

The Renaissance in Local Anesthesia



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I have a relationship with the following companies that may be relevant to this presentation.
I am a paid consultant to:

Septodont, Inc



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PAIN

The greatest fear
dental patients have
is FEAR of PAIN

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PAIN

Clinical definition:

**Pain is whatever a
patient says hurts**

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PAIN

Real pain
Psychological pain

They *BOTH* hurt!

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Painless Injections

How important
- to the patient -
is pain-free dental treatment?

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How Dentists Are Judged By Patients

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2. Does not hurt

1. A painless injection



de St. Georges J. Dentistry Today 23(8): 96-99, August 2007

Menu

15 January 2016

1. Pain & Fear
 - a. Sedation
2. The Drugs
3. Problems achieving effective pain control
4. Buffered lidocaine

Menu

15 January 2016

5. Is the 'Mandibular Block' passe?
6. What's New in Local Anesthesia
 - a. Local Anesthesia Reversal
 - b. C.C.L.A.D
 - c. Nasal Local Anesthetic Mist

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Pain Reaction Threshold

11

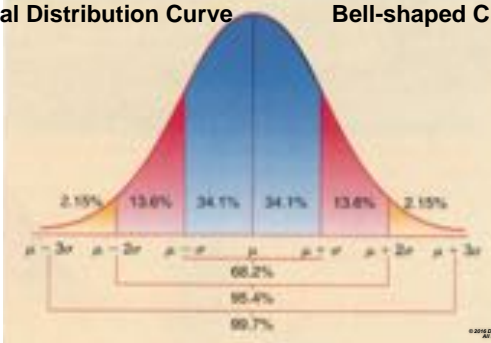
PRT

... that point at which a person interprets a stimulus as painful.

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Normal Distribution Curve Bell-shaped Curve

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Pain Reaction Threshold

70% respond appropriately (Normo-responders)

15% under-respond (Hypo-responders)

15% over-respond (Hyper-responders)

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Pain Reaction Threshold

Sleep-deprivation
Long-term chronic pain
Short-term acute pain
Fear

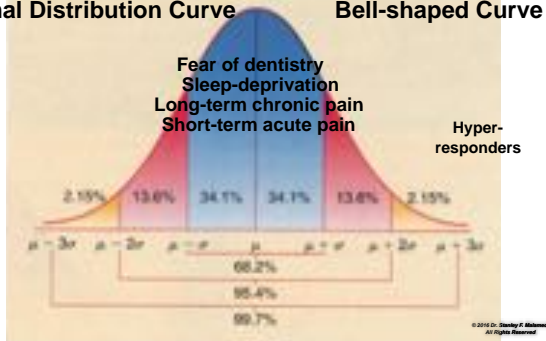
LOWER PRT

Patient overreacts to stimulation
Patient interprets usually non-painful stimuli as noxious

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Normal Distribution Curve Bell-shaped Curve



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LOCAL ANESTHETICS are the
SAFEST and MOST EFFECTIVE
drugs in medicine for the
PREVENTION & MANAGEMENT of pain

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LOCAL ANESTHETICS
are the only drugs that actually
PREVENT PAIN

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Local anesthetics

- Articaine
- Bupivacaine
- Lidocaine
- Mepivacaine
- Prilocaine



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**Deposit a Local
Anesthetic Close to a
Nerve and It
WILL
Produce Pain Control**

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**The *PROBLEM* is
local anesthetics
need to be
INJECTED**



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◦ The act of receiving the LA is *THE* most traumatic part of the dental experience for most patients.

◦ The INJECTION



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Syncope	15,407 (50.3%)	All ages N = 4,307
Mild allergy	2,583 (8.4%)	
Angina Pectoris	2,552 (8.3%)	
Postural hypotension	2,475 (8.1%)	
Seizure	1,595 (5.2%)	
Asthmatic attack	1,392 (4.5%)	
Hyperventilation	1,326 (4.3%)	
Epinephrine Rxn	913 (3.0%)	
Hypoglycemia	890 (2.9%)	
Cardiac Arrest	331 (1.1%)	
Anaphylaxis	304 (1.0%)	
Myocardial Infarction	289 (0.9%)	
L.A. Overdose	204 (0.7%)	

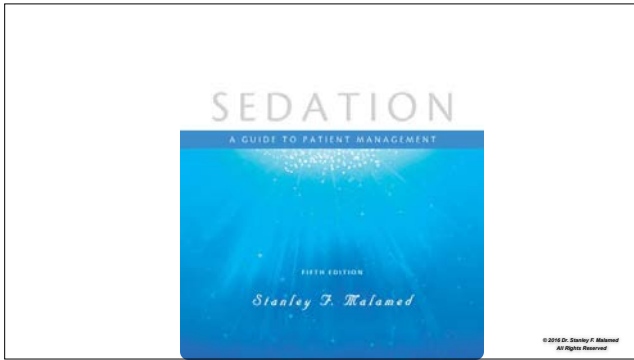
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Treatment Stage	Occurrence
Immediately before Tx	1.5%
During / after LA	54.9%
During treatment	22%
After treatment	15.2%
After leaves office	5.5%

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Medical Emergencies Treatment being performed

Treatment	Occurrence
Tooth extraction	38.9%
Pulp extirpation	26.9%
Unknown	12.3%
Other treatment	9%
Preparation	7.3%
Filling	2.3%
Incision	1.7%



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**The scared dental patient
OVERREACTS
to incoming sensory stimulation,**




**be it visual, auditory,
proprioceptive, or nociceptive**

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**The goal of sedation is
DISTRACTION**



**To take the patients mind off
of what is happening to them
whilst in the dental chair**

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**So, when it comes to managing
fear, our target organ is the brain**



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IATROSEDATION

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- Iatro = Doctor
- Sedation = Relaxation
- Relaxation of the patient through the 'doctors' behavior
- Non-drug techniques of sedation

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Non-drug Techniques of Sedation

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- Chairside demeanor
- Hypnosis
- Acupuncture
- Audioanalgesia
- Video

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PHARMACOSEDATATION

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- Pharm = Drugs
- Sedation = Relaxation
- Techniques of sedation requiring drug administration

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PHARMACOSEDATATION

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Requires the administration of
CNS-depressant drug(s),
altering the patients level of consciousness,
thereby rendering them
less aware of their surroundings

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**A primary GOAL of sedation
(iatro- or pharmaco-)
is to permit the
STRESS-INTOLERANT patient
to receive dental care in a SAFE and
efficient manner.**

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**Another GOAL of sedation is to
PREVENT
the occurrence of
medical emergencies.**

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Routes of Drug Administration

- Oral sedation
- Inhalation sedation
 - N₂O – O₂
- Intravenous sedation
- Intranasal sedation

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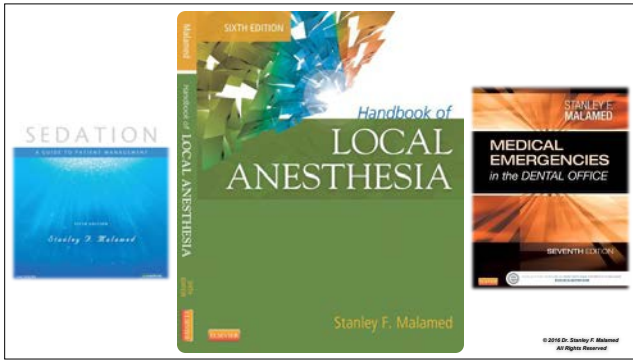
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**Deal with the
FEAR first**

**then PAIN will be
a minor problem**

Milgrom P, Weinstein P, Kleinknecht R, Getz T
Treating fearful dental patients, Reston 1980

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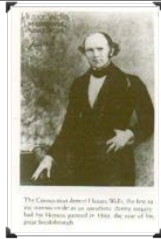


Local anesthetics are the SAFEST and the MOST EFFECTIVE drugs available in medicine for the prevention and management of pain

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11 December 1844

Prof. Colton administers N₂O to Horace Wells while Dr. John Riggs (DDS) extracts one of Well's teeth



ANESTHESIA

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**1844 - 1880's
General Anesthesia**




- Nitrous oxide
- Ether
- Chloroform

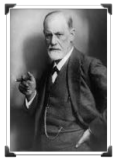
**Appendectomy
Cholecystectomy**

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Cocaine



Karl Koller
1857-1944
Ophthalmologist



Sigmund Freud
1856-1939
Psychiatrist


1885 Vienna, Austria


- Karl Koller & Sigmund Freud
- Topical cocaine used successfully in eye surgery

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Cocaine





1885 Baltimore, MD

- William Stewart Halsted (1852-1922)
- 1885 Excised the inferior dental nerve after blocking it with an injection of a solution of cocaine
- 1885 Discovered that local anesthesia might be produced by intradermal injections of very weak solutions of cocaine and even of water.


