LOCAL ANESTHETICS:
Dentistry’s Most Important Drugs

Stanley F. Malamed, DDS
Dentist Anesthesiologist
Emeritus Professor of Dentistry
Ostrow School of Dentistry of USC
Los Angeles, California, USA

Saratoga Dental Congress
4th District Dental Society
Stanley F. MALAMED, DDS
Dentist Anesthesiologist
Emeritus Professor of Dentistry
Ostrow School of Dentistry of USC
Los Angeles, CA, USA

I have a relationship with the following companies that may be relevant to this presentation.
I am a paid consultant to:
Septodont, Inc
OnPharma
St. Renatus
3M ESPE

1. Current Local Anesthetic Formulations
2. What’s New?
   a. Articaine
   b. LA ‘OFF’ Switch
   c. LA ‘ON’ Switch
3. Maxillary Anesthesia Without Injection
LOCAL ANESTHETICS are the SAFEST and MOST EFFECTIVE drugs in medicine for the PREVENTION & MANAGEMENT of pain.

Local Anesthetic Use in Dentistry

Annual LA usage (approximate)

300 x 10^6 USA (300,000,000)
80 x 10^6 Germany
40 x 10^6 U.K.
Amides have been available since 1948

Esters

Amides

ESTERS
- Cocaine
- Procaine
- Tetracaine
- Benzocaine
- Chloroprocaine
- Propoxycaine

AMIDES
- Articaine
- Bupivacaine
- Lidocaine
- Mepivacaine
- Prilocaine
Local anesthetics
(worldwide)

Articaine
Bupivacaine
Lidocaine
Mepivacaine
Prilocaine

Local Anesthetics by
EXPECTED duration of PULPAL anesthesia

- Short-duration (~30 minutes)
  - Lidocaine 2%, Mepivacaine 3%, Prilocaine 4%
- Intermediate-duration (~60 minutes)
  - Articaine 4%, Lidocaine 2%, Mepivacaine 2%, Prilocaine 3% or 4% (all with vasoconstrictor)
- Long-duration (>90 minutes)
  - Bupivacaine 0.5% (with vasoconstrictor)
Blood flow through area is increased

LA diffuses out of area more rapidly

All injectable local anesthetics are VASODILATORS

Cocaine

Short - Duration LAs

~ 30 minutes

Mepivacaine

3%
No vasoconstrictor

Prilocaine

4%
No vasoconstrictor

Short - duration LAs - USA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset (textbook)</th>
<th>Pulpal</th>
<th>Soft Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mepivacaine 3%</td>
<td>3 - 5 min</td>
<td>20 - 40 min infiltration - nerve block</td>
<td>2 - 3 hours</td>
</tr>
<tr>
<td>Prilocaine 4%</td>
<td>3 - 5 min</td>
<td>10 - 60 min infiltration - nerve block</td>
<td>2 - 4 hours</td>
</tr>
</tbody>
</table>

PLAIN LAs provide a SHORT-DURATION of NOT AS PROFOUND anesthesia
To increase DURATION, and to increaseDEPTH, of anesthesia, a VASOCONSTRICTOR is added to the LA solution.

USA
Epinephrine
Levonordefrin

Worldwide
Epinephrine
Norepinephrine
Felypressin

Intermediate - Duration LAs

~ 60 minutes

Articaine 4% + vasoconstrictor
Lidocaine 2% + vasoconstrictor
Mepivacaine 2% + vasoconstrictor
Prilocaine 4% + vasoconstrictor

Intermediate - duration LAs - USA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset (textbook)</th>
<th>Pulpal</th>
<th>Soft Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine 4%</td>
<td>Epi 1:100k, 1:200k</td>
<td>2 - 3 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Lidocaine 2%</td>
<td>Epi 1:50k, 1:100k</td>
<td>3 - 5 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Mepivacaine 2%</td>
<td>Levonordefrin 1:20k</td>
<td>3 - 5 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Prilocaine 4%</td>
<td>Epi 1:200k</td>
<td>3 - 5 min</td>
<td>60 min</td>
</tr>
</tbody>
</table>

Through addition of a vasoconstrictor, the ensuing BLOOD LEVEL of the local anesthetic is significantly decreased, making the LA drug SAFER by minimizing risk of overdose (toxic reaction).

