Mythbusters – Local Anesthesia Edition

<u>Myth #1</u>: "My Dentist Still Uses Novocain"

We all know this myth is totally BUSTED, but let's briefly look back at the history of Novocain… by the way there is no "e" in Novocain (the brand name for procaine)

Historical Perspective

- The first local anesthetic was Cocaine
- Carl Koller (September 1884) used cocaine as a local anesthetic during a surgical procedure (for glaucoma)
- "The facts are that neither Freud nor I discovered that cocaine is a local anesthetic. This was discovered by Dr. Albert Niemann, who extracted the potent principle from coca leaves in 1860" ~ Dr. Koller (*JAMA* 1941;117(15)1284.)
- Dr. Koller was nominated for the Nobel Prize several times but never received it, mostly because his discovery was made 17 years before the Nobel Prize was created. (www.dentaleconomics.com/articles/print/volume-89/issue-3/features/the-story-of-local-anesthesia.htm)
- William Halsted (November 1884) developed the principles of nerve block using Cocaine
- Infraorbital and IA blocks were performed on him as a "guinea pig" it took him 3 years to overcome his resulting Cocaine addiction (*Ann Surg* 1997 May;225(5):445-58.)
- Due to the unfavorable therapeutic index of Cocaine the search was on for a less toxic compound with LA properties:
  1904 – Alfred Einhorn synthesized the ester Procaine (Novocain)
  1943 – Nils Lofgren synthesized Lidocaine which possessed:
  - Less allergenicity
  - More potency
  - More rapid onset of action
  - First brand name = Xylocaine (Astra Pharmaceutical)

  2000 – Articaine granted FDA approval in the US
  2008 – OraVerse (phentolamine mesylate) approved

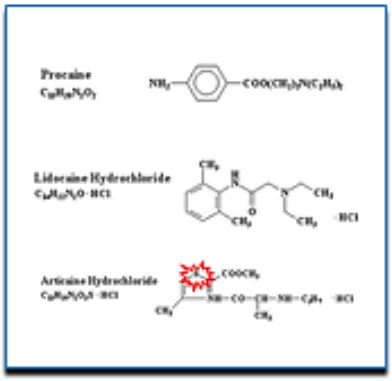
A little more info on Procaine…

- First synthetic injectable local anesthesia used in dentistry
- Produced the greatest amount of vasodilation of all currently used local anesthetics
- Ester type – capable of allergy - PABA
- pKa=9.1, slow onset (6-10 minutes) and at physiologic pH existed as 90% charged (inactive) and 10% uncharged (active)
- Duration of action (epinephrine can be added to prolong action)
- Pulpal anesthesia (mx infiltration) lasts about 5 minutes.
- Soft tissue anesthesia lasts for approximately 30 minutes
- Blocks are not recommended (slow onset, ultra short duration)
- Systemic toxicity negligible because procaine is rapidly destroyed in the plasma

Local Anesthetics – Esters vs. Amides vs. Articaine?

Esters
- Cocaine
- Procaine (Novocain)
- Propoxycaine
- Benzocaine
- Chloroprocaine
- Dyclonine (Cēpacol Maximum Strength)
- Tetracaine (Cēpacol Viractin, Pontocaine)

Amides
- Lidocaine
- Mepivacaine
- Prilocaine
- Bupivacaine
- Etidocaine
- Articaine



Malamed SF. Articaine 30 Years Later. Oral Health, Feb 2016.

LOCAL ANESTHESIA MYTHBUSTERS

Approximate Year of First Clinical Use

- Articaine (mixed Ester and Amide)
- Developed in Germany in 1969
- FDA approved in US 2000 (Europe 1976, Canada 1983)
- Marketed as Articadent®, Septocaine®, Zorcaine®, Orabloc®
- Supplied in 1.7 mL cartridges
- Half-Life is approximately 27 minutes
- Max number of cartridges in an adult is 7

Cocaine	1884
Benzocaine	1900
Procaine	1905
Dibucaine	1929
Tetracaine	1930
Lidocaine	1948
Nesacaine	1955
Mepivacaine	1957
Prilocaine	1960
Bupivacaine	1963
Articaine	1969
Ropivacaine	1992

LOCAL ANESTHESIA MYTHBUSTERS

<u>1.7mL vs. 1.8mL on Local Anesthetic Cartridges</u>

- Average cartridge volume in U.S. is 1.76mL (*JADA* 2007;138:1104–1112.)
- During the approval process for Articaine in the 1990's the FDA asked the manufacturer, "Can you guarantee that each and every cartridge contains at least 1.8mL of solution?" the answer was "No." (Malamed SF. Clinical Action of Specific Agents. In: Handbook of Local Anesthesia. 6th Edition. 2014. p 56.)
- Therefore, manufacturers began printing a volume of 1.7mL on the cartridges

Lots of Brand Names for local anesthetic solutions…
- Retail costs for local anesthetics $30-50
- Exception is Bupivacaine ~$60

Myth #2: "Doctor, I'm allergic to epinephrine!"

Again, we know this myth is BUSTED, but this is such a common patient report that is worth looking into!