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1906

Procaine
Novocaine

1906





Alfred Einhorn
Sc. D.

Nc1ccc(cc1)C(=O)OCCN(C)C + HCl

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ESTERS

1885 to late 1940's

Procaine
 $C_{13}H_{16}N_2O_2$

Nc1ccc(cc1)C(=O)OCCN(C)C

Cocaine

Procaine

Tetracaine


Benzocaine

Chloroprocaine

Propoxycaine

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
Lidocaine 1948
 Mepivacaine 1960
 Prilocaine 1965
 Bupivacaine 1972
 Articaine 2000
 Canada - 1985

dates are for USA
 FDA approvals
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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)


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All injectable local anesthetics are VASODILATORS

Blood flow through area is INCREASED

Cocaine



• LA diffuses OUT of AREA more rapidly

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Short - Duration LAs

~ 30 minutes

Mepivacaine
 3%
 No vasoconstrictor

Prilocaine
 4%
 No vasoconstrictor



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**PLAIN LAs
provide a
SHORT-DURATION
of
NOT AS PROFOUND
anesthesia**

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Short - Duration LAs

Drug	Onset (textbook)	Pulpal	Soft Tissue
Mepivacaine 3%	3 - 5 min	20 - 40 min infiltration - NB	2 - 3 hours
Prilocaine 4%	3 - 5 min	10 - 60 min infiltration - NB	2 - 4 hours

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

Canada
Epinephrine



Worldwide
Epinephrine
Norepinephrine
Felypressin

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Intermediate - Duration LAs

~ 60 minutes



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

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Intermediate - duration LAs

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Drug	Onset (textbook)	Pulpal	Soft Tissue
Lidocaine 2% Epi 1:50k, 1:100k	3 - 5 min	60 min	3 - 5 hours
Articaine 4% Epi 1:100k, 1:200k	2 - 3 min	60 min	3 - 5 hours
Mepivacaine 2% Epi 1:100k	3 - 5 min	60 min	3 - 5 hours
Prilocaine 4% Epi 1:200k	3 - 5 min	60 min	3 - 8 hours

Epi = Epinephrine (Adrenalin)

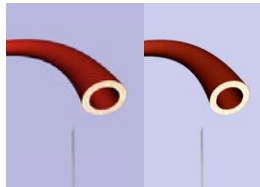
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Through addition of a vasoconstrictor, the ensuing **BLOOD LEVEL** of the local anesthetic is significantly decreased, making the LA drug **SAFER** by minimizing risk of overdose (toxic reaction)

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Epinephrine



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Local Anesthetic Blood Levels

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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

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Vasoconstrictor - Advantages

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1. Increased depth of anesthesia
2. Increased duration of anesthesia
3. Decreased toxicity (increased safety)

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Local Anesthetics by
EXPECTED duration of PULPAL anesthesia

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Intermediate-duration (~60 minutes)

Articaine 4%, Lidocaine 2%, Mepivacaine 2%,
Prilocaine 4% (all with vasoconstrictor)

Approximately 90% of all local anesthetics
used by **North American** dentists are
intermediate-duration drugs



Long - Duration LAs

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> 90 minutes



Bupivacaine 0.5% + vasoconstrictor

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Long - Duration LAs

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Drug	Onset (textbook)	Pulpal	Soft Tissue
Bupivacaine 0.5%	Epi 1:200k	6 -10 min	90 - 180 min (up to 7 hours NB)
			up to 12 hours (NB)

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Bupivacaine 0.5% with vasoconstrictor

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- Not indicated for:

Rarely indicated for administration to children (long
duration soft tissue anesthesia = increased risk of self-inflicted
soft tissue injury)



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Bupivacaine 0.5% with vasoconstrictor

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



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Post-Surgical Pain Control

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Pre-surgical NSAID po 1 hr. prior to appointment
 • Ibuprofen 600 mg PO 1 hour prior to surgery



LA of choice for surgery

- Articaine, Lidocaine, Mepivacaine

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

- Bupivacaine (nerve block preferred)

NSAID on timed basis (q4,6,8h) for xx days

- Ibuprofen 600 mg QID PO

Post-surgical telephone call early evening



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Maximum Recommended Dosages

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Drug	Mg/kg	Absolute maximum	Mg/kg	Absolute maximum (cartridges)
Articaine HCl	7	n/a	7 5 (children)	500 (7)
Bupivacaine HCl	***	90	2	200 (10)
Lidocaine HCl	7	500	7	500 (13)
Mepivacaine HCl	6.6	400	6.6	400 (11) (7 for 3% plain)
Prilocaine HCl	8	600	8	500 (8)

USA

Jan-Dec2014

By MARKET SHARE
(2014)



Lidocaine	49.35%
Articaine	34.86%
Mepivacaine	9.82%
Bupivacaine	3.3%
Prilocaine	2.7%

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Carpule or Cartridge?

March 1922

- Carpule® is a registered trademark of the glass dental cartridge by the Cook-Waite Company (Kodak)



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Cartridge Volume

1.8 mL v. 1.7 mL



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USA Dental Cartridges - VOLUME

Robertson, D. Nusstein, J. Reader, A. Beck, M. McCartney, M. The anesthetic efficacy of articaine in buccal infiltration of mandibular posterior teeth. J Am Dent Assoc. Aug;138(8): 1104-12. 2007.

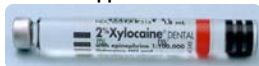
The mean (\pm standard deviation [SD]) amount expressed from the articaine cartridges in milliliters was 1.76 ± 0.023 mL (SD) and from the lidocaine cartridges was 1.76 ± 0.022 mL.

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North American Dental Cartridges

- 2 mL glass tube
- 0.2 mL silicone stopper



- 1.8 mL LA solution
- 1.7 mL as per FDA regulation
 - ~1.76 mL actual volume

Calculate dosage as
1.8 mL per cartridge

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What's New in Local Anesthesia?

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What's NEW in Local Anesthesia

- **Buffered LA** - The LA 'ON' Switch
- **Intranasal Local Anesthetic Mist**
- **C-CLAD** - Computer-Controlled Local Anesthetic Delivery
- **Phentolamine mesylate** - The LA 'OFF' Switch
- **Articaine** - Mandibular Infiltration

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How long does it take for pulpal anesthesia to develop?

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Intermediate - duration LAs

Drug	Onset (textbook)	Pulpal	Soft Tissue	
Lidocaine 2%	Epi 1:50k, 1:100k	3 - 5 min	60 min	3 - 5 hours
Articaine 4%	Epi 1:100k 1:200k	2 - 3 min	60 min	3 - 5 hours
Mepivacaine 2%	Epi 1:100k	3 - 5 min	60 min	3 - 5 hours
Prilocaine 4%	Epi 1:200k	3 - 5 min	60 min	3 - 8 hours

Epi = Epinephrine (Adrenalin)

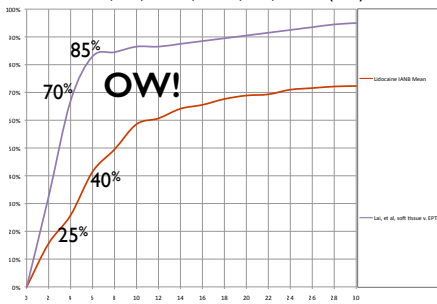
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**Some doctors use
soft tissue anesthesia
as a sign of
pulpal anesthesia**

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30 Minute Time Course for IANB Soft Tissue Analgesia (sharp dental explorer)
Lai, et al, OOOOE, Vol 102, No 4, P 462-68 (2006)



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**Soft tissue anesthesia
is *NEVER*
a guaranteed sign of
pulpal anesthesia**

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**Is there a guarantee?
YES!**



General Anesthesia

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Is there a guarantee?



