ARE YOU NUMB YET?

THE ANATOMY OF LOCAL ANESTHESIA PART 1: PHARMACOLOGY

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Patients rate *"painless injections"* as the most important criteria in evaluating their dentist (or hygienist)

de St Georges J. *How dentists are judged by patients*, Dentistry Today, Vol. 23, August 2004

90% of all patients report being anxious about going to the dentist or hygienist and receiving a shot. Friedman & Krochak, 1998

White Coat Syndrome

90% of all patients report being anxious about going to the dentist or hygienist and receiving a shot. Friedman & Krochak, 1998

Patient anxiety

→ Practitioner anxiety

The majority of dentists and hygienists report high personal stress levels when giving injections

Peltier B et al, *The injection procedure as a source of stress for dentists*, Gen Dent, NovDec 1995

PHYSIOLOGIC FACTORS FOR DENTAL ANESTHESIA INJECTIONS

Success versus Failure

Physiology of Anesthetic Agents

- How do we assess anesthesia?
  - Question the patient
  - Probe the area
  - } Soft tissue only
  - Electric pulp tester
  - Cold test
  - } Pulpal tissue
- 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)
  - Delayed pulpal onset: occurs in the mandible of 19 – 27% of patients (even though soft tissue is numb)
    - Delayed over 30 minutes in 8%

Nusstein J et al. *The challenges of successful mandibular anesthesia*, Inside Dentistry, May 2008

Physiology of Anesthetic Agents

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

Agent	Lipid Solubility	Protein Binding
Lidocaine	2.9	65%
Mepivacaine	1	75%
Prilocaine	1.5	55%
Articaine	49.5	95%

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

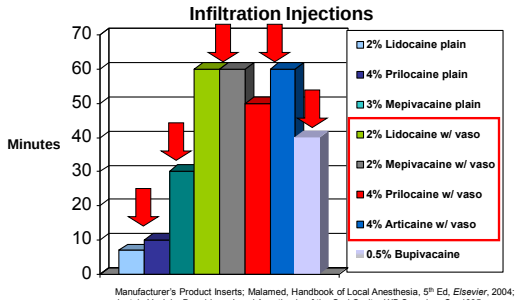
- Advantages of infiltrations
  1. Faster onset
  2. Simple
  3. Safe
  4. Good hemostasis (with vasoconstrictor)
- Disadvantages of infiltrations
  1. Multiple injections for multiple teeth
  2. Shorter duration of anesthesia

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

Blocks versus Infiltrations

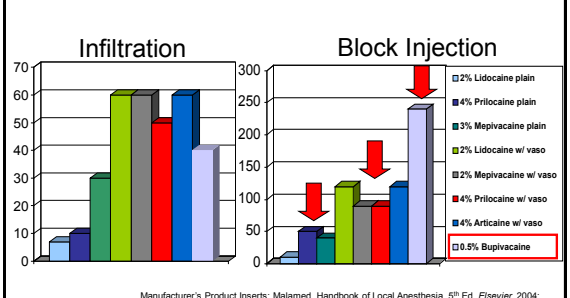
- Duration of pulpal anesthesia:



Manufacturer's Product Inserts; Malamed, Handbook of Local Anesthesia, 5th Ed, *Elsevier*, 2004; Jastak, Yagiela, Donaldson, Local Anesthesia of the Oral Cavity, *WB Saunders Co*, 1995

Blocks versus Infiltrations

- Duration of pulpal anesthesia:



Manufacturer's Product Inserts; Malamed, Handbook of Local Anesthesia, 5th Ed, *Elsevier*, 2004; Jastak, Yagiela, Donaldson, Local Anesthesia of the Oral Cavity, *WB Saunders Co*, 1995

Blocks versus Infiltrations

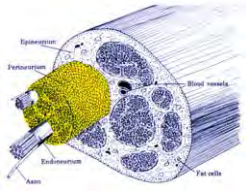
- Duration of anesthesia and onset:
  1. Dependent upon anesthetic agent
     - Concentration
     - Diffusion to/from the site
     - Lipid solubility
     - Protein binding to receptor sites
  2. Dependent upon technique, block versus infiltration
  3. Dependent upon vasoconstrictor presence, but NOT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

*Malamed, Handbook of Local Anesthesia, 5th Ed, *Elsevier*, 2004

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)

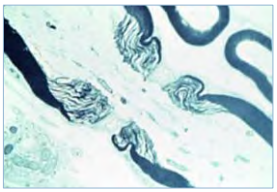
DeJong RH, Physiology and Pharmacology of Local Anesthesia, 1970



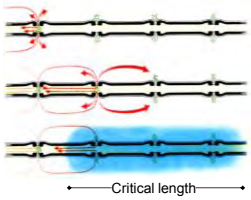
Jastak, Yagiela, Donaldson, Local Anesthesia of the Oral Cavity, *WB Saunders Co*, 1995

Physiology of Anesthetic Agents

3. Critical length = 3 nodes minimum (5 mm)
   Anesthetic volume, tissue space & density



Node of Ranvier



Critical length

Evers & Haegerstam, Introduction to Dental Local Anesthesia, *Mediglobe*, 1990

Physiology of Anesthetic Agents

- The "right" volume depends on many variables
  - For infiltration injections, ½ to ¾ cartridge is generally ideal

Brunetto et al, *Anesthetic efficacy of 3 volumes of lidocaine with epinephrine in maxillary infiltration anesthesia*, Anesth Prog 55, 2008

  - For an inferior alveolar nerve block,
    - Less than ½ cartridge tends to be ineffective
    - ¾ – 1 cartridge is ideal

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

Physiology of Anesthetic Agents

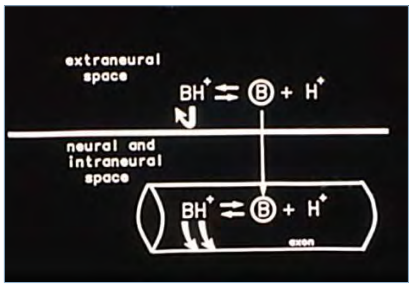
- How do local anesthetics work?
- The Henderson – Hasselbalch equation:

$$\text{Log}\ \frac{\text{Base}}{\text{Acid}} = \text{pH} - \text{pK}_a$$

pK_a = affinity for hydrogen ions (H+)

Physiology of Anesthetic Agents

- How do local anesthetics work?