Pharmacokinetics of Epinephrine

- Naturally occurring
- It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system
- Onset of action: 1-2 minutes
- Duration of action: 1-2 minutes
- Acts directly on alpha and beta adrenergic receptors (50:50, alpha constricts and beta dilates)
- Antagonizes the effects of histamine
- Stimulates the liver to produce and raise blood glucose levels
- Increases HR, cardiac contractility, and systemic vascular resistance
- Increases myocardial oxygen demand

Epinephrine – Historical Progression

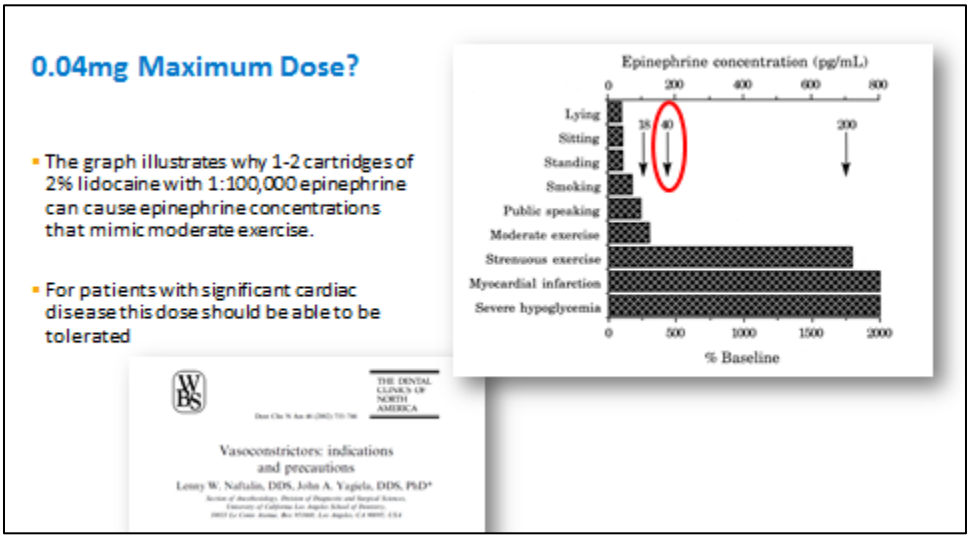
- In 1986, the AHA emphasized safety by concluding, "Vasoconstrictor agents should be used in local anesthesia solutions during dental practice only when it is clear that the procedure will be shortened or the analgesia rendered more profound. When a vasoconstrictor is indicated, extreme care should be taken to avoid intravascular injection. The minimum possible amount of vasoconstrictor should be used."

- Malamed and Bennet, proposed 0.04mg as a maximum dose of epinephrine for patients with severe cardiac disease

Table I. Contraindications to vasoconstrictors in dentistry

Absolute contraindications
Heart diseases
a. Unstable angina
b. Recent myocardial infarction
c. Recent coronary artery bypass surgery
d. Refractory arrhythmias
e. Untreated or uncontrolled severe hypertension
f. Untreated or uncontrolled congestive heart failure
Uncontrolled hyperthyroidism
Uncontrolled diabetes
Sulfite sensitivity; steroid-dependent asthma
Pheochromocytoma
Relative contraindications
Patients taking tricyclic antidepressants
Patients taking phenothiazine compounds
Patients taking monoamine oxidase inhibitors
Patients taking nonselective β-blockers
Cocaine abuser

References:
Dent Clin North Am 2002;46(4):733-46.
Oral Surg Oral Med Oral Pathol 1992;74:679-86.



The "Reaction"

- But what about those patients who suffer from the following symptoms after local anesthetic injection?
- Heart palpitations or racing heartbeat
- Pale, sweaty skin
- Dizziness
- Nervousness
- Headache
- Most likely to occur during IANB
- Rates of positive aspiration for IANB :
    - 5.8% in approximately 6000 injections (Ann Anat 1999;181:105-6.)
    - 8.1% in 731 injections (JADA 1999:130:496-9)
    - Other authors have suggested a wider range (2.6-30%) with factors such as needle size and anatomy playing a role (JADA 1992;123:69-73)
    -

Technique	Needle Gauge	Needle Length
Palatal Approach (ASA)	30	Ultrashort
PSA Nerve Block	27	Short
Infiltration	27	Short
Buccal (Long) Nerve Block	27	Short
PDL Injection	27	Short
IA Nerve Block	25	Long
Gow-Gates Nerve Block	25	Long
Vazirani-Akinosi Nerve Block	25	Long

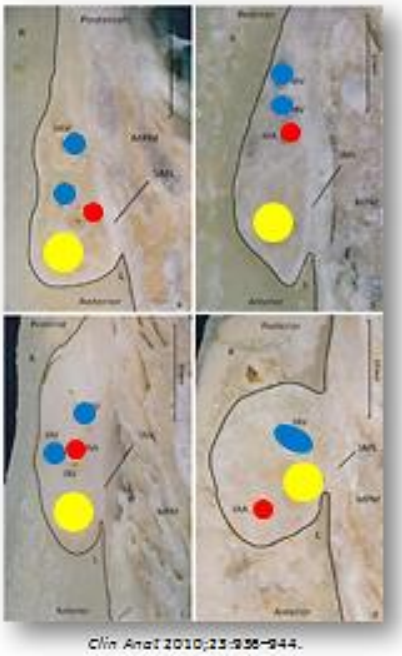
Source: Malamed SF. Handbook of Local Anesthesia. 2004, 5th Ed. p 106.