Epinephrine
Levonordefrin
Local Anesthetic Blood Levels

- **MEPIVACAINE**
  - 5 mg/kg - NO epinephrine - PEAK LEVEL 1.2 ug/mL
  - 5 mg/kg - Epi 1:200,000 - PEAK LEVEL 0.7 ug/mL

- **LIDOCAINE**
  - 400 mg - NO epinephrine - PEAK LEVEL 2.0 ug/mL
  - 400 mg - Epi 1:200,000 - PEAK LEVEL 1.0 ug/mL

Long - Duration LAs

> 90 minutes

**Bupivacaine 0.5% + vasoconstrictor**

Long - duration LAs - USA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset (textbook)</th>
<th>Pulpal</th>
<th>Soft Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine</td>
<td>Epi 1:200k</td>
<td>6 -10 min</td>
<td>90 - 180 min (up to 7 hours)</td>
</tr>
</tbody>
</table>

Bupivacaine 0.5% with vasoconstrictor

- Indicated for:
  - Dental therapy of > 2 hour duration
  - Post-surgical pain control
**Post-surgical pain control**

Pre-surgical NSAID po 1 hr. prior to appointment
- Ibuprofen 600 mg QID PO

LA of choice for surgery
- Articaine, Lidocaine, Mepivacaine

Long-acting LA at end of surgery just prior to discharge of patient
- Bupivacaine

NSAID on timed basis (q4,6,8h) for xx days
- Ibuprofen 600 mg QID PO

Post-surgical telephone call early evening

---

**Bupivacaine 0.5% with vasoconstrictor**

- Not indicated for:
  - Rarely indicated for administration to children (long duration soft tissue anesthesia = increased risk of self-inflicted soft tissue injury)

---

**Maximum recommended therapeutic dosages**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mg/kg</th>
<th>Absolute maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine HCl</td>
<td>7</td>
<td>n/a</td>
</tr>
<tr>
<td>Bupivacaine HCl</td>
<td>***</td>
<td>90</td>
</tr>
<tr>
<td>Lidocaine HCl</td>
<td>7</td>
<td>500</td>
</tr>
<tr>
<td>Mepivacaine HCl</td>
<td>6.6</td>
<td>400</td>
</tr>
<tr>
<td>Prilocaine HCl</td>
<td>8</td>
<td>600</td>
</tr>
</tbody>
</table>

---

**Local Anesthetics by EXPECTED duration of PULPAL anesthesia**

- Short-duration (~30 minutes)
  - Mepivacaine 3%, Prilocaine 4%

- Intermediate-duration (~60 minutes)
  - Articaine 4%, Lidocaine 2%, Mepivacaine 2%, Prilocaine 3% or 4% (all with vasoconstrictor)

- Long-duration (>90 minutes)
  - Bupivacaine 0.5% (with vasoconstrictor)
**USA**

By MARKET SHARE

<table>
<thead>
<tr>
<th>Local Anesthetic</th>
<th>Market Share 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>49.35%</td>
</tr>
<tr>
<td>Articaine</td>
<td>34.86%</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>9.82%</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>3.3%</td>
</tr>
<tr>
<td>Prilocaine</td>
<td>2.7%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>84.21%</strong></td>
</tr>
</tbody>
</table>

**Jan-Dec 2014**

---

**What’s NEW in Local Anesthesia**

- **Articaine - Mandibular Infiltration**
- **The LA ‘OFF’ Switch**
- **The LA ‘ON’ Switch**
- **Maxillary Anesthesia without Injection**

---

**Articaine HCl**

*by Mandibular Infiltration in Adults*

---

**Buccal infiltration - ARTICAINE**

**Mandibular infiltration**

John Meechan (UK)

Al Reader (USA)
Articaine infiltration as a **sole** injection for mandibular anesthesia