BH+ = acidic, ionized form:

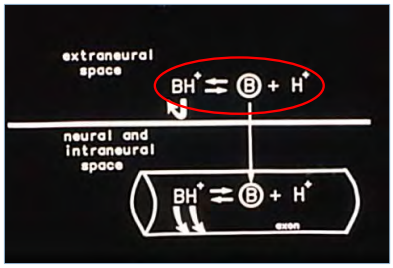
Can't pass through nerve membrane (water soluble)

B = basic, unionized form:

Can pass through nerve membrane (lipid soluble)

Physiology of Anesthetic Agents

- Reasons for delayed or failed onset
  - Disassociation rate



BH+ = acidic, ionized form:

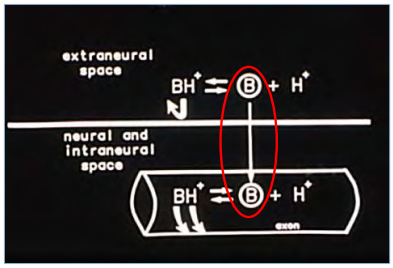
Can't pass through nerve membrane (water soluble)

B = basic, unionized form:

Can pass through nerve membrane (lipid soluble)

Physiology of Anesthetic Agents

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



BH+ = acidic, ionized form:

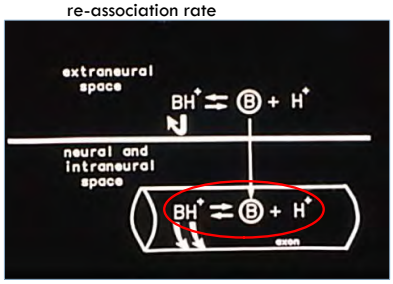
Can't pass through nerve membrane (water soluble)

B = basic, unionized form:

Can pass through nerve membrane (lipid soluble)

Physiology of Anesthetic Agents

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



BH+ = acidic, ionized form:

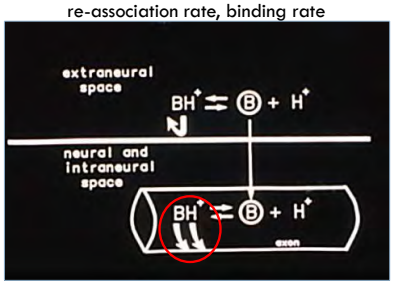
Can't pass through nerve membrane (water soluble)

B = basic, unionized form:

Can pass through nerve membrane (lipid soluble)

Physiology of Anesthetic Agents

- 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

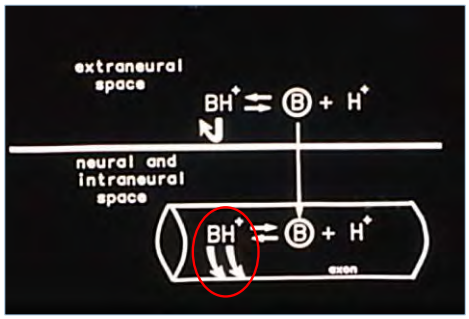
Is this failed anesthesia?

Frequency dependent conduction

Wait!
I Still Feel That!

Physiology of Anesthetic Agents

- Frequency dependent conduction



Anesthesia Delivery Assistance Devices

- Devices that vibrate – Frequency dependent conduction
  - Vibration stimulates nerves, allowing greater anesthetic access to receptor sites to produce better anesthesia

Newer version, the VibraJect R3, $359.00

Anesthesia Delivery Assistance Devices

- The Gate Control Theory of Pain
  - Upon injection of anesthetic solution:
    - Nociceptors send pain messages 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
  - The vibration sensations reach the brain first and cause release from inhibitory interneurons, blocking the C fiber pain stimulation by "closing the pain gate"

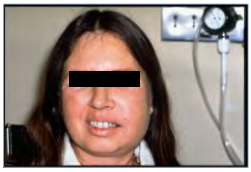
Reasons for Anesthetic Failures

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

Wong MKS & Jacobsen PL, *Reasons for local anesthesia failures*, JADA Vol 123, Jan 1992

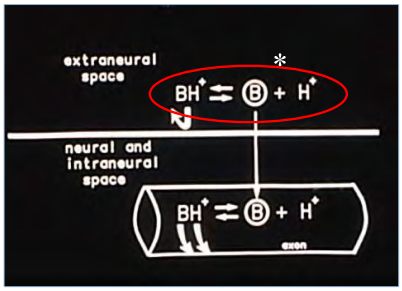
Reasons for Anesthetic Failures

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



Reasons for Anesthetic Failures

4. Inflammation and infection



Increased tissue acidity (decreased pH)

Decreased anesthetic disassociation

Decreased anesthetic effect

*Injecting too much anesthetic, or injecting it too fast, may decrease the tissue buffering capacity

Reasons for Anesthetic Failures

4. Inflammation and infection

Normal tissue	pH = 7.4	24% of injected anesthetic is unionized **B**
Intraneuronal	pH = 7.0	11.2 % to **B**
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
- First, give a block injection
  - Well away from the site of any local inflammation or infection
    - The low pH will prevent the disassociation of the anesthetic agent
  - A needle should not be inserted into an area of active infection, such as a periapical abcess
    - The volume of anesthetic is likely to increase the pain
    - There is the potential for spreading the infection

Troubleshooting Anesthesia

- The "Hot" Tooth
- First, give a block injection
  - The Gow-Gates mandibular division block has a significantly higher success rate than all other techniques

Gow-Gates	52%
Vazirani-Akinosi	41%
Conventional IA	36%
Buccal-plus-lingual infiltration	27%

All with 4% articaine with 1:100,000 epinephrine

  - No technique was fully acceptable by itself

Aggarwal V et al, *Comparative evaluation of anesthetic efficacy of Gow-Gates mandibular conduction anesthesia, Vazirani-Akinosi technique, buccal-plus-lingual infiltrations, and conventional inferior alveolar nerve anesthesia in patients with irreversible pulpitis*, O Surg O Med O Path O Radio Endo, Vol. 109 No 2, Feb. 2010

Troubleshooting Anesthesia

- The "Hot" Tooth
- First, give a block injection
  - Well away from the site of any local inflammation or infection
- Second, give a periodontal ligament (PDL) or intraosseous injection
  - Intraosseous injections are more reliable and have better duration
- Or, give a buccal &/or lingual infiltration with articaine (or prilocaine)

Hasse et al, *Comparing anesthetic efficacy of articaine versus lidocaine as a supplemental buccal infiltration of the mandibular first molar after an inferior alveolar nerve block*, JADA Vol 139 No 9, Sept 2008

Kanaa et al, *Articaine buccal infiltration enhances the effectiveness of lidocaine inferior alveolar nerve block*, Int Endo J 42, 2009

Infiltration Anesthesia

- Works well for the maxilla, but the mandible…
  - Work fairly well for anteriors and bicuspids
  - Widely varying 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

Robertson et al, *The anesthetic efficacy of articaine in buccal infiltration of mandibular posterior teeth*, JADA Vol 138 No 8, 2007
Meechan, Practical Dental Local Anesthesia, *Quintessence*, 2002

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

Brandt RG et al, *The pulpal anesthetic efficacy of articaine versus lidocaine in dentistry: A meta-analysis*, JADA 142(5), May 2011

    - Articaine was 4 times more effective, with greater duration, than lidocaine as an infiltration injection when used for teeth diagnosed with irreversible pulpitis

Ashraf H et al, *Efficacy of articaine versus lidocaine in block and infiltration anesthesia administered in teeth with irreversible pulpitis: A prospective, randomized, double-blind study*, JOE Vol 39(1) Jan 2013

Troubleshooting Anesthesia

- The "Hot" Tooth
- 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.