Location of the Nerve and Vessels in the Mandible

Transverse sections of the right mandibular ramus at the level of the lingula of four representative specimens

These specimens show the inferior alveolar nerve to be located posterolateral to the tip of the lingula

The location of the inferior alveolar artery and vein(s) varies significantly with the inferior alveolar artery being posterior or posterolateral



Clin Anat 2010;23:936–944.

Take home message…

"The addition of a suitable vasoconstrictor in adequate concentration increases the efficiency of local anaesthetic preparations and reduces the toxicity; their presence is therefore desirable. There is far greater danger of untoward reactions from the use of preparations without a vasoconstrictor than from the small amount of adrenaline normally present."
(*Aust Dent J* 1968 Feb;13(1):65-9.)

Recommendations:

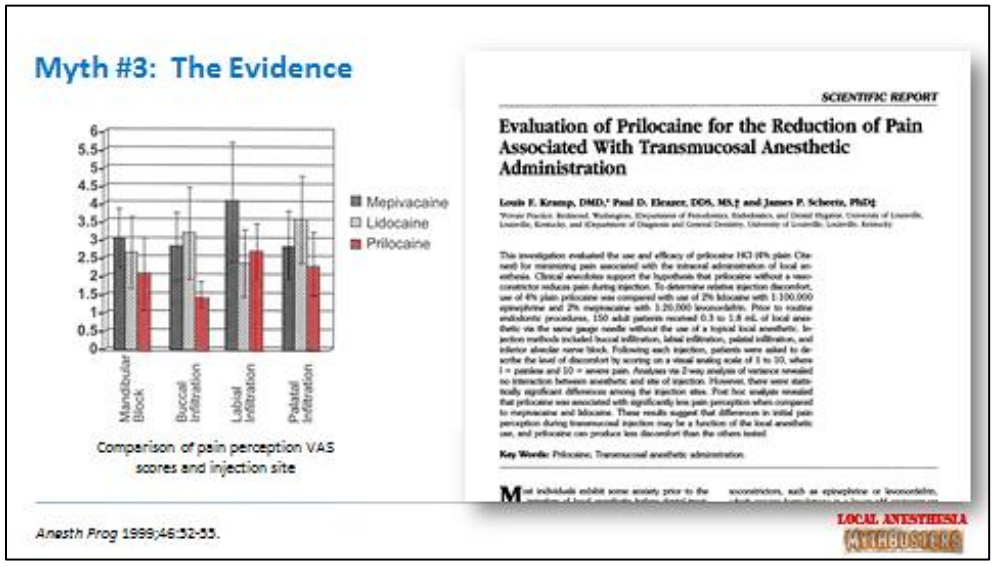
- The "Reaction" is most likely to occur during IANB in the mandible
- Use the right size needle (avoid 30ga for IANB in adults and kids) (*Dent Clin North Am* 2010;54:745–756.)
- Aspirate (twice)
- Slow injection technique – fast injection technique may cause back pressure within the vessel and decrease chances of positive aspiration (*Ann Anat* 1999;181:105-106)
- Consider reduced/no epinephrine dose formulations:
  - 4% articaine with 1:200,000 (multiple brands)
  - 4% Citanest Forte with 1:200,000 epi (Prilocaine, Dentsply Sirona)
  - 3% mepivacaine (multiple brands)
  - 4% Citanest (Prilocaine, Dentsply Sirona)
  - 2% Xylocaine (Lidocaine, Dentsply Sirona), last available 2011 in the U.S. (*Pediatr Dent* 2015 Sep-Oct;37(5):71-77)

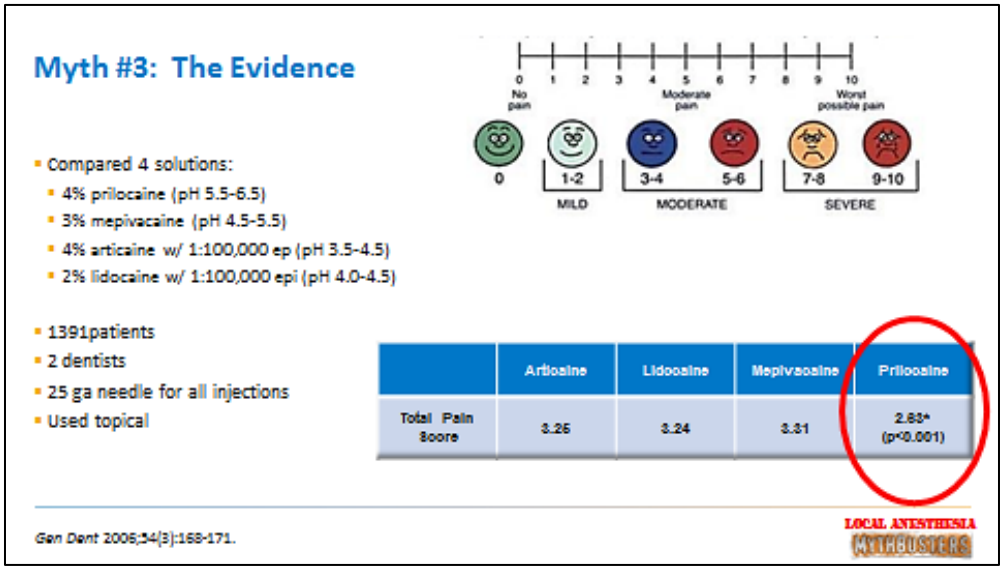
<u>Myth #3: "First, I give a local anesthetic without epinephrine to my patients, because it stings less."</u>