<table>
<thead>
<tr>
<th>Design:</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 60</td>
<td></td>
</tr>
<tr>
<td>Infiltration mandibular buccal fold by #30</td>
<td></td>
</tr>
<tr>
<td>• Lidocaine 2% + epi 1:100K</td>
<td></td>
</tr>
<tr>
<td>• Articaine 4% + epi 1:100K</td>
<td></td>
</tr>
<tr>
<td>Randomized</td>
<td></td>
</tr>
<tr>
<td>At least 7 days apart</td>
<td></td>
</tr>
<tr>
<td>60 on right side</td>
<td></td>
</tr>
<tr>
<td>60 on left side</td>
<td></td>
</tr>
<tr>
<td>1.8 mL in 60 seconds</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EPT</th>
<th>2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teeth tested: 1\textsuperscript{st} and 2\textsuperscript{nd} molar, 1\textsuperscript{st} and 2\textsuperscript{nd} premolar</td>
<td></td>
</tr>
<tr>
<td>• Baseline</td>
<td></td>
</tr>
<tr>
<td>• EPT @ 1 min = molars</td>
<td></td>
</tr>
<tr>
<td>• EPT @ 2 min = premolars</td>
<td></td>
</tr>
<tr>
<td>• EPT @ 3 min = Control (contralateral canine)</td>
<td></td>
</tr>
<tr>
<td>• Repeated cycle every 3 minutes for 60 minutes</td>
<td></td>
</tr>
<tr>
<td>Criteria for success:</td>
<td></td>
</tr>
<tr>
<td>No response to 2 or more consecutive 80uA tests</td>
<td></td>
</tr>
</tbody>
</table>
The anesthetic efficacy of articaine in buccal infiltration of mandibular posterior teeth

Pulp test every 3 min
SUCCESS = 80/80 on 2 consecutive tests

<table>
<thead>
<tr>
<th>Tooth</th>
<th>Articaine</th>
<th>Lidocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandibular 2nd Molar</td>
<td>75%</td>
<td>45%</td>
</tr>
<tr>
<td>Mandibular 1st Molar</td>
<td>87%</td>
<td>57%</td>
</tr>
<tr>
<td>Mandibular 2nd Premolar</td>
<td>92%</td>
<td>67%</td>
</tr>
<tr>
<td>Mandibular 1st Premolar</td>
<td>86%</td>
<td>61%</td>
</tr>
</tbody>
</table>

p value for all: >.0001

Results -2:
The onset of successful anesthesia was significantly faster for articaine than lidocaine for all 4 teeth tested

<table>
<thead>
<tr>
<th>Tooth</th>
<th>Articaine onset (min) +/- Standard Deviation</th>
<th>Lidocaine onset (min) +/- Standard Deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd molar</td>
<td>4.6 +/- 4.0</td>
<td>11.1 +/- 9.5</td>
<td>.0001</td>
</tr>
<tr>
<td>1st molar</td>
<td>4.2 +/- 3.1</td>
<td>7.7 +/- 4.3</td>
<td>.0002</td>
</tr>
<tr>
<td>2nd premolar</td>
<td>4.3 +/- 2.3</td>
<td>6.9 +/- 6.6</td>
<td>.0014</td>
</tr>
<tr>
<td>1st premolar</td>
<td>4.7 +/- 2.4</td>
<td>6.3 +/- 3.1</td>
<td>.0137</td>
</tr>
</tbody>
</table>

Thiophene ring: > lipid solubility

Meechan JG, Ledvinka JI.
Pulpal anaesthesia for mandibular central incisor teeth: a comparison of infiltration and intraligamentary injections.
Int Endod J 35:629-634, 2002
Design:
Articaine 4% + epi 1:100K
Lidocaine 2% + epi 1:80K
Infiltration buccal fold by lateral incisor
• 0.5 mL
Infiltration buccal & lingual by lateral incisor
  0.5 mL per site
EPT q 3 min for 45 minutes

Results-1:
Infiltration buccal fold by lateral incisor
  94% articaine; 70% lidocaine
Infiltration buccal & lingual by lateral incisor
  97% articaine; 88% lidocaine

Advantages
- Profound pulpal anesthesia
  30 to 40 minute duration of pulpal anesthesia
- Minimal accessory soft tissue anesthesia
- Tongue
Disadvantage
I can’t think of any, unless it doesn’t work!

Comment
The research required articaine infiltration by tooth #30
In clinical situations you would logically infiltrate the articaine in the buccal fold adjacent to the tooth to be treated.