Hargreaves & Keiser, *Local anesthetic failure in endodontics: Mechanisms and management*, Endodontic Topics, 2002

Troubleshooting Anesthesia

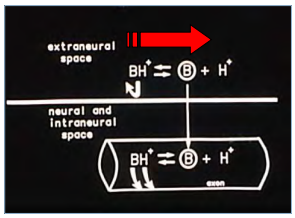
- There is no contraindication for combining any of the amide anesthetic agents
  - Using plain anesthetic for "pre-injection", then using anesthetic with vasoconstrictor
    - Anesthetic with vasoconstrictor: pH ~3.5
    - Plain anesthetic: pH ~6.5
    - Plain has less "burning" sensation
  - Plain anesthetics have better dissociation in a site of infection (but will wash out faster!)
  - Using a plain anesthetic first may mildly increase cardiovascular side-effects of vasoconstrictors

WHAT'S NEW IN DENTAL LOCAL ANESTHESIA?

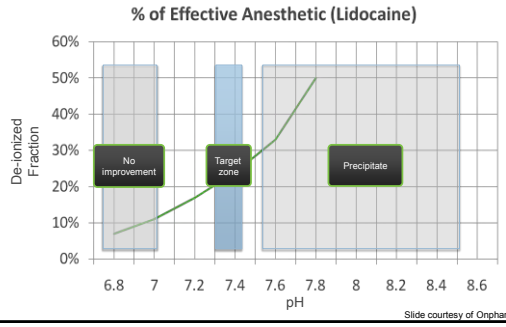
Buffered Anesthetics
Inhalation Local Anesthesia

Buffering of Local Anesthetics

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

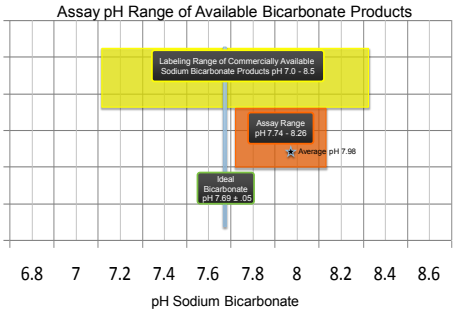


Buffering of Local Anesthetics



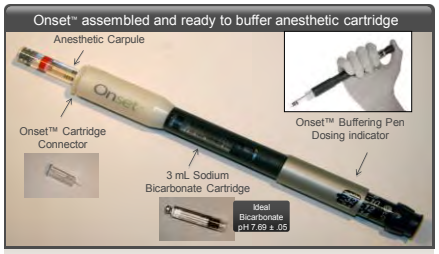
Slide courtesy of Onpharma

Buffering of Local Anesthetics



Slide courtesy of Onpharma

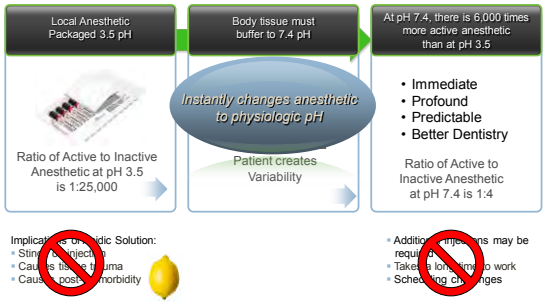
New Technology: OnSet



OnSet mixing pen: insert anesthetic cartridge, mix, load in syringe, and inject – for best results, inject within 30 seconds of mixing

Slide courtesy of Onpharma

New Technology: OnSet



Slide courtesy of Onpharma

New Technology: OnSet

- 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 Research: Intranasal Delivery

- Utilizing the BD ACCUSPRAY® technology currently used in the Flumist® nasal product
- The goal is to produce a regional block enabling invasive quadrant dentistry on maxillary (& mandibular?) teeth

Information courtesy of St. Renatus

New Research: Intranasal Delivery

- Anesthetic enters the trigeminal neural pathway within the nasal cavity
  - Orofacial structures can be targeted
  - Particularly effective for the maxilla
- "Sniff" administration
  - Non-invasive, painless, rapid
  - Patients could self-administer
- Phase 3 clinical trials are in progress to submit the product to the FDA for approval

Information courtesy of St. Renatus

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

Pharmacology of Anesthetic Agents

- 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

Pharmacology of Anesthetic Agents

- Lidocaine HCl:
  1. 2% plain (not available in dental cartridges)
     - Pulpal anesthesia for 5 to 10 minutes
     - Soft tissue anesthesia for 1 to 2 hours
  2. 2% with 1:100,000 or 1:50,000 epinephrine
     - Pulpal anesthesia for 1 to 2 hours
     - Soft tissue anesthesia for 3 to 5 hours
  3. Xylocaine, Octocaine, Lignospan, etc.

Pharmacology of Anesthetic Agents

- Mepivacaine HCl:
  1. 3% plain
     - Pulpal anesthesia for 20 to 40 minutes
     - Soft tissue anesthesia for 2 to 3 hours
  2. 2% with 1:20,000 levonordefrin (Neo-Cobefrin)
     - Pulpal anesthesia for 1 to 1 ½ hours
     - Soft tissue anesthesia for 3 to 5 hours
  3. Carbocaine, Polocaine, Isocaine, Scandonest, etc.