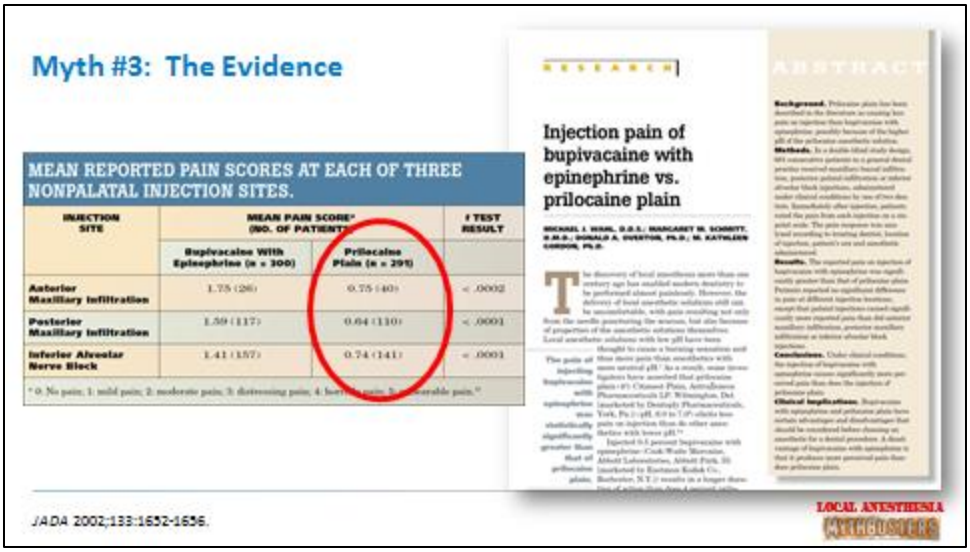
Background: Some dentists believe that by using a plain local anesthetic solution (ie, no epi) that the patient won't feel a pinch, sting, or burn at injection

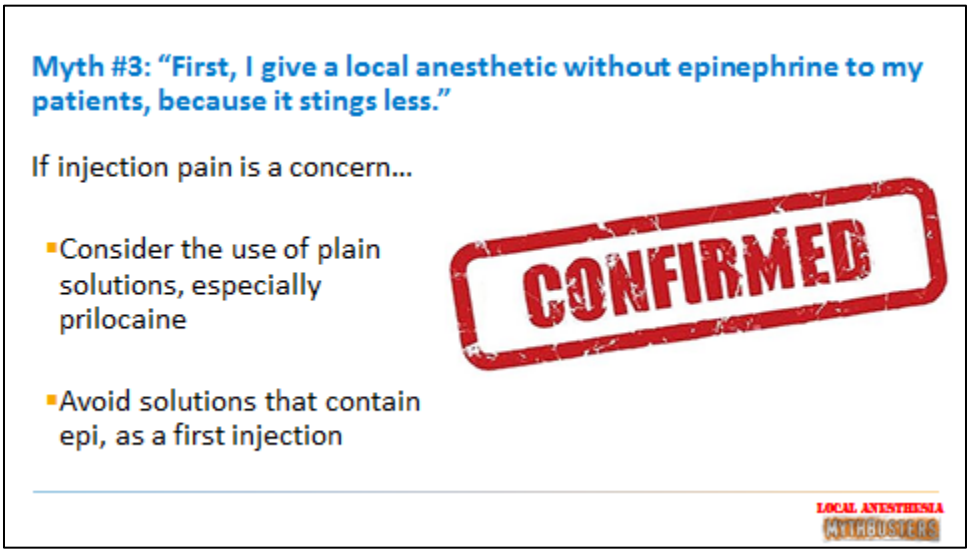
Could be related to pH. It is well-known that solutions containing a vasconstrictor (eg, epi) have a lower pH then plain solutions

Local Anesthetic Ph (Source: *Compend Contin Educ Dent* 2016 May;37(5):e6-e12.)
Average pH of solutions containing epinephrine: 3.82
Average pH of plain solutions: 6.34









One more thing… who has heard of buffering local anesthetics?