Articaine infiltration as a supplement to IANB

- IANB’s at each of 2 visits = 2% lidocaine + epi 1:80K
- One visit = 4% articaine + epi 1:100K infiltration buccal fold 1st molar (2.0 mL)
- One visit = ‘dummy injection’ buccal fold 1st molar
- Pulp test for 45 minutes
Articaine infiltration as a supplement to IANB

**1\textsuperscript{st} Molar**

- Success: 33 (91.7%)
- Failure: 16 (44.4%)

**1\textsuperscript{st} Premolar**

- Success: 32 (88.9%)
- Failure: 12 (33.3%)

**Anesthesia success**

<table>
<thead>
<tr>
<th>Anesthesia infiltration</th>
<th>Success n (%)</th>
<th>Failure n (%)</th>
<th>McNemar Test P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA + a-caine infiltration</td>
<td>33 (91.7)</td>
<td>16 (44.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IA + dummy infiltration</td>
<td>24 (66.7)</td>
<td>7 (19.4)</td>
<td>0.021</td>
</tr>
</tbody>
</table>

The local anesthetic “OFF SWITCH”

**Phentolamine Mesylate**
PLAIN LAs provide a SHORT-DURATION of NOT VERY PROFOUND anesthesia.

To increase DURATION, and to increase DEPTH, of anesthesia, a VASOCONSTRICTOR is added to the LA solution.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset (textbook)</th>
<th>Pulpal</th>
<th>Soft Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine 4%</td>
<td>Epi 1:100k</td>
<td>2 - 3 min</td>
<td>3 - 5 hours</td>
</tr>
<tr>
<td></td>
<td>Epi 1:200k</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lidocaine 2%</td>
<td>Epi 1:50k</td>
<td>3 - 5 min</td>
<td>3 - 5 hours</td>
</tr>
<tr>
<td></td>
<td>Epi 1:100k</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mepivacaine 2%</td>
<td>Levonordefrin 1:20k</td>
<td>3 - 5 min</td>
<td>3 - 5 hours</td>
</tr>
<tr>
<td>Prilocaine 4%</td>
<td>Epi 1:200k</td>
<td>3 - 5 min</td>
<td>3 - 8 hours</td>
</tr>
</tbody>
</table>

The PROBLEM, on occasion, is RESIDUAL SOFT TISSUE ANESTHESIA.

Epi = Epinephrine (Adrenalin)
13% of pediatric patients receiving IANB suffer post-treatment traumatic injury to soft tissues.

<table>
<thead>
<tr>
<th>Age</th>
<th>% with soft tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4 years</td>
<td>18%</td>
</tr>
<tr>
<td>4 - 7</td>
<td>16%</td>
</tr>
<tr>
<td>8 - 11</td>
<td>13%</td>
</tr>
<tr>
<td>12+</td>
<td>7%</td>
</tr>
</tbody>
</table>

Phentolamine mesylate is a vasodilator (an alpha adrenergic antagonist) that increases vascular perfusion in the area of injection. This increased perfusion leads to an increased rate of the LA diffusing out of the nerve into the cardiovascular system, thereby decreasing the duration of residual soft tissue anesthesia.

The local anesthetic “OFF SWITCH”
Phentolamine Mesylate

Local Anesthesia Reversal

Does it work?
Phentolamine Mesylate

OraVerse

- Conservative dental treatment
- Non-surgical periodontics (SRP)
- Pediatric dentistry
- Medically compromised patients:
  - e.g.: Diabetics
- Geriatric patients
- Special needs patients
- Post-mandibular implants

The local anesthetic “ON SWITCH”

Buffered Local Anesthetics
Alkalinized Local Anesthetics
How long does it take for pulpal anesthesia to develop?

Intermediate - duration LAs - USA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset (textbook)</th>
<th>Pulpal</th>
<th>Soft Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine 2%</td>
<td>Epi 1:50k, 1:100k</td>
<td>3 - 5 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Mepivacaine 2%</td>
<td>Levonordefrin 1:20k</td>
<td>3 - 5 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Prilocaine 4%</td>
<td>Epi 1:200k</td>
<td>3 - 5 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Articaine 4%</td>
<td>Epi 1:100k, 1:200k</td>
<td>2 - 3 min</td>
<td>60 min</td>
</tr>
</tbody>
</table>

Epi = Epinephrine (Adrenalin)

Six-Hour Time Course for Pulpal Analgesia (EPT)
IANB Second Premolar

95% of patients will (eventually) get numb if given a 45-minute waiting period.

45 minutes

So the question is:

How long does it REALLY take for pulpal anesthesia to develop?
30-Minute Time Course for Pulpal Analgesia - Lidocaine IANBs
Data from 28 PRP Studies - 1078 Subjects (1991 - 2008)

The SPAGHETTI graph

IANB - Lido
28 peer-reviewed trials
N = 1078

Infiltration - Lido
8 peer-reviewed trials
N = 416

IANB - Articaine
5 peer-reviewed trials
N = 222

30 Minute Time Course for IANB Soft Tissue Analgesia (sharp dental explorer)

At 4 minutes:
70% soft tissue numb
25% pulpal anesthesia
At 6 minutes:
85% soft tissue numb
40% pulpal anesthesia

Soft tissue anesthesia **is** NEVER a guaranteed sign of pulpal anesthesia
Is there a guarantee?