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

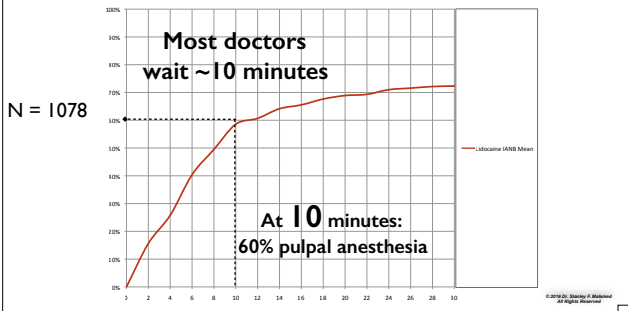


*Assumes no pulpal involvement

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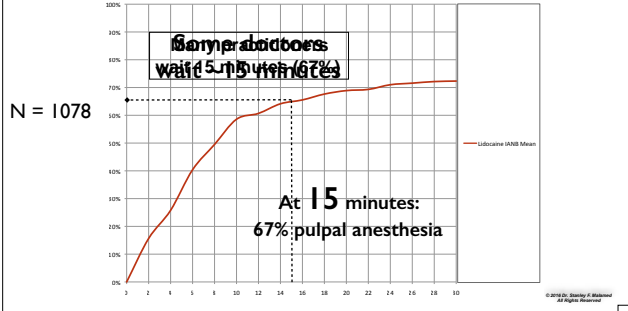
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30-Minute Time Course for Pulpal Analgesia - Lidocaine IANBs
Average for 28 PRP Studies - 1078 Subjects (1991 - 2008) with Lidocaine IANB Mean



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30-Minute Time Course for Pulpal Analgesia - Lidocaine IANBs
Average for 28 PRP Studies - 1078 Subjects (1991 - 2008) with Lidocaine IANB Mean



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IANB: Lidocaine + epinephrine

% clinically effective pulpal anesthesia

25% at 4 minutes

40% at 6 minutes

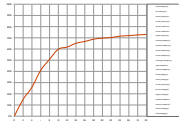
60% at 10 minutes

67% at 15 minutes

95% at 45 minutes

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Can we speed the onset of anesthesia . . . with Articaïne?

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Why do doctors LIKE articaïne?

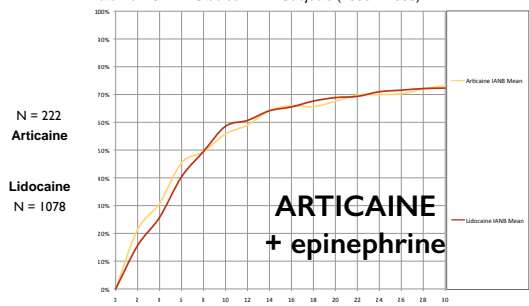
Anecdotal comments from dentists:

- “It works better”
- “I don’t miss as often”
- “Hard to get ‘numb’ patients are easier to numb with articaïne”
- “It works faster”

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30-Minute Time Course for Pulpal Analgesia - Articaïne IANBs
Data from 5 PRP Studies – 222 Subjects (1990 – 2008)



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Can we speed the onset of anesthesia with Articaïne?

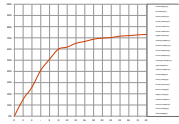


NO



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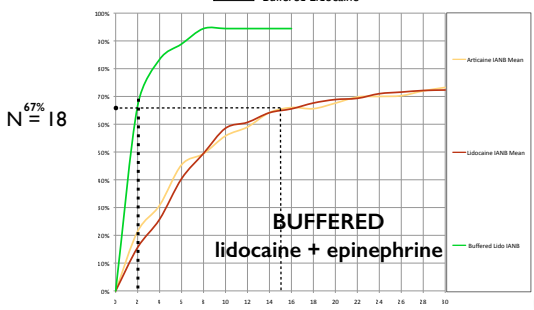
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Can we speed the onset of anesthesia . . .
by changing the pH of the LA solution?

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



90

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

😊 **YES** 😊

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The local anesthetic
"ON SWITCH"
Buffered Local Anesthetics
Alkalinized Local Anesthetics

92

Local anesthetics are **INSOLUBLE** in water.



93

We inject the acid-salt of the local anesthetic



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Six-Hour Time Course for Pulpal Analgesia (EPT) pH of Local Anesthetics



- pH
 - 'Plain' LA solution = ~6.5
 - Vasoconstrictor LA solution = ~3.5
 - Lemon juice = 3.3



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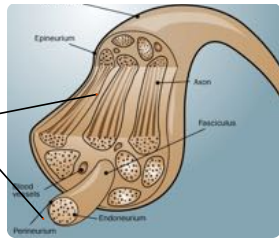


- So . . . inside the LA cartridge we have three things: **RN** **H⁺** and **RNH⁺**

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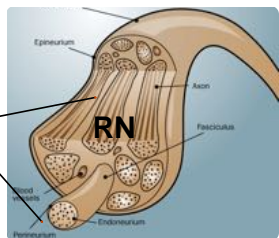
The LA must diffuse through the nerve membrane to block Na⁺ channels

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RN is LIPID SOLUBLE and CAN cross the lipid-rich nerve membrane

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RNH⁺ CANNOT cross the nerve membrane

RN % Un-ionized (RN) LA RN

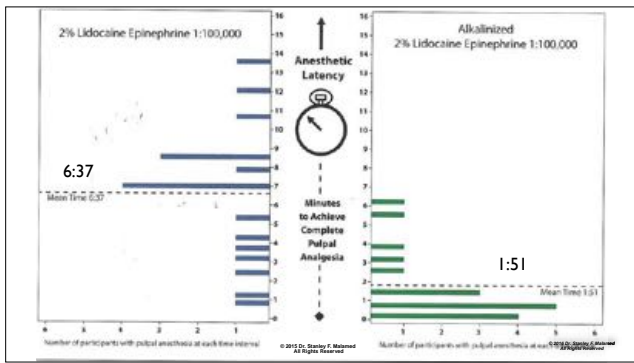
99

pH	Lidocaine pKa 7.9	Articaine pKa 7.8	Mepivacaine pKa 7.6	Bupivacaine pKa 8.1
3.5 (with epi)	0.004 RN	0.005 RN	0.008 RN	0.003 RN

The higher the pH
of the LA solution
the greater the percentage
of RN ions

100





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What IS buffering?



The addition of a chemical agent to a solution which increases its pH (towards the body's normal pH of 7.4 [7.35 - 7.5])

NaBicarbonate

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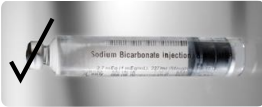
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What has happened to make LA buffering a reality in dentistry?

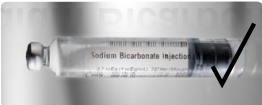
Stabilization
of the
NaBicarbonate Solution

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pH = 7.35 → 

BUFFERING
with
Sodium Bicarbonate

→ pH = 7.35 

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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

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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)

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The Onset® approach

Mandibular anesthesia - IANB

Administer buffered lidocaine IANB
DO NOT LEAVE THE PATIENT !!!
You know if your block is successful in 2 minutes

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The Onset® approach

Mandibular anesthesia - IANB

4. Check for pulpal anesthesia:
EPT or Endo-Ice
5. In 2 minutes following IANB
either begin tooth preparation or
readminister LA



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The Onset® approach

Maxillary anesthesia

Follow same procedure for maxillary teeth.

Onset time is at least as rapid
- if not faster -
following infiltration

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Anutra Medical www.anutramedical.com

Anutra Local Anesthetic Delivery System

Time is of the essence, pain is not an option.



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Effect of Buffered 4% Lidocaine on the Success of the Inferior Alveolar Nerve Block in Patients with Symptomatic Irreversible Pulpitis: A Prospective, Randomized, Double-blind Study

Jared Schellenberg, DDS, MS, Melissa Drum, DDS, MS,[†] Al Reader, DDS, MS,[‡] John Nusstein, DDS, MS,[§] Sara Fowler, DMD, MS,[¶] and Mike Beck, DDS, MA^{||}*

(J Endod 2015;41:791–796)

JOE

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We concluded that a 4% buffered lidocaine formulation did not result in a statistically significant increase in the success rate or a decrease in injection pain of the IAN block for mandibular posterior teeth in patients with symptomatic irreversible pulpitis.



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Previous studies by the Ohio State group have demonstrated that 4% lidocaine + epinephrine did **NOT** increase success in Symptomatic Irreversible Pulpitis

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This paper, concluding that buffered lidocaine did not increase clinical success in SIP, demonstrates the difficulties in achieving pain control in acutely infected teeth

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If you truly believe that the use of a buffered local anesthetic is going to be the answer to this problem, that you will be able to adequately anesthetize a tooth with SIP with 1 or 2 cartridges of buffered LA, you are simply kidding yourself - or you are delusional!

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Two to three cartridges of buffered LA will likely work 20% to 30% of the time.

However . . . buffering will allow you to proceed with your LA algorithm more rapidly.

You will know within 2 minutes, not 10-15, if block has worked.