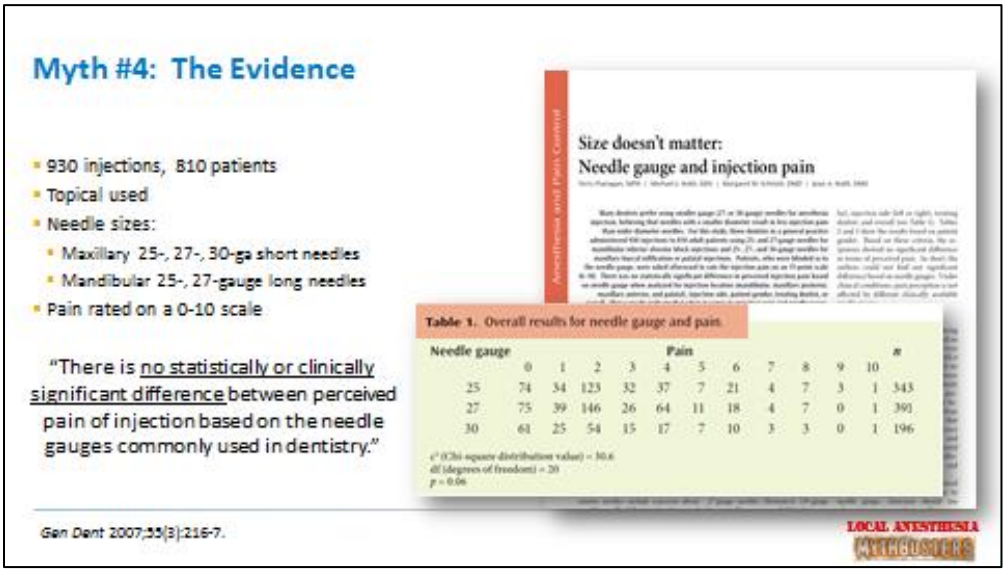
- Local anesthetic buffering involves adding Sodium Bicarbonate to low pH solutions to raise the pH closer to physiologic levels
- Possible benefits include:
- Faster onset
- Better efficacy
- Less injection pain
    - The data on whether buffering decreases injection pain is equivocal (*Gen Dent* 2015;63(6):74-78.)
    - All the studies look at buffered vs. non-buffered lidocaine or articaine
    - We need to look at buffered vs. prilocaine!

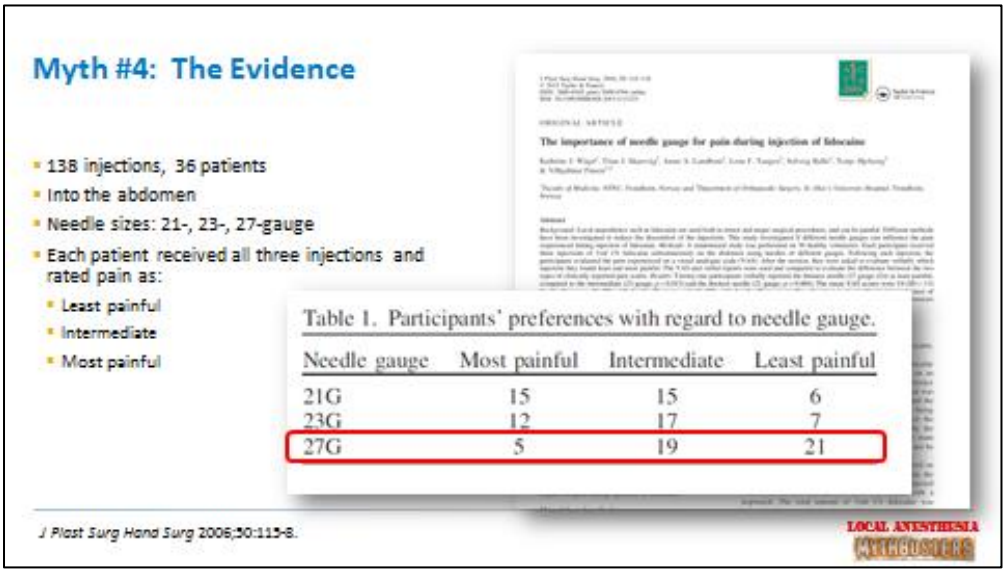
Myth #4: "I use small needles for my injections because they are less painful to the patient compared to larger needles."