Pharmacology of Anesthetic Agents

- Prilocaine HCl:
  1. 4% plain = Citanest
     - Pulpal anesthesia for 40 to 60 minutes*
     - Soft tissue anesthesia for 2 to 3 hours
  2. 4% with 1:200,000 epinephrine = Citanest forte
     - Pulpal anesthesia for 1 to 1 ½ hours
     - Soft tissue anesthesia for 3 to 8 hours

  * Only if via block technique; 5 - 10 minutes as infiltrate

Pharmacology of Anesthetic Agents

- Articaine HCl:
  1. 4% with 1:100,000 or 1:200,000 epinephrine
     - Pulpal anesthesia for 1 to 1 ½ hours
     - Soft tissue anesthesia for 2 to 4 hours
  2. Septocaine, Zorcaine, Articadent, Orabloc (U.S.) Ultracaine, Septanest (Canada, Europe)

Pharmacology of Anesthetic Agents

- Bupivacaine HCl:
  1. 0.5% with 1:200,000 epinephrine
     - Long-acting by block injection only
     - Pulpal anesthesia for 1 ½ to 4 hours, up to 7 hours
     - Soft tissue anesthesia for 5 to 12 hours
  2. Marcaine, Vivacaine

Pharmacology of Anesthetic Agents

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

Pharmacology of Anesthetic Agents

- Common usage:
  - Long procedures: more than 2 hours or for post-operative analgesia
    1. Bupivacaine 0.5% with vasoconstrictor (as block)
  - Difficult to anesthetize patients:
    1. Prilocaine 4% with vasoconstrictor
    2. Articaine 4% with vasoconstrictor

CRA Newsletter, June 2001

Pharmacology of 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

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

Pharmacology of Anesthetic Agents

- Adverse reactions to anesthetic agents:
  1. 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

Pharmacology

- Adverse reactions to anesthetic agents:
  1. Psychogenic reactions
     - Management of syncope:
       - Lay patient supine with legs above head
       - Maintain airway; may administer O_2

Pharmacology

- Treating local anesthetic complications
  - First and foremost, maintain the airway

In 1960, Moore reported successful control of local anesthetic-induced seizures in 84 of 93 patients using a positive-pressure oxygen mask

Moore DC, Bridenbaugh LD, *Oxygen: the antidote for systemic reactions from local anesthetic drugs*, JAMA 15;174, Oct 1960

Pharmacology

- Adverse reactions to anesthetic agents:
  1. Psychogenic reactions
     - Management of syncope:
       - Lay patient supine with legs above head
       - Maintain airway; may administer O_2
       - Monitor pulse, blood pressure & breathing
       - Loosen tight collar; keep patient warm
       - Calmly reassure the patient

Pharmacology

- Adverse reactions to anesthetic agents:
  2. 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

Pharmacology

- Adverse reactions to anesthetic agents:
  2. Allergic reactions
     - Mild
       - Rash, skin itches, runny nose and eyes (leaky capillaries)
     - Moderate
       - Asthmatic wheezing (respiratory constriction)
     - Severe
       - Anaphylaxis: <u>may develop within minutes</u>!
       - CV system relaxes, BP drops, shock, failure

Pharmacology

- Adverse reactions to anesthetic agents:
  2. Allergic reactions
     - Anaphylaxis
       - Initial signs and symptoms:
         warm moist skin, apprehension, diffuse erythema/hives, itching, angioedema
       - Subsequent signs:
         abdominal cramps, vomiting, <u>wheezing</u>, dyspnea, difficulty talking

Progressive signs and symptoms develop <u>very quickly</u>!

Pharmacology

- Adverse reactions to anesthetic agents:
  2. Allergic reactions: mild to moderate

<u>Reactions</u>	<u>Treatment</u>
Uticaria Angioneurotic edema Mucous membrane congestion	- Diphenhydramine (Benadryl) 25 to 50 mg orally if no respiratory or circulatory compromise - Continue every 6 hours for 2 to 3 days - Bronchodilator: Albuterol or Alupent inhaler

Pharmacology

- Adverse reactions to anesthetic agents:
  2. Allergic reactions: severe

Reactions	Treatment
Anaphylaxis	- Have front desk call 911
Airway restriction	- Give positive pressure O_2
Hypotension	- Epinephrine 1:1000 (Epi pen)
"something wrong"	0.3 – 0.5 cc subcutaneously,
"sick feeling"	repeat every 10 – 15 mins. if needed
	- Diphenhydramine 2 mg/kg
	IV or IM

Pharmacology

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

Pharmacology of Anesthetic Agents

- Adverse reactions to anesthetic agents:
  2. Allergic reactions
     - The antioxidant for the vasoconstrictor:
       Sodium metabisulfite (0.50 mg/ml)
     - Possible sulfite sensitivity, especially for corticosteroid-dependent asthmatics (10 – 20%)
       - Ask about food sensitivities:
         Dried fruits, beer and wine, salami and pepperoni-type meats: all have sulfites

Bush RK et al, *Prevalence of sensitivity to sulfiting agents in asthmatic patients*, Am J Med Vol 81, 1986
Canfield DW & Gage TW, *A guideline to local anesthetic allergy testing*, Anesth Prog Vol 34, 1987

Pharmacology of Anesthetic Agents

- Adverse reactions to anesthetic agents:
  2. Allergic reactions
     - If a patient is allergic to the amide anesthetics:
     1. Have patient patch tested (skin "prick" test followed by intradermal injection) for all amides and for at least one ester anesthetic
     2. A challenge test to duplicate symptoms can be used if there is no response to skin testing; this is more reliable
     3. May use 1% diphenhydramine (Benadryl) with 1:100,000 epinephrine as an alternative anesthetic
        Short duration, may require multiple injections

Canfield DW & Gage TW, *A guideline to local anesthetic allergy testing*, Anesth Prog Vol 34, 1987

Pharmacology

- 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

- Adverse reactions to anesthetic agents:
  3. Toxic reactions: Contributing factors
     - Type of anesthetic
     - Dosage of anesthetic
     - Route of administration
     - Rate of administration
     - Patient's physical condition and health
       - Includes previous exposure
       - Drug interactions
       - Psychological response

Pharmacology

- Adverse reactions to anesthetic agents:
  3. Toxic reactions: Contributing factors
     - Drugs that alter the functioning of the CNS or CVS may lower the toxicity threshold for local anesthetics
     - This is especially true for drugs that decrease liver or cardiac functions or that stimulate the CNS
     - Limiting the total dose and using anesthetics with vasoconstrictors are the two common means of avoiding local anesthetic toxicity reactions.

Chen AH, *Toxicity and allergy to local anesthesia*, CDA Jour Vol 26 No 9, 1998

Pharmacology

- Local anesthetic dosage
  - Calculating dosage:
    In dental cartridges,
    ~18 mg anesthetic/% concentration
  - 2% lidocaine 36 mg/cartridge*
  - 3% mepivacaine 54 mg/cartridge*
  - 4% prilocaine 72 mg/cartridge*
  - 4% articaine 68 mg/cartridge*

Cartridge volume officially 1.78 to 1.82 ml; all labeled as 1.7 ml.
*These are approximate mg/cartridge numbers

Pharmacology

- Local anesthetic dosage (FDA approved max. dosage)
  1. 2% lidocaine w/epi 3.2 mg/lb
     4% articaine w/epi
  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)

Pharmacology

- Local anesthetic dosage (FDA approved max. dosage)
  - Calculating dosage: 150 lb. adult

2% lidocaine with epinephrine
150 lb. x 3.2 mg/lb. = 480 mg

$$\frac{480 \text{ mg}}{36 \text{ mg/cartridge}} = 13.33 \text{ cartridges}$$

13 cartridges is the maximum for a 150 lb. patient

Pharmacology of Anesthetic Agents

- Local anesthetic dosage (FDA approved max. dosage)
  - Calculating dosage: 150 lb. adult

3% mepivacaine plain
150 lb. x 3.0 mg/lb. = 450 mg
But…400 mg is maximum for any patient!

$$\frac{400 \text{ mg}}{54 \text{ mg/cartridge}} = 7.40 \text{ cartridges}$$

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 lb. x 3.0 mg/lb. = 450 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 ≥ 135 lb.