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Inferior alveolar NB x 2 (or GGMNB) with buffered LIDOCAINE or ARTICAINE

Buccal infiltration at apex of tooth with 0.6 - 0.9 mL of buffered ARTICAINE

PDL (ILI) with LIDOCAINE or ARTICAINE

Intraosseous with buffered ARTICAINE

Intrapulpal

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Onset®

Drug	Onset number
Lidocaine	18 = NB 9 - Infiltration
Articaine 4%	9
Mepivacaine 2% & 3%	9
Prilocaine 4%	9

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Deposit a Local Anesthetic Close to a Nerve and It *WILL* Produce Pain Control

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If local anesthetics are so effective . . .

Then why is achieving effective pain control elusive, on occasion?

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Local Anesthetic Facts & Fiction

125

- Duration of PULPAL ANESTHESIA varies with TYPE of INJECTION
- TIME OF DAY affects local anesthetic efficacy & duration
- HAIR COLOR

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Anesthesiology 2004; 100:415-27

© 2004 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Chronobiology and Anesthesia

Dominique Chassard, M.D., Ph.D.,* Bernard Bruguerolle, M.D., Ph.D.†



Local anesthetics:

- Lidocaine - 1500 40% and 60% increased duration
- Mepivacaine - 1500 69% increased duration
- Articaine - 1400 37% increased clinical effectiveness



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Anesthesiology 2004; 101:279-83

© 2004 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Anesthetic Requirement Is Increased in Redheads

Edwin B. Liem, M.D.,* Chun-Ming Lin, M.D.,† Mohammad-Irfan Suleman, M.D.,† Anthony G. Doufas, M.D., Ph.D.,* Ronald G. Gregg, Ph.D.,§ Jacqueline M. Veauthier, Ph.D.,* Gary Loyd, M.D.,¶ Daniel I. Sessler, M.D.**



Discussion

Anesthetic requirement in redheads was increased 19%, a difference that was highly statistically significant ($P = 0.0004$). The results confirm anecdotal clinical impressions that anesthetic requirement is greater in redheads.



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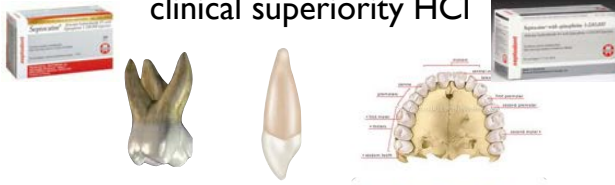
And, when problems achieving clinically adequate pain control occur . . .

Where do they happen?

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128

CLINICAL evidence of Articaine's clinical superiority HCl



- Articaine by maxillary infiltration will - in some instances - provide *PALATAL* soft tissue anesthesia following *BUCCAL* infiltration

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Table 2. How often do you encounter inefficiency of local anesthesia, both infiltration and conduction, during manipulation of various tooth groups?

N = 121

Tooth group	Often	Sometimes	Rarely	Very Rarely	Never
Mandibular Incisors	4	6	17	39	55
Mandibular Canines	4	10	23	39	45
31% Mandibular Premolars	8	29	18	41	25
55% Mandibular Molars	20	47	32	21	1

Staggio SV
Local anesthesia failure problems in conservative dental therapy clinic.
Stomatologia. 2006; 85(6):6-10

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134

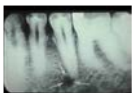
Anesthesia of
**Mandibular Premolars,
Canine, and
Incisors,**
can be easily accomplished

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Incisive NB

aka Mental NB (incorrectly)



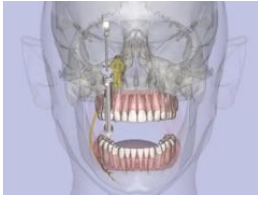
- Needle: 27 gauge short
- Insertion: MB fold at or anterior to mental foramen
- Target: Mental nerve as it exits mental foramen
- Volume: 0.6 mL
- Aspiration: 5.7%

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Incisive NB

aka Mental NB (incorrectly)



Insert needle in buccal fold and advance towards mental foramen

Aspirate
Deposit 0.6 mL outside foramen

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Incisive NB

aka Mental NB (incorrectly)

Apply finger pressure for 2 minutes



Vas = 0 -2

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So, now we're left with those 'darned' mandibular molars!

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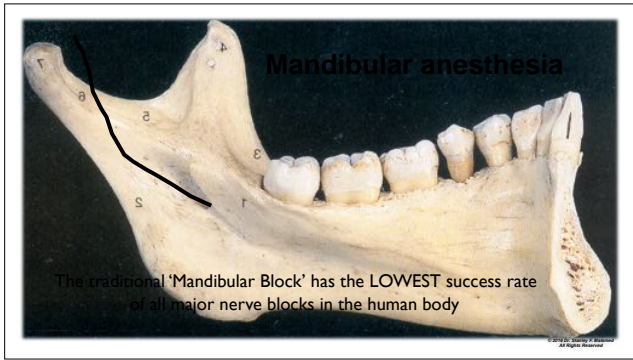
N = 121

	Often	Sometimes			
55%	20	47			

Shapiro DV.
Local anesthesia failure problems in conservative dental therapy clinic.
Stomatologia. 2006; 85(6):e-10

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A basic truism regarding INJECTIONS:

Once a needle penetrates the skin or mucous membrane, every injection is **BLIND**

142


A dentist will administer approximately 30,000 IANBs in the course of a 20-year career



Pogrel MA, Thamby S.
Permanent nerve involvement resulting from inferior alveolar nerve blocks
JADA 2000;131:901-907

143

Mandibular anesthesia

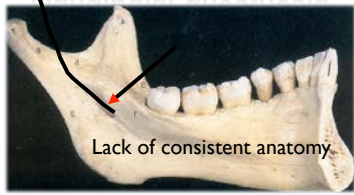


Bone is TOO thick

- *THE* problem with mandibular anesthesia, in the adult, is the density of the cortical plate of bone.
- It precludes the successful administration of suprapariosteal anesthesia.

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Mandibular anesthesia



A second problem with mandibular anesthesia, in the adult, is the lack of consistent landmarks.

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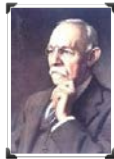
Inferior Alveolar NB

"Mandibular NB"
Inferior Dental Block

The 'HALSTED Approach'



William Stewart Halsted
1852-1922

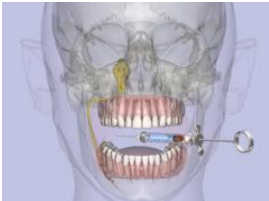


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Inferior Alveolar NB

"Mandibular NB"
Inferior Dental Block



Needle: 25- or 27- gauge long

Insertion: soft tissue on medial border of mandibular ramus

Target: IA nerve on lingual aspect of ramus prior to entering mandibular foramen

Volume: 1.5 mL

Aspiration: 10% - 15%

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Buccal NB

"Long" Buccal

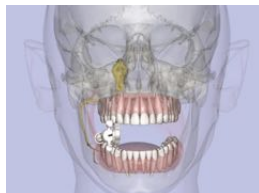
Needle: 25- or 27- gauge long

Insertion: mucus membrane distal and buccal to last mandibular molar

Target: buccal nerve passing over border of ramus

Volume: 0.3 mL

Aspiration: 0.7%



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Following completion of IANB & Buccal NBs . . .

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Seat patient comfortably upright

Speeds onset of anesthesia

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Inferior Alveolar NB

“Mandibular NB”
Inferior Dental Block

150

The experienced dentist administered the IANB by ‘feel’

Needle is advanced towards lingual aspect of body of mandible until bone is contacted.

Dr. ‘feels’ or ‘senses’ that the needle has contacted bone at the appropriate depth (based on years of clinical experience)



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Inferior Alveolar NB

“Mandibular NB”
Inferior Dental Block

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The most common reason for missing the IANB is depositing LA solution too low. (BELOW the mandibular foramen)

The ‘nerve’ is gone!



A little higher is a little better

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The limited success of the IANB has led to the development of alternative techniques:

- Gow-Gates Mandibular Nerve Block
- Vazirani - Akinosi (closed mouth) Mandibular Nerve Block
- Periodontal ligament injection (intraalveolar)
- Intraosseous anesthesia
- Articaine HCl via buccal infiltration

152

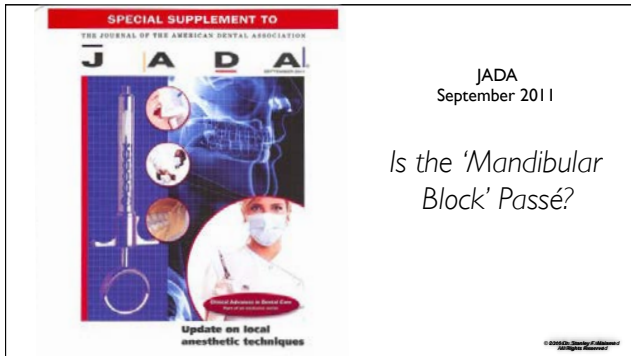
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So the question is:

Is the INFERIOR ALVEOLAR NERVE BLOCK Passé ?