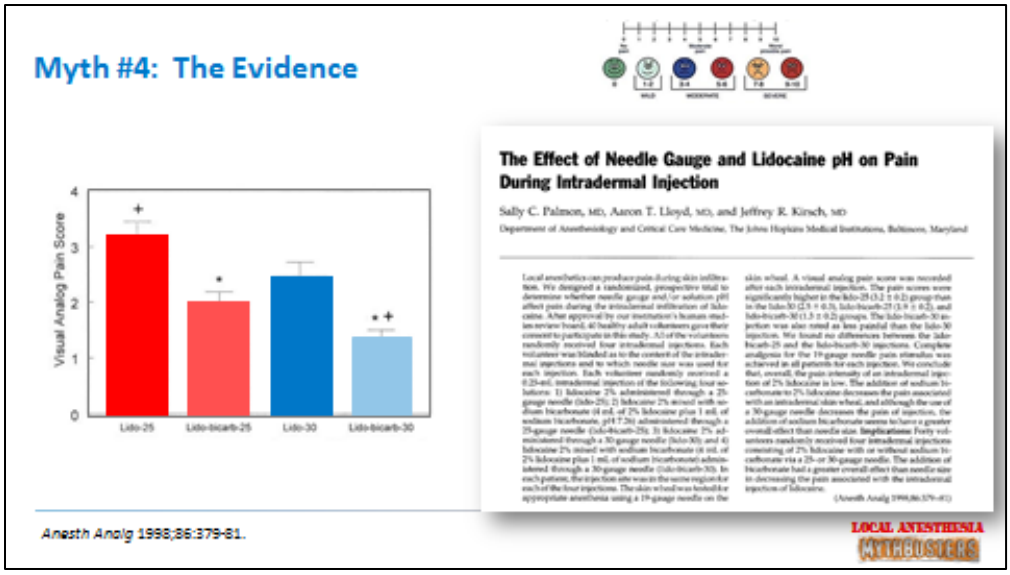
Background: There is a long-standing belief in dentistry that using a smaller gauge needle will cause less discomfort to the patient

This myth has long persisted despite some early evidence:

- "patients are unable to differentiate among 23-, 25-, 27-, and 30-gauge needles" (*NY State Dent J* 1972;38:425-426.)
- "no significant differences in the perception of pain produced by 25-, 27-,and 30-gauge needles during inferior alveolar nerve blocks in adults" (*JADA* 1979;99:822-824.)





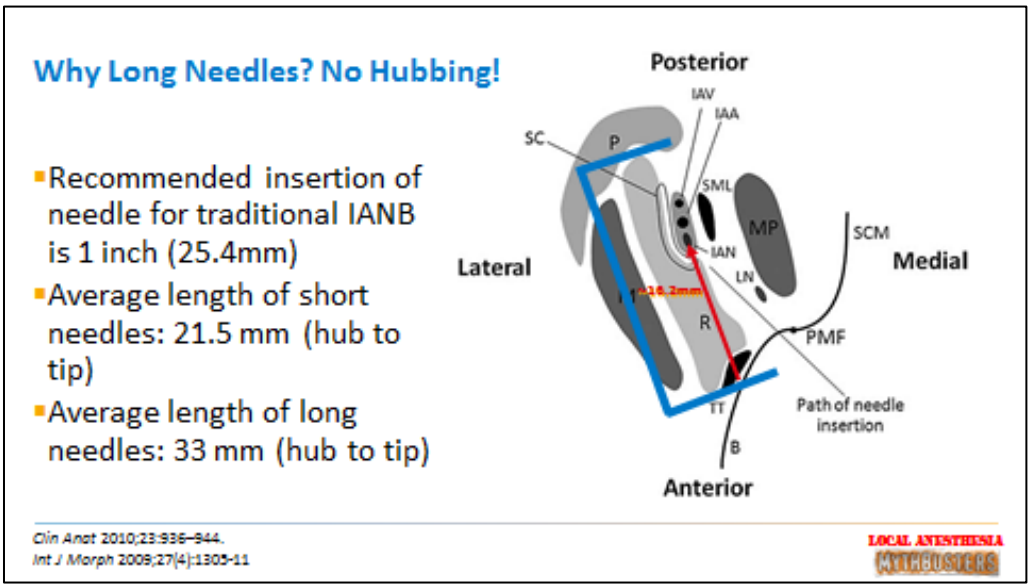


The Verdict…UNCLEAR

Recommendations

- Use the right size needles!
- Why? Not for patient comfort but for reasons such as:
  - Needle deflection
  - Ability to aspirate (less pressure required)
  - Decreased risk of breakage
- For IANB use 25- or 27-ga long needles
- For infiltrations use 27-ga (or 30-ga) short needles
- To help avoid needle breakage:
  - Minimize bending of needles
  - Minimize reorienting needles when in tissue
  - Avoid hubbing the needle

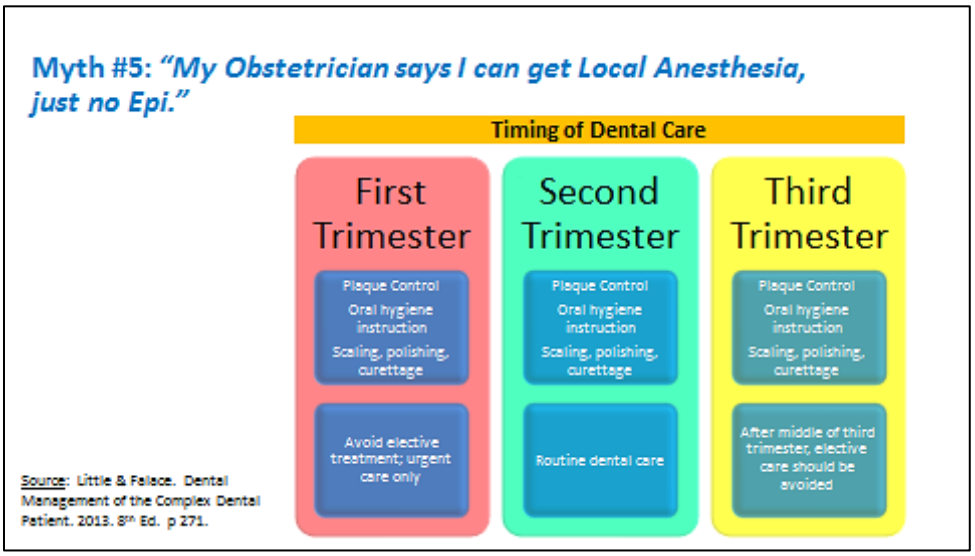
Why Long Needles? No Hubbing!