The best* we have is using an electric pulp tester or Freezing spray (e.g. Endo-Ice)

*Assumes no pulpal involvement

The best* we have is using an electric pulp tester or Freezing spray (e.g. Endo-Ice)

Most doctors wait ~10 minutes


At 10 minutes: 60% pulpal anesthesia

Some doctors wait 15 minutes (67%)

At 15 minutes: 67% pulpal anesthesia

IABN: Lidocaine + epinephrine

% clinically effective pulpal anesthesia
25% at 4 minutes
40% at 6 minutes
60% at 10 minutes
67% at 15 minutes
95% at 45 minutes
Can we speed the onset of anesthesia... with Articaine?

Why do doctors LIKE articaine?

Anecdotal comments from dentists:
- “It works better”
- “I don’t miss as often”
- “Hard to get ‘numb’ patients are easier to numb with articaine”
- “It works faster”

Can we speed the onset of anesthesia with Articaine?

NO

30-Minute Time Course, Pulpal Analgesia, IANB, Lidocaine, Articaine

N = 222
Articaine

N = 1078
Lidocaine

ARTICAINE + epinephrine
Can we speed the onset of anesthesia . . .
by buffering the LA solution?

Can we speed the onset of anesthesia . . .
by changing the pH of the LA solution?

Can we speed the onset of anesthesia
by buffering the solution?

YES
The local anesthetic “ON SWITCH”

Local anesthetics are INSOLUBLE in water.

Hydrochloric acid is added to make the drug water-soluble.

We inject the acid-salt of the local anesthetic.
Let’s look at the anesthetic cartridge

- pH
  - ‘Plain’ LA solution (mepivacaine 3%) = ~6.5
  - Vasoconstrictor LA solution = ~3.5
  - Lemon juice = 3.3

Lidocaine = RN

- Hydrochloric acid = $H^+$

The more acidic the solution, the greater the number of $H^+$

Some $H^+$ attach to RN forming $RNH^+$
So... inside the LA cartridge we have three things: RN, H⁺, and RNH⁺.

RN is lipid soluble and can cross the lipid-rich nerve membrane.

RNH⁺ cannot cross the nerve membrane.

The LA must diffuse through the nerve membrane to block Na⁺ channels.

% Un-ionized (RN) LA

<table>
<thead>
<tr>
<th>pH</th>
<th>Lidocaine pKa 7.5</th>
<th>Articaine pKa 7.8</th>
<th>Mepivacaine pKa 7.6</th>
<th>Bupivacaine pKa 8.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>RN</td>
<td>3.5 (with epi)</td>
<td>0.004</td>
<td>0.005</td>
<td>0.008</td>
</tr>
</tbody>
</table>
The body will SLOWLY buffer the anesthetic solution to a pH of 7.4.

The human body is a magnificent buffering machine.

BUFFERING with Sodium Bicarbonate.

pH = 7.35
Patients were appointed twice.

- Received IANB each time
  - At least 1 week between appointments
- Pulp tested mandibular premolar prior to start
- IANB administered
  - Traditional lidocaine + epi 1:100k (pH ~3.5)
  - Buffered lidocaine + epi 1:100k (pH 7.35)

Timer started

- Endo-ice applied to premolar q20sec until no response
- Confirmed with EPT
- Onset of anesthesia when BOTH tests negative

Clinical Data – Pain Free Injections

44% of buffered anesthetic patients experienced zero injection pain

6% of traditional anesthetic patients experienced zero injection pain
Clinical Data – Patient Preference

72% of patients rated buffered anesthetic as the more comfortable injection.