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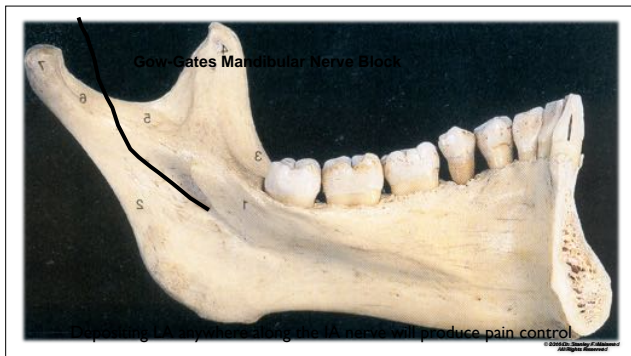
154



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1973 ... **Gow-Gates Mandibular Nerve Block**

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Gow-Gates Mandibular Nerve Block

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Anesthesia

- Mandibular teeth to midline
- Buccal soft tissues to midline
- Anterior 2/3 of tongue and floor of oral cavity
- Lingual soft tissues and periosteum
- Body of mandible, inferior portion of ramus
- Skin over zygoma, posterior portion of cheek, and temporal region



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Gow-Gates Mandibular Nerve Block

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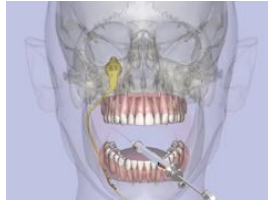
Needle: 25 gauge long

Insertion: At height of ML cusp of maxillary 2nd molar, just distal to 2nd molar

Target: Lateral aspect of condylar neck

Volume: 1.8 to 3.0 mL

Aspiration: < 2%



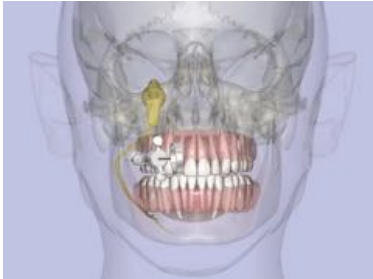
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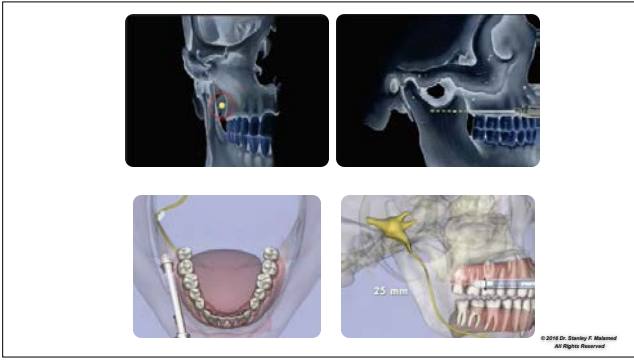
159

Akinosi-Vazirani Mandibular NB Vazirani-Akinosi Mandibular NB

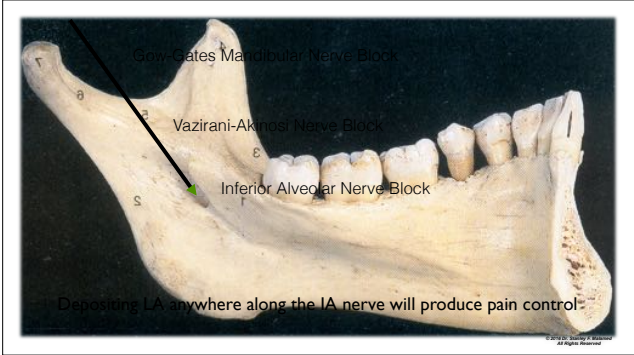
160



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162

Periodontal ligament injection: a clinical evaluation

RE Walton and BJ Abbott *JADA* October 1, 1981 103(4): 571-575

1982 . . . Periodontal Ligament Injection (PDL)
aka **Intraligamentary Injection (ILI)**

163

Periodontal Ligament Injection (PDL, ILI)

- 27 gauge short needle
- Place interproximally
- **SLOWLY** deposit 0.2 mL per root

164

165

1980's . . . Intraosseous Anesthesia (10)

The Stabident System of intraosseous anesthesia

Leonard M, J Amer Dent Assoc October 103(4): 571-575, 1981

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Nusstein J, Reader A, Nist R, Beck M, Meyers WJ.
Anesthetic efficacy of the supplemental intraosseous injection of 2%
lidocaine with 1:100,000 epinephrine in irreversible pulpitis.
J Endodont 24(7):487-491, 1998

**88% successful
mandibular molars**

Parente SA, Anderson RV, Herman WW, Kimbrough WF, Weller RN.
Anesthetic efficacy of the supplemental intraosseous injection for
teeth with irreversible pulpitis.
J Endodont 24(12):826-828, 1998

**91% successful
mandibular molars**

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Intraosseous Anesthesia (10)

Stabident SYSTEM
Intraosseous Anesthesia for the New Century

Stabident System is a revolutionary new intraosseous anesthesia system. It is designed to provide superior anesthesia for the most difficult cases. The system consists of a Stabident System Intraosseous Anesthetic System (SAS) and a Stabident System Intraosseous Anesthetic System (SIAS).

Stabident System Intraosseous Anesthetic System (SAS)

- Provides superior anesthesia for the most difficult cases.
- The SAS is designed to provide superior anesthesia for the most difficult cases.
- The SAS is designed to provide superior anesthesia for the most difficult cases.

Stabident System Intraosseous Anesthetic System (SIAS)

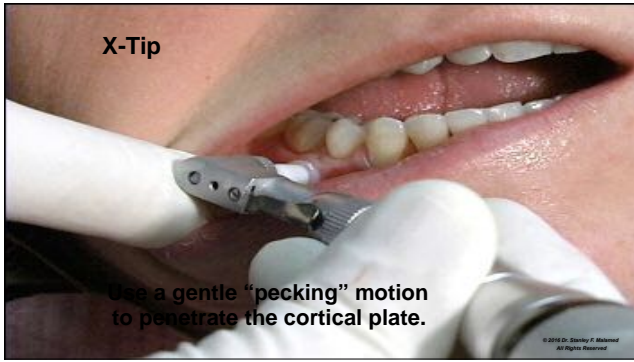
- Provides superior anesthesia for the most difficult cases.
- The SIAS is designed to provide superior anesthesia for the most difficult cases.
- The SIAS is designed to provide superior anesthesia for the most difficult cases.

Flairfax Dental

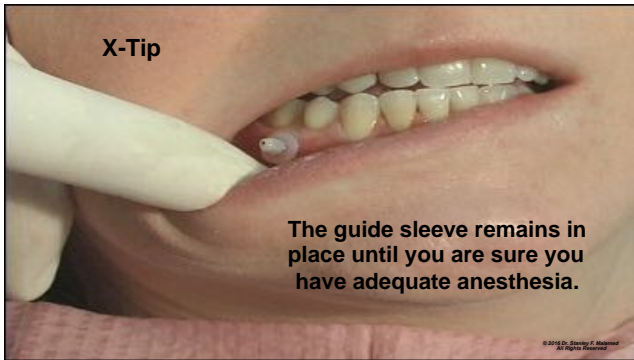
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Intraosseous Anesthesia (IO)


<p>ADVANTAGES</p> <ul style="list-style-type: none"> Relatively comfortable Single / multiple tooth anesthesia No lip / tongue 	<p>DISADVANTAGES</p> <ul style="list-style-type: none"> Highly vascular region LA OD Vasopressor "shakes" use 1:200k or plain Can't locate hole with needle
--	--

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Intraseptal (Crestal) Anesthesia

Application of Crestal Anesthesia for Treatment of Class I Caries in Posterior Mandibular Teeth

Koroush Taheri Talesh¹ and Shiva Solahaye Kahnemouli^{2,*}



J Dent Res Dent Clin Dent Prospect.
Winter 2011 5(1): 17-22, 2011



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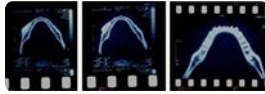
172

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Intraseptal (Crestal) Anesthesia

Percentage (number) of successful anesthesia achieved by crestal anesthesia (CA) and inferior alveolar nerve block (IANB) techniques

Tooth*	CA	IANB
First premolar	96 (16)	82 (17)
Second premolar	98 (26)	83 (21)
First molar	100 (52)	85 (45)
Second molar	100 (40)	88 (36)
Third molar	100 (19)	93 (15)



J Dent Res Dent Clin Dent Prospect.
Winter 2011 5(1): 17-22, 2011

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Intraseptal (Crestal) Anesthesia

	Crestal	IANB	
Onset	7.00 +/- 0.71	3.30 +/- 0.67	<0.001
Duration	23.10 +/- 2.13	32.10 +/- 2.02	<0.05
Pain	1.54 +/- 0.18	3.44 +/- 0.22	<0.001
Volume	0.4 mL +/- 2.07	1.99 mL	

J Dent Res Dent Clin Dent Prospect.
Winter 2011 5(1): 17-22, 2011

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Intraseptal (Crestal) Anesthesia



Figure 15-8. Area of insertion for an intraseptal injection.