Myth #5: "My Obstetrician says I can get Local Anesthesia, just no Epi."

Changes in 2014:

- On 12/13/2014, the FDA published the Pregnancy and Lactation Labeling Final Rule (PLLR), which changed the labeling requirements for the pregnancy and lactation sections for prescription drugs and biological agents
- The final rule removed the pregnancy letter categories, and created descriptive subsections
- Labeling changes from this rule begin on June 30, 2015. Previously approved drugs from June 30, 2001 will switch to the new labeling gradually.
- This rule does not apply to OTC medications



What is a TERATOGEN?

Any agent that can disturb the development of an embryo or fetus. Teratogens may cause a birth defect in the child. Or a teratogen may halt the pregnancy outright. The classes of teratogens include radiation, maternal infections, chemicals, and drugs.

Category	FDA Pregnancy Risk Factor Definitions
A	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 animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women or 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 studies in animals have revealed adverse effects on the fetus (teratogenic, embryocidal, or other) and there are no controlled studies in women or studies in women and animals are not available. Drugs 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	Studies in animals or human beings have demonstrated fetal abnormalities or there is 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. The drug is contraindicated in women who are or may become pregnant.
N	FDA has not classified the drug

The Facts:

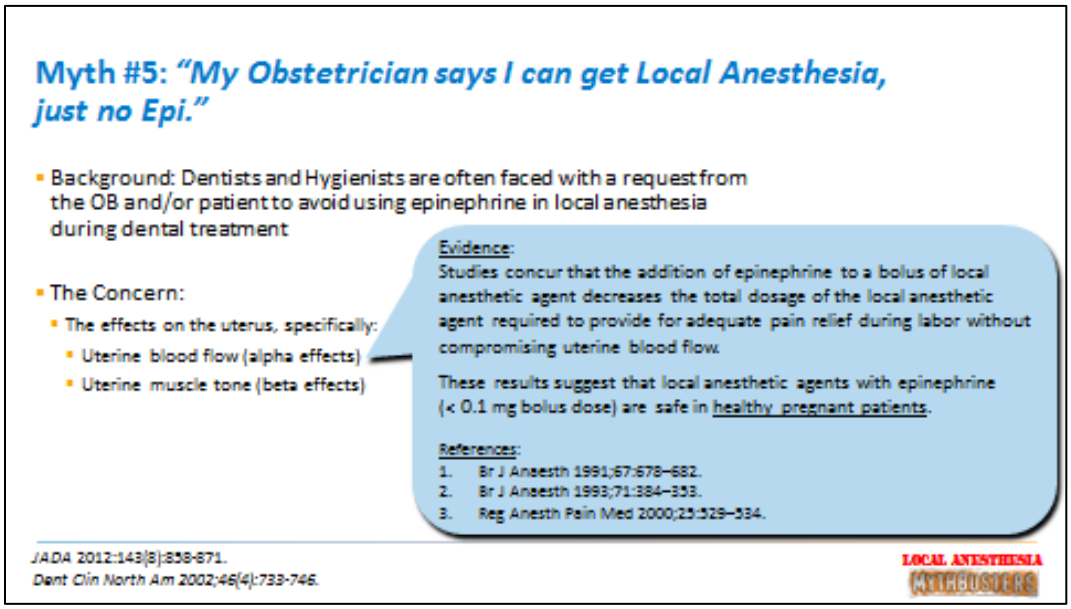
- Medication use during pregnancy is common; two out of every three women take prescription medications during pregnancy. (*American Journal of Obstetrics and Gynecology* 2004; 191:398-407.)
- Medication use during pregnancy still causes great anxiety and misunderstanding among both the public and health care professionals.
- The majority of birth defects have an unknown cause, however one early publication estimated that 2-3% of birth defects are thought to be caused by medications taken during pregnancy. (*Teratology* 1973; 7:3-15.)

Local Anesthetics	Pregnancy Category	Safe during Pregnancy?	Safe during breastfeeding?
Articaine	C	Use with Caution	Use with caution
Bupivacaine	C	Use with Caution	Yes
Lidocaine (with or without epinephrine)	B	Yes	Yes
Mepivacaine (with or without levonordefrin)	C	Use with Caution	Yes
Prilocaine	B	Yes	Yes
Benzocaine (topical)	C	Use with caution	Use with caution
Dyclonine (topical)	C	Yes	Yes
Lidocaine (topical)	B	Yes	Yes
Tetracaine (topical)	C	Use with caution	Use with caution

Source: *JADA* 2012:143(8):858-871.