Pharmacology

- Local anesthetic dosage (FDA approved max. dosage)
  - Calculating dosage: 150 lb. adult

4% prilocaine plain or with epinephrine
150 lb. x 4.0 mg/lb. = 600 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 ≥ 150 lb.

Pharmacology

- Local anesthetic dosage (FDA approved max. dosage)
  - Calculating dosage: 150 lb. adult

4% articaine with epinephrine
150 lb. x 3.2 mg/lb. = 480 mg

$$\frac{480\ \text{mg}}{68\ \text{mg/cartridge}} = 7.05\ \text{cartridges}$$

8 cartridges is the maximum for a 150 lb. patient

Pharmacology

- Local anesthetic dosage (FDA approved max. dosage)
  - Calculating dosage: For children
    - Maximum recommended dosage is 2.0 mg/lb. for all anesthetics, and use of a vasoconstrictor is strongly recommended
    - Note: Children have a higher metabolic rate, which means that more anesthetic enters their bloodstream in a shorter time.
    - Hence the reduction of maximum dosage to 2.0 mg/lb. for children for all anesthetics

Malamed, Handbook of Local Anesthesia, 5th Ed, *Elsevier*, 2004

Pharmacology

- Local anesthetic dosage (FDA approved max. dosage)
  - Calculating dosage: For children

Age	Average weight in lbs.	Cartridges of 2% lidocaine
2	32	1.7
3	37	2.0
4	45	2.5
5	49	2.7
6	54	3.0
7	60	3.3
8	70	3.8
9	82	4.5
10	94	5.2
11	105	5.8
12	122	6.7
13	136	7.5

Pharmacology

- Local anesthetic dosage
  - Calculating dosage: For adults
  - Using 2.0 mg/lb for all anesthetics, the lowest maximum for any anesthetic
  - 150 lb. adult:
    - 2% lidocaine w/epi or 2% mepivacaine w/levo = 8.33 cartridges
    - 3% mepivacaine plain = 5.55 cartridges
    - 4% prilocaine or 4% articaine = 4.16 cartridges

Pharmacology

- Local anesthetic dosage
  - Using 2.0 mg/lb. for all anesthetics, the lowest maximum for any anesthetic, for 150 lb. adult:
    - 2% lidocaine w/epi or 2% mepivacaine w/levo ≈ 8 cartridges
    - 3% mepivacaine plain ≈ 5 cartridges
    - 4% prilocaine or articaine ≈ 4 cartridges
  - Maximum dosage for 150 lb. adult:
    - 2% lidocaine w/epi = 13 cartridges
    - 2% mepivacaine w/levo = 11 cartridges
    - 3% mepivacaine plain = 7 cartridges
    - 4% prilocaine = 8 cartridges
    - 4% articaine = 7 cartridges

Pharmacology of Anesthetic Agents

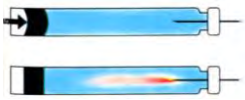
- Local anesthetic dosage
  - Factors to keep in mind:
    1. The time interval of injections is important
       - The half-life of lidocaine in the bloodstream is 90 minutes; for articaine the half-life is <30 minutes
       - Half-life is a serum phenomenon related to potential toxicity; it is not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

Pharmacology

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

Pharmacology

- 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



Evers & Haegerstam, Introduction to Dental Local Anaesthesia, *Mediglobe*, 1990

Pharmacology

- 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

Pharmacology

- Vasoconstrictors in local anesthetics
  - Absolute contraindications:
    - Unstable angina
    - Myocardial infarction within 6 months
    - Coronary artery bypass surgery within 3 months
    - Refractory arrhythmias
    - Untreated or uncontrolled hypertension
    - Untreated of uncontrolled congestive heart disease
    - Uncontrolled diabetes or other endocrine diseases

Pérusse, Goulet, Turcotte, *Contraindications to vasoconstrictors in dentistry: Part I*, O Surg O Med O Pathol, Vol 74 No 5, Nov 1992

Pharmacology

- Vasoconstrictors in local anesthetics
  - 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

- 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)
      American Heart Association and American Dental Association, 1964
    - 1:100,000 epinephrine = 0.018 mg/cartridge
      1:200,000 epinephrine = 0.009 mg/cartridge
      Management of dental problems in patients with cardiovascular disease, JADA Vol 68 No 3, 1964
      American Dental Society of Anesthesiology, The Pulse Vol 41 No 1, 2008

Pharmacology

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

Pharmacology

- Vasoconstrictors in local anesthetics
  - Epinephrine has its primary effect on the alpha 1 receptors
    - In patient's with controlled hypertension, use of local anesthetics with vasoconstrictor is OK.
      - Can initially give up to a maximum of 2 cartridges of anesthetic with 1:100,000 epinephrine, then wait at least 10 minutes.
      - If no problems arise in that time, additional cartridges may be used judiciously.

Pharmacology

- Vasoconstrictors in local anesthetics
  - Epinephrine has its primary effect on the alpha 1 receptors
    - Patients on alpha 1 blockers (vasodilators like *minipress*) have decreased anesthetic duration
    - Patients on beta 1 blockers have an increased alpha 1 response
      - Increased anesthetic duration
      - Increased peripheral blood pressure
      - Risk greatest with nonselective beta blockers (*propanolol & timolol*); fewer problems with *atenolol & Lopressor*

Pharmacology

- Vasoconstrictors in local anesthetics
  - Levonordefrin (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

Pharmacology

- Vasoconstrictors in local anesthetics
  - 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 (*propanolol [Inderal], timolol*)
    - Patients taking recreational drugs (cocaine, methamphetamines, etc.) or ADD/ADHD medications*

Pérusse, Goulet, Turcotte, *Contraindications to vasoconstrictors in dentistry: Part I,* O Surg O Med O Pathol, Vol 74 No 5, Nov 1992
*ADA/PDR Guide to Dental Therapeutics, 5th Ed, 2009