Clinical Data – Onset less than 2 minutes

Buffering Lidocaine HCl

- Lidocaine 2% + epinephrine 1:100,000 = pH 3.5
  BUFFERED
- Lidocaine 1.75% + epi 1:125,000 + CO2 + NaHCO3 = pH 7.4
  - More dilute
  - 6,000x more active ions to enter nerve

Buffered Local Anesthetics

When buffering is done properly the following advantages can be expected from the increase in pH:

1. More comfortable injection for patient
   - pH of anesthetic 7.35 to 7.5
2. More rapid onset on pulpal anesthesia
3. More profound anesthesia
4. Less post-injection soreness
5. No effect on duration of action
6. No increase in LA blood level (safety)
Administer buffered lidocaine IANB

2. DO NOT LEAVE PATIENT !!!
3. You will know if your block is successful in 2 minutes
Check for pulpal anesthesia:
  EPT or Endo-Ice
In 2 minutes following
IANB begin tooth preparation

The Onset® approach

Maxillary anesthesia

Follow same procedure for maxillary teeth.
Onset time is at least as rapid
- if not faster -
following infiltration

ADA Center for Evidence Based Dentistry

Increasing the pH of lidocaine with sodium bicarbonate decreased pain on injection and augmented patient comfort and satisfaction.

ADA Evidence Quality Rating = Good

The local anesthetic

“ON SWITCH”

Buffered Local Anesthetics
Alkalinized Local Anesthetics
Intranasal Local Anesthesia in the Maxilla

Illicit drugs: Cocaine

- Emergency medicine
  - Pediatric grand mal status . . . Midazolam
- Pediatric sedation (dentistry) . . . Midazolam
Intranasal Local Anesthetic

KOVANAZE™

3% Tetracaine
- Ester-type local anesthetic
- Commonly used by ENT surgeons
- Has 'track record' as safe & effective IN

Oxymetazoline
- Vasoconstrictor
- Active ingredient in 'Afrin' & other nasal decongestants

- NDA (New Drug Application) filing anticipated second quarter 2015; anticipated FDA approval in early 2016 for USA
- The goal is to administer a local anesthetic to provide pulpal anesthesia on teeth numbers 4 through 13 (#1.1 to 1.5 and 2.1 to 2.5)
- All planned FDA Phase 1, 2 & 3 Clinical Trials Completed in Fall 2013
Maxillary anesthesia without injection

- Phase 2 Clinical Trial: 2009
- Dr. Sebastian Ciancio, SUNY Buffalo
- Nasal spray of local anesthetic provides pulpal anesthesia to maxillary anterior teeth

Intranasal Local Anesthetic

PHASE 2 CLINICAL TRIAL

3% Tetracaine
Oxymetazoline
(active ingredient in Afrin nasal spray)
Sprayed into R & L nares
N=48

Injectable (lidocaine + epi)
94% success
1st molar to 1st molar

94% success
Kovanaze™

84% success - 1st molar to 1st molar
100% success - premolar to premolar

16% failure on 1st molar

What’s New in Local Anesthesia

In the more distant future

Light-activated / Light-inactivated Local Anesthetic

Optical control of pain-sensing neurons. QAQ selectively enters pain sensing neurons and silences their activity (top, green light). Illumination with violet light (bottom) quickly restores signal conduction.
Now for a change of subject

A basic truism regarding ANATOMY:
Everybody is different

We teach ‘normal’ anatomy:
  Insert the needle here
  Advance 25 mms
  Aspirate
  Deposit the drug
We HOPE the nerve is in the area

A basic truism regarding INJECTIONS:
Once a needle penetrates the skin or mucous membrane, every injection is BLIND

A basic truism regarding LOCAL ANESTHETICS:
LAs are chemicals that interrupt nerve conduction (producing anesthesia) transiently (hopefully)
Another truism regarding LOCAL ANESTHETICS

ALL LAs are neurotoxic
(they can damage nerves)

If all LAs were equally neurotoxic
the % of cases of paresthesia would be
equal to the drugs % market share

50% of market share = 50% of cases of paresthesia
25% of market share = 25% of cases of paresthesia
Ratio should be 1.0

% Cases of paresthesia

% Market share

A basic truism regarding PARESTHESIA:

Paresthesia has existed
ever since injections
were first administered

Just the Facts
Articaine
and
Paresthesia
Haas, D A. Lennon, D.
A 21 year retrospective study of reports of paresthesia following local anesthetic administration.

