anesthetic:**

- Contains a thiophene ring rather than a benzene ring — increases lipid solubility
- Contains both ester and amide chemical groups

---

**Attributes of Articaine**

1. Fast onset
   - 1 to 6 minutes
2. Greater diffusion/penetration
   - Often obtain adequate anesthesia with infiltrations alone
3. More profound anesthesia
4. Greater success
   - With hard to anesthetize patients
   - Fewer missed blocks
5. Low allergenicity
   - Amide characteristic
6. Rapid metabolism → reduced risk of toxicity
   - Ester characteristic
   - Half-life in bloodstream 27 minutes (lidocaine 90 minutes)

---

Clinical Research Associates, June 2001
Potential for Nerve Injury

In 1995, Haas DA & Lennon D published:

A 21 year retrospective study of reports of paresthesia following local anesthetic administration, J Can Dent Assoc, Vol 61 No 4

Articaine (Septocaine) and prilocaine (Citanest) were more likely to be associated with paresthesia injuries compared with other anesthetics, and this was statistically significant when compared to the distribution of use.

Potential for Nerve Injury

- Focused only on reports of paresthesia
- “All forms of altered nerve sensation”
- All cases involving surgery were excluded (304)
- 143 paresthesias “from injection alone”
- Average = 6.8 paresthesias per year
  - High = 20 (1990); low = 0 (1973 & 1979)

Potential for Nerve Injury

- All 143 paresthesias in mandibular arch
- 92 involved tongue; 42 lower lip; 9 both
- Number of reported cases low until 1984, then gradually increased
- Articaine introduced in Canada in 1983
- 102 cases where anesthetic(s) used were known
  - Articaine 49.0%  Lidocaine 4.9%
  - Prilocaine 42.2%  Mepivacine 3.9%

Potential for Nerve Injury

- In 1993, 14 paresthesias occurred from an estimated 11,000,000 injections
- Incidence of 1 paresthesia/785,000 injections
- Of the 14 paresthesias
  - 10 were with articaine, 4 with prilocaine
    - Probability of paresthesia using articaine = 2.27/million injections
    - Probability of paresthesia using prilocaine = 1.7/million injections

Potential for Nerve Injury

- Conclusions:
  - Articaine (Septocaine) and prilocaine (Citanest) were more likely to be associated with paresthesia injuries compared with other anesthetics
  - This was statistically significant when compared to the distribution of use
  - Although it can occur, the risk of paresthesia from injection itself is extremely low
  - This extremely low risk does not warrant advising every patient prior to injection

Clinical Research Associates, in a study of 13,000 patient treatments by 94 dentists using articaine, reported 2 paresthesias.
- Both were associated with “mandibular” blocks
- Both resolved: Incidence = 0.03%

CRA follow-up 2005: 73% of articaine paresthesias were with “mandibular” regional nerve block injections
Potential for Nerve Injury

In a second publication by Haas and Gaffen using the same source:

- 182 paresthesias from 1999 to 2008
- 180 associated with the inferior alveolar nerve block
- 172 inferior alveolar block alone
- 8 inferior alveolar block combined with 1 or more other injections
- Incidence of 1/609,000 injections

Gaffen AS & Haas DA, Retrospective review of voluntary reports of non-surgical paresthesia in dentistry, J Can Dent Assoc, Vol 75 No 8, October 2009

Potential for Nerve Injury

From the U.S. FDA Adverse Event Reporting System data:

- 248 paresthesias from 1997 to 2008
- 94.5% associated with the inferior alveolar nerve block
- Articaine associated injuries 3.6 times greater than expected
- Prilocaine associated injuries 7.3 times greater than expected

Garisto et al, Occurrence of paresthesia after dental local anesthetic administration in the United States, J Am Dent Assoc, Vol 141, July 2010

If Injury Does Occur

- Anesthesia-induced nerve injuries are VERY rare (Temporary 0.13 – 0.54%; permanent 0.0001 – 0.01%)