Pharmacology

- 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**

Boakes AJ et al, *Interactions between sympathomimetic amines and antidepressant agents in man*, Brit Med Jour Vol 1, 1973

Lexi-Comp Tricyclic Antidepressant update, Feb. 2012

Pharmacology

- 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

Moore PA, *Adverse drug interactions in dental practice: Interactions associated with local anesthetics, sedatives, and anxiolytics*, JADA Vol 130, 1999

Pharmacology

- Other local anesthetic complications
  - Excessive doses 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

Moore PA, *Adverse drug interactions in dental practice: Interactions associated with local anesthetics, sedatives, and anxiolytics*, JADA Vol 130, 1999

Pharmacology

- Safest local anesthetics during pregnancy and breast-feeding:
  - Lidocaine and prilocaine (B), all others are C

Donaldson M & Goodchild JH, Pregnancy, breast-feeding and drugs used in dentistry, JADA 143 (8), August 2012

Pharmacology

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

CATEGORY	DEFINITION
A	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
B	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
C	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; drug should be given only if the potential benefit justifies the potential risk to the fetus
D	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 for a serious disease for which safer drugs cannot be used or are ineffective)
X	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 the use of the drug in pregnant women clearly outweighs any possible benefit; use of the drug is contraindicated in women who are or may become pregnant

* Sources: U.S. Food and Drug Administration.[3,10]

Pharmacology

- Safest local anesthetics during pregnancy and breast-feeding:
  - Lidocaine and prilocaine (B), all others are C
  - Risk of methemoglobinemia with topicals (benzocaine, tetracaine) and injectable prilocaine
  - Epinephrine is OK!

Donaldson M & Goodchild JH, Pregnancy, breast-feeding and drugs used in dentistry, JADA 143 (8), August 2012

Pharmacology

- Metabolism of local anesthetics
  - Amide agents primarily biotransformed in the liver by P-450 cytochrome enzymes
  - Articaine begins rapid biotransformation in the bloodstream due to its ester moiety, then completed in the liver
    - 90 – 95% metabolized in the blood stream; 5 – 10% metabolized in the liver
    - Articaine may be a better local anesthetic agent for patients with impaired liver function

Pharmacology

- Metabolism of local anesthetics
  - 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

Pharmacology

- 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

Pharmacology

- 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 <u>all</u> patients.

Pharmacology

- 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.
  3. Monitor the patient for unusual reactions both during and after the injection.

Pharmacology

- 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

- Safety Guidelines for local anesthesia (contd.)
  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 <u>partially</u> 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 <u>with a different anesthetic agent</u>
  - If a different anesthetic, or combination of anesthetics, is found to work better for a patient, <u>record that fact</u> and start with that anesthetic at the next appointment

Pharmacology

- 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.

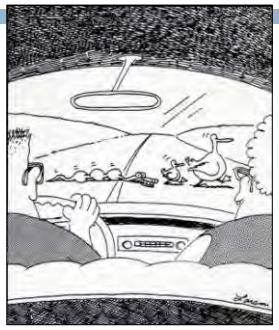
Jong RH & Bonin JD, *Mixtures of local anesthetics are no more toxic than the parent drugs*, Anesthes Vol 54 No 3, 1981

Pharmacology

- 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**

Pharmacology

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



Pharmacology

- 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)

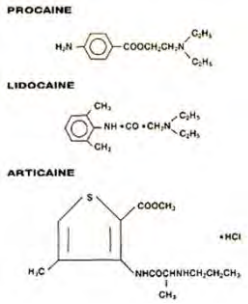
- Released in the U.S. in 2000
  - Released in Europe in 1975 (Germany), and in Canada in 1983

Prilocaine (Citanest & Citanest forte)

- Released in the U.S. in 1965
  - Released in Europe in 1960, Canada shortly thereafter

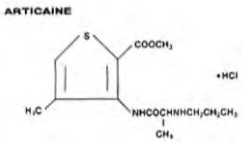
4% Dental Anesthetic Agents

- 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



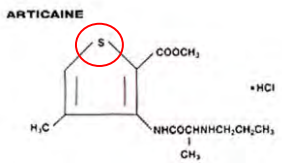
4% Dental Anesthetic Agents

- Articaine is a unique "hybrid" amide anesthetic:
  - Classified as an amide agent because it has the low allergenicity rate of other amides
  - Ester group means it is metabolized in both the bloodstream and the liver
  - Shorter plasma half-life potentially reduces risk of toxicity



4% Dental Anesthetic Agents

- Articaine anesthetic:
  - One reason for the delay in releasing articaine in the U.S. was the presence of **sulfur** in the thiophene ring
  - There have been no adverse reactions reported



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
   - Ester characteristic
   - Half-life in bloodstream 27 minutes (lidocaine 90 minutes)

CRA, June 2001

4% Dental Anesthetic Agents

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.

Haas DA & Lennon D, *A 21 year retrospective study of reports of paresthesia following local anesthetic administration*, J Can Dent Assoc Vol 61 No 4, 1995

Nerve Paresthesia 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)

Haas DA & Lennon D, *A 21 year retrospective study of reports of paresthesia following local anesthetic administration*, J Can Dent Assoc Vol 61 No 4, 1995

Nerve Paresthesia 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%

Haas DA & Lennon D, *A 21 year retrospective study of reports of paresthesia following local anesthetic administration*, J Can Dent Assoc Vol 61 No 4, 1995

Nerve Paresthesia 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

Haas DA & Lennon D, *A 21 year retrospective study of reports of paresthesia following local anesthetic administration*, J Can Dent Assoc Vol 61 No 4, 1995

Nerve Paresthesia 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
  - The extremely low risk does not warrant advising every patient prior to injection

Haas DA & Lennon D, *A 21 year retrospective study of reports of paresthesia following local anesthetic administration*, J Can Dent Assoc Vol 61 No 4, 1995

Nerve Paresthesia Injury

CRA, 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 Newsletter, June 2001

CRA follow-up 2005: 73% of articaine paresthesias were with "mandibular" nerve block injections

CRA Newsletter, June 2005

Nerve Paresthesia 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 nonsurgical paresthesia in dentistry,* J Canadian DA, Vol 75 No 8, October 2009

Nerve Paresthesia Injury

Distribution of anesthetic agents:

	# of Cases	% of Injuries
Articaine	109	59.9%
Prilocaine	29	15.9%
Lidocaine	23	12.6%
Mepivacaine	6	3.3%
Bupivacaine	0	0.0%
Combination	15	8.2%

- In 99 cases (54.4%), 1 cartridge was used

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

Nerve Paresthesia Injury

Reported incidence of paresthesia:

Prilocaine	1:332,000 injections*
Articaine	1:410,000 injections*
Mepivacaine	1:839,000 injections
Lidocaine	1:2,580,000 injections