Figure 15-9. Orientation of the needle for an intraseptal injection.

J Dent Res Dent Clin Dent Prospect.
Winter 2011 5(1): 17-22, 2011

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ARTICAINE

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Articaine

Ultracain
Septocaine
Articadent
Vivacaine
Septanest
Alphacaine
Zorcaine



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Articaine

4% with
epinephrine
1:100,000
1:200,000



Synthesized in Germany 1969
Introduced Germany 1976
Canada 1985
USA 2000

1st & only Local anesthetic designed for dentistry

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Articaine 4% Epinephrine 1:100,000 & 200,000



Duration of pulpal anesthesia (infiltration) = 60 minutes
Duration of pulpal anesthesia (nerve block) = 60 minutes
Duration of soft tissue anesthesia = 3 - 5 hours

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Articaine infiltration
as a **sole** injection
for mandibular anesthesia

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The anesthetic efficacy of articaine in buccal infiltration of mandibular posterior teeth

Douglas Robertson, DDS, MS; John Neustein, DDS, MS; Al Reader, DDS, MS; Mike Beck, DDS, MA; Melissa McCortney, DDS, MS
JADA 138(8):1104-1112, 2007

Results -1:

	Articaine	Lidocaine
Pulp test every 3 min		
Mandibular 2 nd Molar	75%	45%
Mandibular 1 st Molar	87%	57%
Mandibular 2 nd Premolar	92%	67%
Mandibular 1 st Premolar	86%	61%

p value for all: >.0001

SUCCESS = 80/80 on 2 consecutive tests

2007

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The anesthetic efficacy of articaine in buccal infiltration of mandibular posterior teeth

Douglas Robertson, DDS, MS; John Neustein, DDS, MS; Al Reader, DDS, MS; Mike Beck, DDS, MA; Melissa McCortney, DDS, MS

Results -2:

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

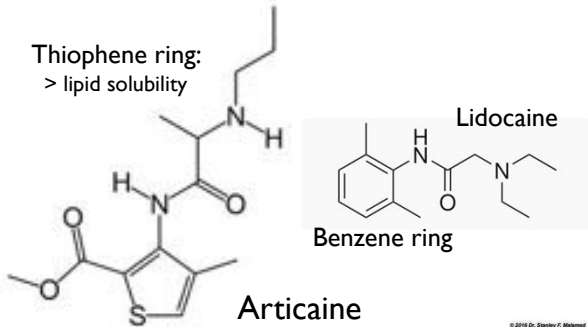
Tooth	Articaine onset (min) +/- Standard Deviation	Lidocaine onset (min) +/- Standard Deviation	P value
2 nd molar	4.6 +/- 4.0	11.1 +/- 9.5	.0001
1 st molar	4.2 +/- 3.1	7.7 +/- 4.3	.0002
2 nd premolar	4.3 +/- 2.3	6.9 +/- 6.6	.0014
1 st premolar	4.7 +/- 2.4	6.3 +/- 3.1	.0137

2007

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182

Thiophene ring:
> lipid solubility



Articaine

183



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

2002

Mandibular Incisors

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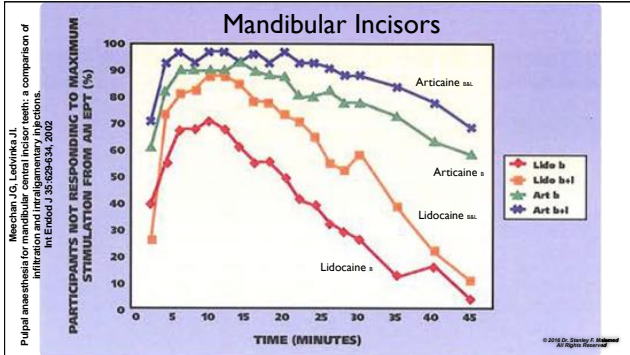
184

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Results-1:

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

2002



186

187

Discussion:

The increased success rate for infiltration in the adult mandibular incisor region is thought to be due to the fact that the cortical plate of bone, both buccal and lingual, is quite thin and might provide little resistance to infiltration.

2002

Buccal infiltration -
ARTICAINE

Advantages

- Profound pulpal anesthesia
- 30 to 40 minute duration of pulpal anesthesia
- Minimal accessory soft tissue anesthesia
- Tongue

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Buccal infiltration -
ARTICAINE

Disadvantage
I can't think of any,
unless it doesn't work!

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Buccal infiltration -
ARTICAINE

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.

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Articaine infiltration
as a **supplement**
to IANB

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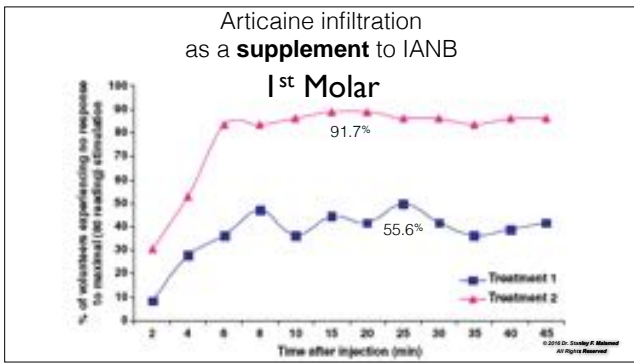
Kanaa JM, Whitworth JM, Corbett IP, Meehan JG
Articaine buccal infiltration enhances the effectiveness of lidocaine inferior alveolar nerve block.
Int Endodont J 42:238-246, 2009

- 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

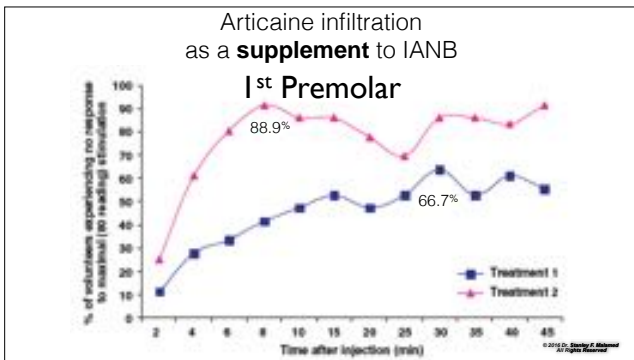


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194

Is the 'Mandibular' Block Passé?

Perhaps
NOT YET, but ...
you've got
great options

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- Is the 'Mandibular' Block Passé?
- Options:
- Incisive (mental) nerve block
 - Gow-Gates mandibular nerve block
 - Akinosi-Vazirani nerve block
 - PDL, Intraosseous, Intraseptal
 - Articaine by mandibular infiltration
 - Buffered local anesthetic
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Recommendation
Premolars, Canine, Incisors

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Incisive NB

- Buffered lidocaine or articaine
- 0.6 mL

If ineffective:

- PDL or Intraseptal

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Recommendation
Canine or Incisor

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Infiltration of buffered articaine
◦ 0.5 mL buccal fold for ~10 minute treatment

Infiltration of buffered articaine
◦ 0.5 mL buccal **AND** lingual for 15 - 30 minute treatment

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Recommendation
Posterior teeth

199

IANB or GGMNB utilizing

- Buffered lidocaine or articaine, followed by
- Buffered articaine buccal infiltration at apex of tooth
- 0.5 mL

If ineffective:

- PDL, IO or Intraseptal

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The local anesthetic
“OFF SWITCH”
Phentolamine Mesylate

200

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"Doctor,
Do I have to be
frozen for so long?"