- Most paresthesias are reversible, resolving within 2 to 8 weeks

- Mandibular nerve injuries are far more common than maxillary

- The vast majority of nerve injuries are associated with the conventional IA block injection technique

Nerve Paresthesia Injury

- Theories of causes:
  1. Injury due to direct contact of the needle with the nerve (traumatic injury)
  2. Injury due to direct contact of the anesthetic solution with the nerve (toxicity injury)
  3. Injury due to hematoma within the nerve sheath or in close proximity to the nerve (compression injury)
  4. Injury due to stretching of the nerve (morphology injury)*

Nerve Paresthesia Injury

- Theories of causes:
  1. Injury due to direct contact of the needle with the nerve (traumatic injury)

Meechan, Practical Dental Local Anaesthesia, Quintessence, 2002


Experiments have shown that the needle will usually pass between nerve fascicles

Blunt injury may occur if the nerve is pinned against bone

A blunted, barbed needle tip may injure the nerve upon withdrawal after contacting bone

Meechan, Practical Dental Local Anaesthesia, Quintessence, 2002
Nerve Paresthesia Injury

- Theories of causes:
  1. Injury due to direct contact of the anesthetic solution with the nerve (toxicity injury)
  2. All agents are neurotoxic, however, the higher the concentration, the higher the risk of causing neurotoxicity

<table>
<thead>
<tr>
<th>US usage</th>
<th>Prilo</th>
<th>Lido</th>
<th>Mepiv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injuries</td>
<td>13%</td>
<td>23%</td>
<td>62%</td>
</tr>
</tbody>
</table>

Injury correlation with anesthetic agent

- Articaine + lidocaine, prilocaine + lidocaine, bupivacaine: <2% each

Conclusion: Prilocaine appears to have the highest incidence of injury; articaine less risk than prilo.

- The rapid breakdown of articaine and the apparent inactivity of its metabolites imply that articaine is a safer local anesthetic agent than other available agents.
  1. Two very important points must be emphasized:
     1. Articaine, like lidocaine, has a maximum dose of 3.2 mg/lb for healthy adults
     2. Articaine, like prilocaine, is a 4% solution; patients will tolerate fewer cartridges as compared with a 2% solution*

*Articaine has 72 mg of anesthetic/cartridge; lidocaine has 36 mg of anesthetic/cartridge

- To reduce the risk of nerve injury when using prilocaine (Citanest) or articaine (Septocaine):
  1. Inject less, usually about half the dosage, than for lidocaine or mepivacaine
  2. Inject that reduced volume more slowly – about twice as long as the rate with lidocaine or mepivacaine – particularly with the inferior alveolar nerve block technique
Potential for Nerve Injury

What is the most likely cause of injury?

- One single cause is unlikely
- It appears that it may be the higher dose of drug (neurotoxicity) combined with a mechanical insult that predisposes the nerve to injury.

- Use of higher concentration anesthetic solutions may be a factor, but is clearly not the exclusive cause of nerve injury.

Gaffen AS & Haas DA, Retrospective review of voluntary reports of nonincidental paresthesia in dentistry, J Canadian Dent Assoc, Vol 75 No 8, October 2009

Nerve Paresthesia Injury

- To reduce the risk of nerve injury when using prilocaine (Citanest) or articaine (Septocaine):
  - 75 – 95% of all paresthesia injuries from injections are with the inferior alveolar block injection
  - Due to apparent potential neurotoxicity injury, prudent clinicians may consider avoiding use of high-concentration (4 percent) anesthetic formulations for inferior alveolar nerve blocks in cases where there are viable alternatives.


- Prevention:
  - There is no guaranteed method to prevent nerve injuries due to injections.

- Such injuries are not de facto indications of improper technique; they are a risk of carrying out intraoral injections.

- What is the influence of technique?
  - Is a 4% anesthetic a wise choice with a conventional inferior alveolar nerve block?