*Significantly greater frequency of paresthesia than expected based upon frequency of usage

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

Nerve Paresthesia 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
    - Prilocaine associated injuries 7.3 times greater than expected
    - Articaine associated injuries 3.6 times greater than expected

Garisto et al, *Occurrence of paresthesia after dental local anesthetic administration in the United States,* JADA, Vol 141, July 2010

Nerve Paresthesia Injury

- Anesthesia-induced nerve injuries are VERY rare (Temporary 0.15 – 0.54%; permanent 0.0001-0.01%)

Hillerup S, Jensen R, *Nerve injury caused by mandibular block analgesia,* Int J Oral Maxillofac Surg Vol 35, 2006

- Most paresthesias are reversible, resolving within 2 to 8 weeks
- Mandibular nerve injuries are far more common than maxillary
- The lingual nerve is involved over two times more often than the inferior alveolar nerve

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)

* Pogrel MA et al, *Nerve damage associated with inferior alveolar nerve blocks,* JADA Vol 126, 1995

Nerve Paresthesia Injury

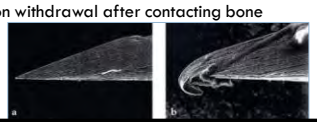
- Theories of causes:
  1. Injury due to direct contact of the needle with the nerve (traumatic injury)
- Incidence of "electric shock" injection:
  - Occurs once every one to two weeks in "average" practices
  - Approximately 8% of these result in some form of paresthesia
  - Incidence of permanent paresthesia is very low from these injections

Pogrel MA et al, *Nerve damage associated with inferior alveolar nerve blocks*, JADA Vol 126, 1995

Nerve Paresthesia Injury

- Theories of causes:
  1. Injury due to direct contact of the needle with the nerve (traumatic injury)
     - 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 Anesthesia, *Quintessence*, 2002



Nerve Paresthesia Injury

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

	Lido	Mepiv	Prilo
US usage	62%	23%	13%
Injuries	48%	5%	47%

Pogrel MA & Thamby S, *Permanent nerve involvement resulting from inferior alveolar nerve blocks*, JADA Vol 131, 2000

Nerve Paresthesia Injury

- Theories of causes:
  2. Injury due to direct contact of the anesthetic solution with the nerve (toxicity injury)
     - Injury correlation with anesthetic agent

	Lido	Mepiv	Prilo	Arti
US usage	54%	15%	6%	25%
Injuries	35%	0%	30%	30%

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

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

Pogrel MA, *Permanent nerve damage from inferior alveolar nerve blocks – an update to include articaine*, CDA Jour Vol 36 No 4, April 2007

Nerve Paresthesia Injury

- Theories of causes:
  2. Injury due to direct contact of the anesthetic solution with the nerve (toxicity injury)

It is noteworthy that in Denmark, where prilocaine is marketed as a 3% solution, 2 studies have linked paresthesia to 4% articaine use, but not to prilocaine use.

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

Nerve Paresthesia Injury

- 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.
- 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*

Isen DA, *Articaine: Pharmacology and clinical use of a recently approved local anesthetic*, Dentistry Today Vol 19 No 11, Nov 2000

*Articaine has 68 mg of anesthetic/cartridge; lidocaine has 36 mg of anesthetic/cartridge

Nerve Paresthesia Injury

- Local anesthetic dosage
  - FDA approved max. dosage for 150 lb. adult:
    - 2% lidocaine w/ epi = 13 cartridges
    - 4% prilocaine = 8 cartridges
    - 4% articaine = 7 cartridges
- 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

Wynn RL et al, *Paresthesia associated with local anesthetics: A perspective on articaine*, General Dentistry (Journal AGD), Nov/Dec 2003

Nerve Paresthesia Injury

- 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

Wynn RL et al, *Paresthesia associated with local anesthetics: A perspective on articaine*, General Dentistry (Journal AGD), Nov/Dec 2003

  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

Nerve Paresthesia 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.

Gaffen AS & Haas DA, *Retrospective review of voluntary reports of nonsurgical paresthesia in dentistry*, J Canadian DA, 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
  3. 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.

Hillerup S et al, *Trigeminal nerve injury associated with injection of local anesthetics: Needle lesion or neurotoxicity*, JADA 142(5), May 2011

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*, JADA Vol 131, 2000

Nerve Paresthesia Injury

- Theories of causes:
  4. Injury due to stretching of the nerve (morphology injury)

Mason DA, *Lingual nerve damage following lower third molar surgery*, Int J Oral Maxillofac Surg 17, 1988

     - 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

Brann CR et al, *Factors influencing nerve damage during lower third molar surgery*, Brit Dent Jour Vol 186 No 10, May 1999

     - Histologic studies of structure of lingual vs. inferior alveolar nerve

Pogrel MA et al, *Lingual nerve damage due to inferior alveolar nerve blocks: A possible explanation*, JADA Vol 134, Feb 2003

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.

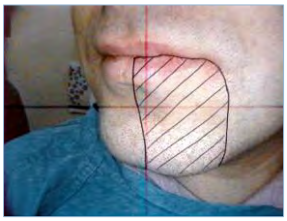
Haas DA, *Localized complications from local anesthesia*, CDA Jour Vol 26 No 9, 1998

What is the influence of technique?

- Inferior alveolar block versus alternatives?

Nerve Paresthesia Injury

- Management of nerve injuries:
  1. 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

Krafft TC & Hickel R, *Clinical investigation into the incidence of direct damage to the lingual nerve caused by local anesthesia*, J Craniomaxillofac Surg Vol 22 No 5, 1994

*Smith MH & Lung KE, *Nerve injuries after dental injection: A review of the literature*, J Can Dent Assoc Vol 72 No 6, 2006

Nerve Paresthesia Injury

- Management of nerve injuries:
  3. 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
  4. If no improvement after 2 weeks, consider referral to a neurologist or to an oral surgeon familiar with management of nerve injuries.

Most injuries will show some sign of improvement within 2 weeks

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.

Haas DA, *Localized complications from local anesthesia*, CDA Jour Vol 26 No 9, 1998

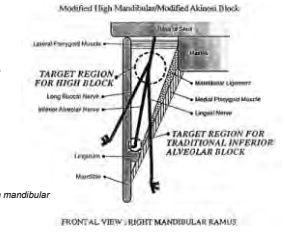
Dentists and dental hygienists must carefully weigh the risks and benefits of the agent and the technique preferred for each clinical situation.

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

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



Wolfe SH, *The Wolfe nerve block: A modified high mandibular nerve block*, Dentistry Today, June/July 1992

WHAT ALTERNATIVES DO WE HAVE TO INJECTIONS?