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Intermediate - duration LAs

Drug	Onset (textbook)	Pulpal	Soft Tissue	
Lidocaine 2%	Epi 1:50k, 1:100k	3 - 5 min	60 min	3 - 5 hrs
Articaine 4%	Epi 1:100k 1:200k	2 - 3 min	60 min	3 - 5 hrs
Mepivacaine 2%	Epi 1:100k	3 - 5 min	60 min	3 - 5 hrs
Prilocaine 4%	Epi 1:200k	3 - 5 min	60 min	3 - 8 hrs

Epi = Epinephrine (Adrenalin)

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

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13% of pediatric patients receiving IANB suffer post-treatment traumatic injury to soft tissues.



Age	% with soft tissue
< 4 years	18%
4 - 7	16%
8 - 11	13%
12+	7%



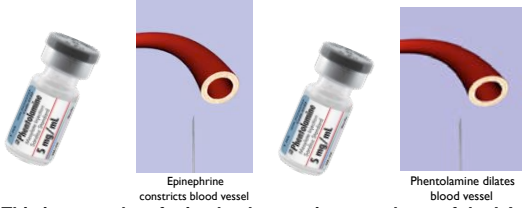
College C, Feigl R, Wandera A, Strange M. Bilateral versus unilateral mandibular block anesthesia in a pediatric population. *Pediatr Dent.* 22(6):453-457, 2000.

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- Phentolamine mesylate is a vasodilator (an alpha adrenergic antagonist) that increases vascular perfusion in the area of injection.

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- 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.

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Local Anesthesia Reversal

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0.23 mg/mL - dental

5.0 mg/mL - medical

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Local Anesthesia Reversal

207

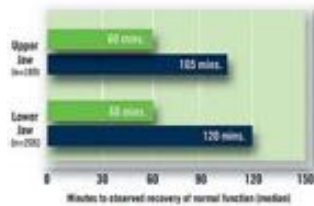


0.23 mg/mL - dental

Does it work?

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YES!



YES!

OraVerse
Phentolamine Mesylate

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UPPER LIP	
Control	133 minutes
PM	50 minutes
Accelerated by:	83 minutes

LOWER LIP	
Control	155 minutes
PM	70 minutes
Accelerated by:	85 minutes

Perception of normal appearance and function Accelerated by 60 min.

Restoration of normal function Accelerated by 60 min.

Restoration of normal sensation of tongue Accelerated by 65 min.

Thanks to:
Suzete Brasil, Erica Dicterow, Fariba Neumann & Joan Ong

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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

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The local anesthetic "OFF SWITCH" Phentolamine Mesylate

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New & Exciting

C-CLAD

Computer-Controlled Local Anesthetic Delivery

INTRANASAL LOCAL ANESTHETIC MIST

Tetracaine + Oxymetazoline

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Computer-Controlled Local Anesthetic Delivery 'C-CLAD'

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C-CLAD



STA-Wand

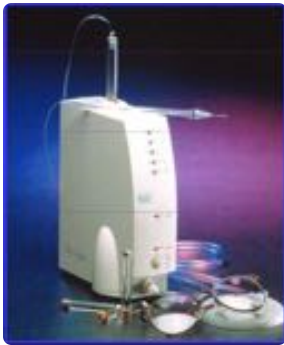


Quick Sleeper

The ability to administer what are considered to be
"PAINFUL" injections
(palatal, PDL)
(almost) painlessly and successfully

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The WAND

The 1st CCLAD system
1998



Dr. Mark Hochman

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Hochman M, Chiarello D, Hochman C, Lopatkin R, Pergola S.

Clinical Research

Computerized local anesthesia vs. traditional
syringe technique: Subjective pain response.

NYS Dental Journal – 1997

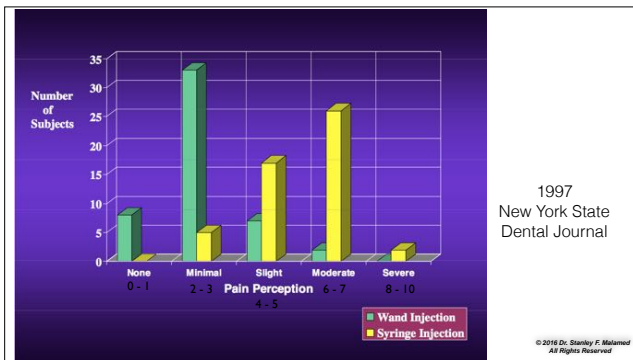
Method & Material

- 50 patients (dentists)
- Palatal injection
- Each patient served as a control
- Subjects blinded to technique
- VAS scale, subjective pain scoring
- 3 examiners performed testing

CCLADS: Fixed flow-rate = 0.005ml/sec = 2 minutes.
Handheld syringe: Maintained injection for 2 minutes.

1997
New York State
Dental Journal

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C-CLAD & Pediatrics

TABLE 2
EFFECTIVENESS OF INTRASULCULAR ANESTHESIA IN FIRST AND SECOND PRIMARY MOLARS.

TREATMENT	NUMBER (PERCENTAGE) OF TEETH IN WHICH ANESTHESIA WAS EFFECTIVE			
	First Primary Molar		Second Primary Molar	
	Mandible	Maxilla	Mandible	Maxilla
Amalgam or Resin-Based Composite Restoration	58 (100)	8 (100)	55 (95)	16 (94)
Professional Stainless Steel Crowns	9 (90)	0 (0)	15 (94)	1 (100)
Extraction	3 (38)	6 (86)	7 (88)	5 (100)
Palpation	7 (78)	1 (100)	8 (87)	6 (75)
TOTAL	57 (88)	15 (88)	85 (90)	28 (90)

CONCLUSION
CDS-IS is a safe, efficient and reliable technique to achieve adequate anesthesia in children's primary molars, primarily for amalgam, resin-based composite or stainless steel crown restorations. The effectiveness is not related to sex or to tooth location (first or second primary molars). In addition, unlike intraligamentary anesthetic delivered via a high-pressure syringe, low-pressure CDS-IS anesthesia does not increase the incidence of FDP. ■

J Amer Dent Assoc 136(10):1418-1425, 2005

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C-CLAD & Pediatrics

What this paper adds

- Intraligamentary injection delivered to primary molars by a C-CLAD does not damage the underlying permanent dental bud in children 4.1 years and older.

Why this paper important to paediatric dentists

- Paediatric dentist will be free to use C-CLAD-III in primary molars in children aged 4.1 and older without worrying about the consequence of this technique on the underlying developing dental bud.
- Increasing usage of C-CLAD-III in children will increase the cooperation of the children during administration of local anaesthesia
 - decrease the prevalence of traumatic injuries to soft tissue following insertion of local anaesthesia
 - decrease the discomfort associated with the feeling of anaesthesia of soft tissue.

Int J Pediatr Dent 20:270-275, 2010

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“New” & Exciting

Intranasal Local Anesthesia in the Maxilla

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Intranasal Drug Administration

- **Emergency medicine**
 - Pediatric grand mal status . . . Midazolam
- **Pediatric sedation (dentistry) . . . Midazolam**

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Intranasal Local Anesthetic Mist



Intranasal Local Anesthetic Mist

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KOVANAZE™

KOVANAZE™

KOVANAZE™

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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 OTC nasal decongestants

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KOVANAZE™ KOVANAZE™ KOVANAZE™

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Safety and Efficacy of a Novel Nasal Spray for Maxillary Dental Anesthesia
S.F. Canalis*, M.C. Halperin†, J. Apple†, E.A. Parker, Jr.†, C.E. Parker, D.A. Goldberg†, S.D. Seligson† and E.A. Alshuler*

Journal of Dental Research :92(suppl 1):43S-48S, 2013

Group 1	N = 45	Group 2
	N = 30	N = 15
3 doses (at 0, 4, 8 minutes) in each nostril tetracaine 3% + oxymetazoline 0.05%		3 doses in each nostril buffered saline nasal spray
+		+
Sham infiltration injection		Active-control infiltration injection (1.8 mL lidocaine 2% + epi 1:100k)

Dental procedure begins 15 minutes after initial nasal spray



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Journal of Dental Research :92(suppl 1):43S-48S, 2013

Data collection sites

- Distal to apex of tooth (maxillary 1st molar) at deepest point in buccal vestibule
- Apical to maxillary lateral incisor at deepest point in labial vestibule
- Incisive papilla of the hard palate
- At junction of alveolar process & hard palate medial to maxillary 2nd premolar

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Journal of Dental Research :92(suppl 1):43S-48S, 2013

Study End Points

- Proportion of patients who received NO rescue anesthesia
- Proportion of patients who had a global VAS score of < 85 mm (less than moderate pain) upon completion of treatment