Haas DA, Localized complications from local anesthesia, J Calif Dent Assoc, Vol 28 No 9, 1990

Nerve Paresthesia Injury

- Theories of causes:
  - 3. Injury due to hematoma within the nerve sheath or in close proximity to the nerve (compression injury)
    - Intraneuronal bleeding (hematoma) is neurotoxic
    - Compression may cause temporary loss of blood supply (ischemia) to part or all of the nerve distal to the injury site
    - May heal with fibrotic scar tissue producing permanent compression injury to the nerve distal to the injury site

Pogrel MA & Thamby S, Permanent nerve involvement resulting from inferior alveolar nerve blocks, J Am Dent Assoc, Vol 131, 2000

Nerve Paresthesia Injury

- Theories of causes:
  - 4. Injury due to stretching of the nerve (morphology injury)
    - Physical tearing of the nerve unlikely
    - Ischemic incident of stretched nerve possibility supported by studies of
      - General anesthesia vs. local anesthesia extraction cases - 5 fold greater injury rate
      - Histologic studies of structure of lingual vs. inferior alveolar nerve: fewer fascicles, more easily injured

Haas DA, Localized complications from local anesthesia, J Calif Dent Assoc, Vol 28 No 9, 1990

Nerve Paresthesia Injury

- Prevention:
  - There is no guaranteed method to prevent nerve injuries due to injections.

- Such injuries are not de facto indications of improper technique; they are a risk of carrying out intraoral injections.

- What is the influence of technique?
  - Is a 4% anesthetic a wise choice with a conventional inferior alveolar nerve block?

Haas DA, Localized complications from local anesthesia, J Calif Dent Assoc, Vol 28 No 9, 1990

Nerve Paresthesia Injury

- Management of nerve injuries:
  - See the patient immediately and document the injury carefully
  - Mark the area of abnormal sensation on a photograph
  - Use to compare area of affect at follow-up visits

Nerve Paresthesia Injury

- Management of nerve injuries:
  1. See the patient immediately and document the injury carefully
  2. Advise the patient that the symptoms may continue for an indefinite time
     - 85% (to 94%)* of injuries caused by injections recover spontaneously within 2 to 12 weeks
     - ~5% will recover within 9 months
     - Up to 10% of remaining injuries will likely never recover completely


- Contact the patient after 24 hours
  - If symptoms have improved, GREAT!
  - If no improvement, use careful judgment to set up intervals for follow-up visits

Most injection-type injuries will show some sign of improvement within 2 – 4 weeks

4. If no improvement after 2 – 4 weeks, consider referral to a nerve injury specialist.

Bagheri SC & Meyer RA, When to refer a patient with a nerve injury to a specialist, J Am Dent Assoc, Vol. 145(8), August 2014

Nerve Paresthesia Injury

- The No Fault Theory

  It is important to note that complications with oral injections are not always preventable, and their occurrence does not necessarily imply poor technique by the dentist or dental hygienist.

  Haas DA, Localized complications from local anesthesia, J Calif Dent Assoc, Vol 26 No 9, 1998

  Dentists and dental hygienists must carefully weigh the risks and benefits of the agent and the technique preferred for each clinical situation.

Anesthetic Agents

- A Practical Armamentarium:
  - 2% Lidocaine with 1:100,000 epinephrine
    - For one to two hour procedures and most block injections
  - 3% Mepivacaine plain
    - For short duration procedures or the rare “no vasoconstrictor” patient
  - 4% Articaine with 1:200,000 epinephrine
    - For infiltrations and “hard to anesthetize” patients
  - 0.5% Bupivacaine with 1:200,000 epinephrine
    - For prolonged pain control and long duration procedures
  - And some buffering agent and OraVerse anesthetic reversal agent

Mandibular Anesthesia

- The risk of nerve injury with administration of prilocaine (Citanest) or articaine (Septocaine) may be reduced by using “high” mandibular division block techniques
  - Gow-Gates technique
  - Vazirani – Akinosi technique


WHAT ALTERNATIVES DO WE HAVE TO INJECTIONS?