Topical Anesthetics

Maxillary Anesthesia

- Techniques to minimize the discomfort of palatal injections
  1. Topical anesthesia
  2. Pressure distraction/analgesia
  3. Slow injection with small volumes
  4. Buccal infiltrations
  5. Explain all that you do to minimize the discomfort

Topical Anesthetics

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

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

Topical Anesthetics

- Lidocaine 2 – 5% (amide)

Note: esters have better absorption through mucosa*

- Benzocaine ≤ 20% (ester)
- Tetracaine 0.2 – 2% (ester)
- Cetacaine (benzocaine 14%, butamben 2%, tetracaine HCl 2% - esters)
- Anbesol (benzocaine 10%, phenol 0.5%, alcohol 70% - ester)
- Compounded topicals: combine amide and ester
  (Profound, Profound PET (Profpet), TAC 20 percent Alternate, TheBestTopicalEver)
  *Therefore, a decreased safety margin, especially with children

Topical Anesthetics

- 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"

Kravitz ND, *The use of compound topical anesthetics*, JADA Vol 138, October 2007

Topical Anesthetics

- Compounded formulas:
  - Maximum recommended dose is unknown
  - Narrow difference between optimal therapeutic dose and toxic dose level
  - Vary in composition, quality, and strength
- Recommendation to avoid tissue sloughing:
  - Apply for maximum of 60 – 90 seconds
  - Rinse area thoroughly after application

Kravitz ND, *The use of compound topical anesthetics*, JADA Vol 138, October 2007

Topical Anesthetics

- Refrigerant application: Pain Ease (Gebauer, Cleveland)

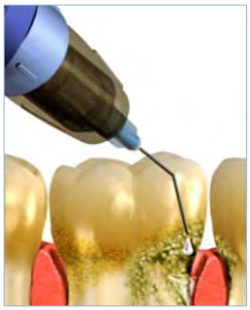
  1,1,1,3,3-pentafluoropropane/1,1,1,2-tetrafluoroethane
  - 5 second application
  - FDA approved for oral tissues
    - Nonirritant to oral mucosa
    - Nontoxic if inhaled
  - Significant reduction in posterior palatal injection pain
    - Good evidence from medical studies
    - Limited dental anecdotal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

Kosaraju A & Vandewalle KS, *A comparison of a refrigerant and a topical anesthetic gel as preinjection anesthetics: A clinical evaluation*, JADA Vol 140, Jan 2009

Topical Anesthetics

- Oraqix

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



Topical Anesthetics

- Oraqix

  2.5% lidocaine, 2.5% prilocaine periodontal gel
  - 30 second onset
  - 20 minute duration (range 14 – 31 min.)
  - Typically, 1 cartridge/quadrant
  - 5 cartridges maximum

Topical Anesthetics

- 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

Anesthetic Reversal Agent

Computer-Controlled Delivery Systems

- The "Wand": Single Tooth Anesthesia (STA) system
  - Milestone Scientific
- The Comfort Control Syringe
  - Dentsply, Inc.
- 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

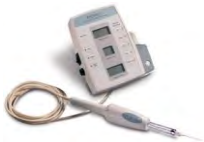
Computer-Controlled Delivery Systems

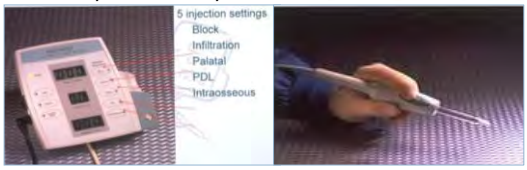
- The "Wand": STA
  - Can give all traditional injections
  - Safer PDL injections
  - Painless palatal injections

Can use for primary or secondary anesthetic injections

Computer-Controlled Delivery Systems

- The Comfort Control Syringe
  - Can give all traditional injections
  - Safer PDL injections
  - Painless palatal injections
  - Primary or secondary anesthesia





Computer-Controlled Delivery Systems

- The Wand STA system
- The Comfort Control Syringe

TABLE 1: PREPROGRAMMED INJECTION RATES

Injection Technique Selection	Injection Rate (cc/sec)	Typical Injection Volume	Typical Injection Time
Block	0.020	Full cartridge	1 min 30 sec
Infiltration	0.017	Full cartridge	1 min 35 sec
Palatal	0.008	Full cartridge	3 min
PDL	0.007	.2cc per root	30 sec per root
Intraosseous	0.020	.9cc	45 sec

(Total Injection Volume and Time are not preset and depend on the clinician manually stopping the injection. The "Injection Technique" selections named on the [redacted] are intended only to be a convenient guide to selecting an injection rate. Your clinical judgement should always prevail in making that selection.)

Needleless Injectors

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

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

INJEX needleless injector system

Electronic Anesthesia

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

    Cell **D**emodulated **E**lectronic **T**argeted **A**nesthesia

An Anesthetic Reversal Agent

- 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
- Restore normal sensation *faster*
- *Accelerate* the return to normal function so patients can speak, smile and drink normally

The Problem

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

Local Anesthetics with Vasoconstrictors	Expected Duration (minutes)	
	Pulpal Anesthesia	Soft Tissue Anesthesia
Articaine 4% + epinephrine 1:100,000	45-60	180-300
Lidocaine 2% + epinephrine 1:100,000	60	180-300
Mepivacaine 2% + levonordefrin 1:20,000	60	180-300
Prilocaine 4% + epinephrine 1:200,000	60-90	180-480

Malamed SF, Handbook of Local Anesthesia, 5th Ed, C.V. Mosby, St. Louis, MO, 2004

Patient Concerns/Complaints

- 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 used in medical indications since 1952
- 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

Hersh EV, Moore PA, Papas AS, et al. *Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults,* JADA Vol. 139 No. 8, Aug 2008

OraVerse Reversal Agent

- 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

Hersh EV, Moore PA, Papas AS, et al. *Reversal of soft-tissue local anesthesia with phentolamine mesylate in adolescents and adults,* JADA Vol. 139 No. 8, Aug 2008

OraVerse Reversal Agent

- Dosage
  - 1:1 ratio to local anesthetic
  - Maximum recommended dose:
    - 2 cartridges for adults & adolescents 12 and older
    - 1 cartridge for patients 6-11 years of age and over 66 lbs.
    - ½ cartridge for children weighing 33-66 lbs.
    - Effective and safe in adults and children aged 6 and over and weighing 33 lbs or more

Evidence from 3 multi-center, double-blinded, randomized, controlled clinical trials involving patients aged 4 through 92

OraVerse Reversal Agent

- 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

OraVerse Reversal Agent

- 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!

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 OnSet buffering agent and OraVerse anesthetic reversal agent

Reasons for Anesthetic Failures

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

"It'll 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

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!

Keys to Success

It's the thought that counts