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Safety and Efficacy of a Novel Nasal Spray for Maxillary Dental Anesthesia

J.D. Caputo^{1*}, M.C. Halbeson², E. Ayoub³, E.A. Parker, Jr.¹, C.E. Parker¹, D.A. Gorkan⁴, S.C. Solberg¹ and E.A. Winkler¹

Results

1. Proportion of patients who received NO rescue anesthesia

25 of 30 (83.3%) in nasal spray group

14 of 15 (93.3%) in lidocaine group

90% of test individuals had anesthesia success from premolar to premolar

Journal of Dental Research
:92(suppl1):43S-48S, 2013

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Safety and Efficacy of a Novel Nasal Spray for Maxillary Dental Anesthesia

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Results

2. Proportion of patients who had a global VAS score of < 85 mm (less than moderate pain) upon completion of treatment

ALL 25 patients who did not receive rescue anesthesia reported less than moderate pain (successful anesthesia)

Journal of Dental Research
:92(suppl1):43S-48S, 2013

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Safety and Efficacy of a Novel Nasal Spray for Maxillary Dental Anesthesia

J.D. Caputo^{1*}, M.C. Halbeson², E. Ayoub³, E.A. Parker, Jr.¹, C.E. Parker¹, D.A. Gorkan⁴, S.C. Solberg¹ and E.A. Winkler¹

Discussion

83.3% success = drug provided anesthesia of maxillary teeth sufficient for performance of restorative procedures in most patients

90% of participants had anesthesia success on teeth #4 (15) through #13 (25)

Journal of Dental Research
:92(suppl1):43S-48S, 2013

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Safety and Efficacy of a Novel Nasal Spray for Maxillary Dental Anesthesia

J.D. Caputo^{1*}, M.C. Halbeson², E. Ayoub³, E.A. Parker, Jr.¹, C.E. Parker¹, D.A. Gorkan⁴, S.C. Solberg¹ and E.A. Winkler¹

Discussion

90% of participants had anesthesia success on teeth #4 (15) through #13 (25)

MSA (middle superior alveolar) & PSA (posterior superior alveolar) nerves consistently provide plural anesthesia to these teeth

Journal of Dental Research
:92(suppl1):43S-48S, 2013

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Nasal Mist KOVANAZE™

83% success
1st molar to 1st molar

90% success
Premolar to premolar

17% failure on 1st molar

Palate

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The cardiovascular effects and pharmacokinetics of intranasal tetracaine plus oxymetazoline

Preliminary findings

J Amer Dent Assoc
143(8):872-880, 2012

Bolin Glennkoppler, DDS, MD; Lawrence M. Levin, DMD, MD; Jui C. Chou, DMD, MD; Anthony T. Cavali, PhD; Matthew Halkicour, MD; Stacy A. Serrin, CGO; Paul A. Moore, DMD, PhD; Elliot V. Harsh, DMD, MS, PhD

Mean maximum changes from baseline in cardiovascular and oxygen saturation parameters.

ANESTHETIC DOSE	MEAN ± STANDARD ERROR OF THE MEAN			
	Heart Rate (Beats/Minute)	Systolic Blood Pressure (mm Hg*)	Diastolic Blood Pressure (mm Hg)	Oxygen Saturation (Percentage)
Maximum Recommended Dose (MRD)†	-6.8 ± 3.6	+5.2 ± 4.0	+8.0 ± 3.3‡	+0.5 ± 0.4
Two-Times MRD‡	-2.6 ± 4.50	+11.4 ± 4.3	+3.1 ± 4.9	-0.3 ± 0.3

* mm Hg; Millimeters of mercury.
† Equal to 18 milligrams tetracaine/0.3 mg oxymetazoline.
‡ Significantly different (P < .05) from baseline value.
§ Equal to 36 mg tetracaine/0.6 mg oxymetazoline.

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Adverse events and expected adverse effects of the intranasal drug.

Five cardiovascular effects and pharmacokinetics of intranasal tetracaine plus oxymetazoline

Bolin Glennkoppler, DDS, MD; Lawrence M. Levin, DMD, MD; Jui C. Chou, DMD, MD; Anthony T. Cavali, PhD; Matthew Halkicour, MD; Stacy A. Serrin, CGO; Paul A. Moore, DMD, PhD; Elliot V. Harsh, DMD, MS, PhD

ADVERSE EVENT OR EXPECTED ADVERSE EFFECT	NO. OF PARTICIPANTS	
	Maximum Recommended Dose (MRD) (N = 42)	Two-Times MRD (N = 42)
Participants With at Least One Adverse Event	6	7
Elevated blood pressure	1	1
Burning sensation in nose, nasal pharynx	0	3
Cut to right hand	0	1
Discomfort at spray site	0	3
Anxious feeling	0	1
Headache	3	3
Itching at back of throat	0	1
Nasal dryness	1	0
Nasal stuffiness (moderate)	1	2
Nausea	0	1
Numbness, altered sensation when breathing nose, mouth's breathing slightly	2	1
Numbness sensation on top of head	0	1
Profusional drip	0	2
Ringing in ear	0	1
Sore throat	1	1
Sore throat	1	0
Throat irritation (moderate)	0	1
Tingling sensation on top of head	1	1
Vomiting	0	1
Participants With at Least One Expected Adverse Effect*	6	11
Runny nose (MRD)	6	9
Nasal stuffiness (MRD)	4	3

* Expected effects include those of mild intensity listed on the package insert for over-the-counter nasal decongestant sprays containing 0.05 percent oxymetazoline.

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Intranasal Local Anesthetic Mist

2016

Intranasal Local Anesthetic Mist

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Whats's New in Local Anesthesia

In the more distant future

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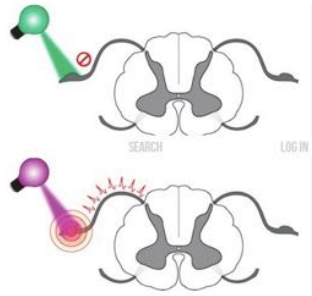
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Light-activated / Light-inactivated Local Anesthetic

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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

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DRUGS

Very Long-Acting Analgesia

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DRUGS

EXPAREL®

(bupivacaine liposome injectable suspension)
PATIENT-FOCUSED PAIN CONTROL

Up to
72 hours

EXPAREL — The Only Single-Dose Local Anesthetic That Controls Pain for Up to 72 Hours

EXPAREL is a local anesthetic that allows bupivacaine in combination with the proven product delivery platform, StearForte®. A single intraperitoneal injection treats pain at the source with reduced opioid requirements for up to 72 hours.

Preclinical studies have demonstrated the safety and efficacy of EXPAREL in patients undergoing herniotomy and herniorrhaphy procedures. The clinical benefit of the alternative decrease in opioid consumption was not demonstrated.

When used as part of a multimodal treatment regimen, EXPAREL can provide non-opioid pain control that lasts as long as the most intense postoperative pain, without the need for sedation, pumps, or other delivery devices.¹

EXPAREL is indicated for administration into the surgical site to produce postoperative analgesia.¹

Efficacy and Safety

The efficacy of EXPAREL was compared to placebo in two multicenter, randomized, double-blind clinical trials conducted in an adult obese population (herniotomy and an orthotopic herniorrhaphy surgical model).

The safety of EXPAREL has been evaluated in 21 clinical trials which include over 1300 subjects in the study population. EXPAREL administration results into the surgical site was evaluated in 10 randomized, double-blind clinical studies involving 800 patients undergoing various surgical procedures. Patients were administered a dose ranging from 80 mg to 332 mg of EXPAREL.

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Ultra Long-Acting Analgesia

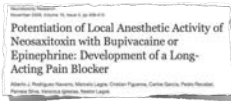
Neosaxitoxin

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Neosaxitoxin

Over 1 week of analgesia (in rodents)
without histologic or functional sequelae



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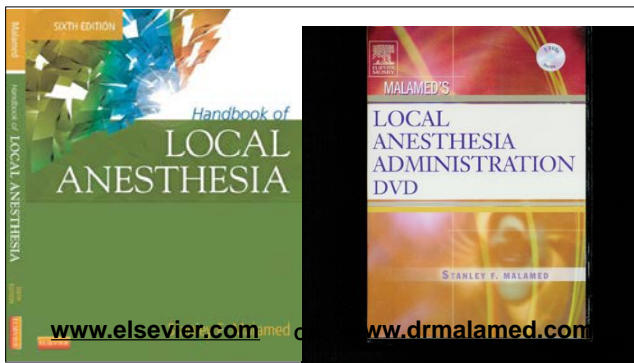
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