Topical Anesthetics
### Topical Anesthetics

- Penetrate 2 – 3 mm
- Adequate anesthesia for minor/superficial procedures
- Pre-injection anesthesia for all techniques

---

### Compounded formulas:

- **Profound** – 10% lidocaine, 10% prilocaine, 4% tetracaine
- **Profound PET** (Profpet) – same as above plus 2% phenylephrine, more viscous
- **TAC 20 percent Alternate** – 20% lidocaine, 4% tetracaine, 2% phenylephrine
- **TheBestTopicalEver** – 12.5% lidocaine, 12.5% tetracaine, 3% prilocaine, 3% phenylephrine

Are neither FDA regulated nor unregulated:

“Unapproved drug products whose benefits may not outweigh their risks”

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### Refrigerant application: Pain Ease (Gebauer, Cleveland)

- 1,1,1,3,3-pentafluoropropane/1,1,1,2-tetrafluoroethane
- 5 second application
- FDA approved for oral tissues
- Nonirritant to oral mucosa
- Nontoxic if inhaled
- Significant reduction in posterior palatal injection pain
- Good evidence from medical studies
- Limited dental anecdotal reports

---

### EMLA = Eutectic Mixture of Local Anesthetics

- 2.5% lidocaine, 2.5% prilocaine
- EMLA cream/topical never approved for intraoral use in the U.S.
- However, we do have…

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**Note:** esters have better absorption through mucosa*

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**Meechan, Practical Dental Local Anesthesia, Quintessence, 2002**

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Topical Anesthetics

- **Oraqix**
  - 2.5% lidocaine, 2.5% prilocaine
  - Approved for intraoral use
  - 30 second onset
  - 20 minute duration (range 14 – 31 min.)

- **Dyclone** (Dyclonine HCl)
  - Currently commercially unavailable
  - Available from compounding pharmacies
  - 0.5%, or 1.0% DS
  - Apply with swab or as a diluted rinse
  - ~45ml for 1 minute (swish & spit)
  - Slow onset, 5 – 10 minutes
  - Duration ~30 minutes

What Other Tools Do We Have?

**Alternative Devices**

- **Computer-Controlled Delivery Systems**
  - The “Wand”: Single Tooth Anesthesia (STA) system
    - Milestone Scientific
  - The Comfort Control Syringe
    - Dentsply, Inc. (This device is no longer marketed)

  - Objective is to deliver the anesthetic at a rate and pressure that is below the threshold of pain
  - Potentially pain-free injections
  - Reduced volumes of anesthetic injected

- **Slow Injection of Anesthetic Solutions**
  - Safety Guidelines for local anesthesia
    - Inject slowly! A maximum rate of 1 minute per cartridge
  - Computer-controlled anesthetic delivery systems:
    - The “Wand”: Single Tooth Anesthesia (STA) system
    - Milestone Scientific
    - The Comfort Control Syringe (no longer marketed)
    - New: Caloject – just now being introduced
    - Aneptico

  - Objective is to deliver the anesthetic at a rate and pressure that is below the threshold of pain
  - Potentially pain-free injections
  - Reduced volumes of anesthetic injected
Computer-Controlled Delivery Systems

- The “Wand”: STA
  - Can give all traditional injections
  - Safer PDL injections
  - Painless palatal injections
  - Can use for primary or secondary anesthetic injections
  - Foot pedal controlled
  - Aspiration enabled

- Calaject
  - Three injection modes
    - Intraligamentary/palatal
    - Infiltrations
    - Regional nerve blocks
  - Cartridge in handpiece
  - Standard needles
  - No disposables
  - Foot pedal controlled
  - Aspiration enabled
  - Handpiece cannot be sterilized