- Overall incidence of paresthesia (all LAs) = 1:785,000
- 2% and 3% LAs = 1:1,250,000
- 4% prilocaine = 1:588,235
- 4% articaine = 1:440,529 (0.000000227%) (2.2699e-06)
- Ontario, Canada

Occurrence of paresthesia after dental local anesthetic administration in the United States

| USA | 0.000000024% | 2.403934e-07 |

Pogrel MA
J. Calif Dent Assoc 40:795-797, 2012 (October)

Permanent Nerve Damage From Inferior Alveolar Nerve Blocks: A Current Update
M. Anthony Pogrel, DDS, MD

Abstract: Permanent nerve involvement has been reported following inferior alveolar nerve blocks. This study provides an update on cases reported to one unit in the preceding six years. Lidocaine was associated with 35 percent of cases, articaine with 32 percent of cases; and prilocaine with 34 percent of cases. It does appear that inferior alveolar nerve block can cause permanent nerve damage with any local anesthetic, but the incidences may vary.

<table>
<thead>
<tr>
<th>% Cases of paresthesia</th>
<th>% Market share</th>
<th>2007</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td></td>
<td>0.64</td>
<td>0.5</td>
</tr>
<tr>
<td>Articaine</td>
<td></td>
<td>1.19</td>
<td>0.97</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td></td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Prilocaine</td>
<td></td>
<td>4.96</td>
<td>3.25</td>
</tr>
</tbody>
</table>

M. Anthony Pogrel, DDS, MD
<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Year</th>
<th>%   Lingual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haas, Lennon</td>
<td>Canada</td>
<td>1995</td>
<td>70.6</td>
</tr>
<tr>
<td>Hillerup</td>
<td>Denmark</td>
<td>2006</td>
<td>77</td>
</tr>
<tr>
<td>Kingon, Sambrook</td>
<td>Australia</td>
<td>2011</td>
<td>80</td>
</tr>
<tr>
<td>Garristo, Haas</td>
<td>USA</td>
<td>2010</td>
<td>92.7</td>
</tr>
</tbody>
</table>

So, why is it that the lingual nerve is primarily involved in cases of paresthesia?

“The Lingual Nerve is In the Way”

Professor Dr. Stanley F. Malamed

- IMO . . . IF it’s the distribution of the lingual nerve (loss of taste, paresthesia) . . .

It’s MECHANICAL

Not chemical
Paresthesia in dentistry

> 95% of reported cases occur in the MANDIBLE

Of these the overwhelming percentage involve only the lingual nerve

Paresthesia in dentistry

Is rarely observed in the maxilla
- < 5%
- Yet 1/2 of all dental care is in the upper arch

Paresthesia in dentistry

Is rarely (no reported cases) observed following:
- Gow-Gates mandibular nerve block
- Vazirani-Akinosi mandibular nerve block
  **No lingual nerve in area**
- Only occasionally following mental/incipise nerve block

Paresthesia and 4% Anesthetics

Articaine is used in medicine:
- Ophthalmology
- Orthopedic surgery
  - Arthroscopic, hand, foot
- Plastic and reconstructive surgery
Articaine in Medicine

Local and Regional Anesthesia
Local and Regional Anesthesia 2012:5 23–33

Articaine: a review of its use for local and regional anesthesia

Marc Snoeck
Department of Anesthesia, Canisius-Wilhelmina Hospital, Nijmegen, The Netherlands

Question:
Is it possible that articaine is so specifically neurotoxic that it only affects nerves within the mouth and more specifically the lingual nerve?

Answer:
NO!
So, what should YOU do?

Benefit v. Risk

The doctor *MUST* always consider the BENEFIT to be gained from use of a procedure or drug versus the RISK involved in the procedure or drug.

ONLY when the benefit to be gained CLEARLY OUTWEIGHS the risk should the procedure be done or the drug administered.

ALL reports claiming an increased risk of paresthesia with articaine are ANECDOTAL

There is absolutely NO scientific evidence articaine has a greater risk of paresthesia than other LAs

So, what should YOU do?

🌟 Continue to use Articaine by IANB block
IF you are unconvinced:
☆ Use Lidocaine or Mepivacaine for IANB
☆ NOT Prilocaine
☆ Follow Lidocaine IANB with Articaine buccal infiltration
☆ At apex of tooth being treated
☆ ½ cartridge

LOCAL ANESTHETICS: Dentistry’s Most Important Drugs

Stanley F. Malamed, DDS
Dentist Anesthesiologist
Emeritus Professor of Dentistry
Ostrow School of Dentistry of USC
Los Angeles, California, USA

Saratoga Dental Congress
4th District Dental Society

Thank you for listening . . .

malamed@usc.edu