- The Wand STA system
- The Comfort Control Syringe

<table>
<thead>
<tr>
<th>Injection Technique</th>
<th>Rate (cc/sec)</th>
<th>Typical Depth of Penetration (mm)</th>
<th>Typical Onset</th>
<th>Typical Duration</th>
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<tbody>
<tr>
<td>Infiltration</td>
<td>0.017</td>
<td>0.5-1.0</td>
<td>3 sec</td>
<td>30-45 min</td>
</tr>
<tr>
<td>Palatal</td>
<td>0.008</td>
<td>0.5-1.0</td>
<td>3 sec</td>
<td>30-45 min</td>
</tr>
<tr>
<td>PDL</td>
<td>0.001</td>
<td>2cc per root</td>
<td>3 sec</td>
<td>30-45 min</td>
</tr>
<tr>
<td>Intravenous</td>
<td>0.009</td>
<td>9cc</td>
<td>45 sec</td>
<td></td>
</tr>
</tbody>
</table>

(NO! YES!

- Pressure injectors
  - 2 – 4+ mm depth of penetration
  - Good for infiltrations only
  - Higher incidence of intravascular injection?

Needleless Injectors

- New Product: NumBee needleless infiltration tip
  1. No PDL tissue penetration; anesthetic solution is dripped into the sulcus
  2. Tip is designed to be angled from 0° to 90°
  3. Risk of post-operative discomfort greatly reduced
  4. Risk of injury to bone, developing teeth, etc. eliminated
  5. 60 second onset; about 35 – 40 minutes duration with less anesthetic solution

This was the promise...
Laser Analgesia

- Erbium (Er,Cr:YSGG) lasers may be used for rapid tooth preparation of small lesions using low to high power settings (3 to 8 watts)
  - Direct analgesia: 3 to 4 watts, defocused with quick movements over the occlusal surface for 60 to 90 sec.
  - If inadequate patient comfort, 0.25 to 0.5 watts, defocused on the buccal surface with slow movements 6 mm from the surface for 90 seconds
- Low energy light results in generation of fewer nerve impulses per second, and a greater stimulus is required to initiate an action potential

Hendy J, Understanding laser analgesia of tooth preparations with erbium lasers, J Laser-Assisted Dent, Spring 2015

Laser Analgesia

- A similar technique with deciduous teeth achieves greater analgesia at lower power in less time
  - Probably due to thinner enamel and dentin layers
  - Will have residual analgesia for about 20 to 30 seconds post-preparation of a small lesion
  - Use handpiece and bur or spoon excavator to complete decay removal
  - Always complete the prep with the laser to remove the smear layer
  - Erbium lasers may also be used for soft tissue applications using 3 watts defocused for 90 seconds with constant small movements

Hendy J, Understanding laser analgesia of tooth preparations with erbium lasers, J Laser-Assisted Dent, Spring 2015

Reasons for Anesthetic Failures

1. Anatomical/physiological variations
2. Technical errors of administration
3. Patient anxiety
4. Inflammation and infection
5. Defective/expired solutions

“Why take you a couple of days to get used to them.”

What defines success?

“Adequate anesthesia to insure patient comfort for the duration of the procedure”

- Different for each procedure
- Different for each patient

“I’m your anesthetist and he’s my back-up man.”

Keys to Success

- Anesthetic failures happen
- The “Three Strikes Rule”
  - 3 attempts at anesthesia, then stop
- It’s not about “fault”
  - It’s not the patient’s fault
  - It’s not your fault
- Failures happen

Reschedule the patient!

Reasons for Anesthetic Failures

3. Patient anxiety

Anxiety lowers the threshold of pain. Therefore, even non-painful stimuli are likely to be perceived as painful.

“Try to relax.”
Keys to Success

2. Patient anxiety
   When patients sense that the dentist or dental hygienist is sincere in doing everything possible to insure the patient's comfort,
   *they will relax!*

Keys to Success

The No Fault Theory
   It is important to note that complications with oral injections are not always preventable, and their occurrence does not necessarily imply poor technique by the dentist or dental hygienist.

In Conclusion

It's the thought that counts