The Concern:
The effects on the uterus, specifically:

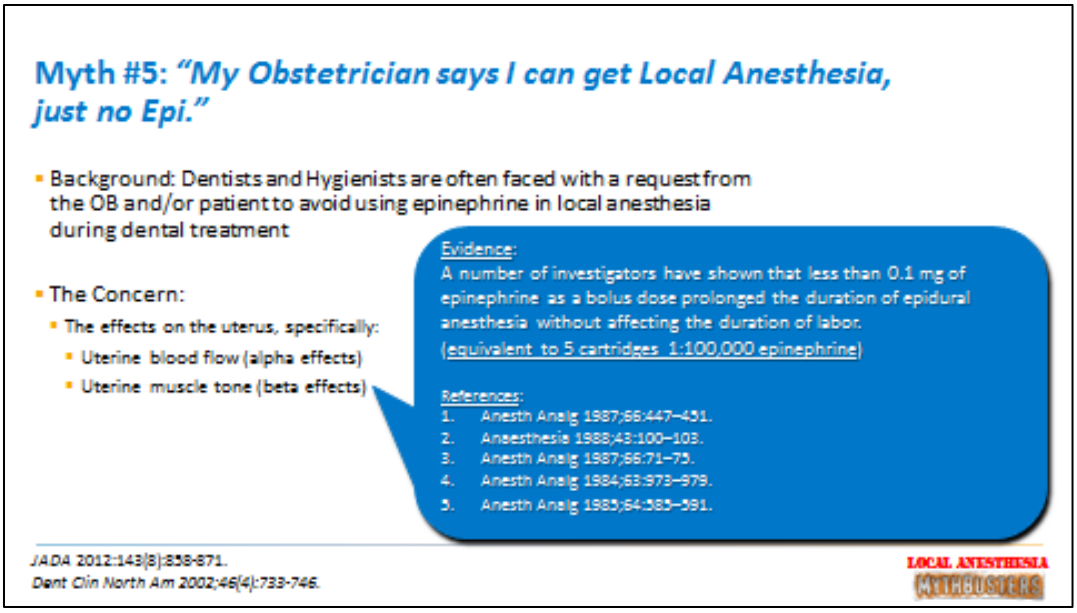
- Uterine blood flow (alpha effects)
- Uterine muscle tone (beta effects)

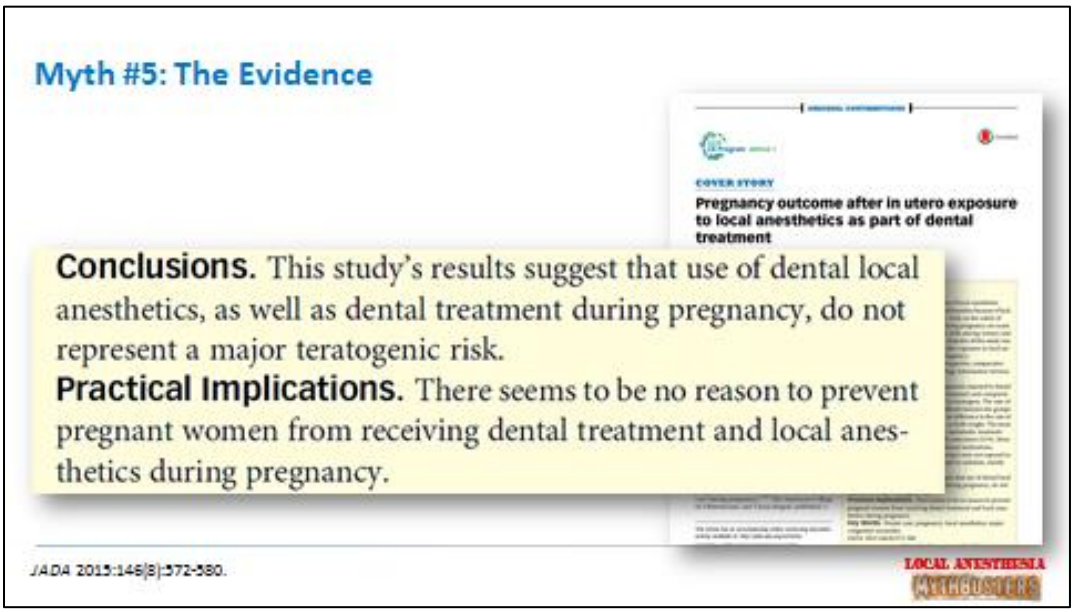


A true contraindication to epinephrine in local anesthetics for pregnant dental patients is if the pregnancy is complicated by hypertension.

References:

Br J Anaesth 1991;67:678–682.
Br J Anaesth 1993;71(3):348–53.





The Verdict…

This myth is BUSTED. Your safest choices if a local anesthetic is indicated for a pregnant patient are:

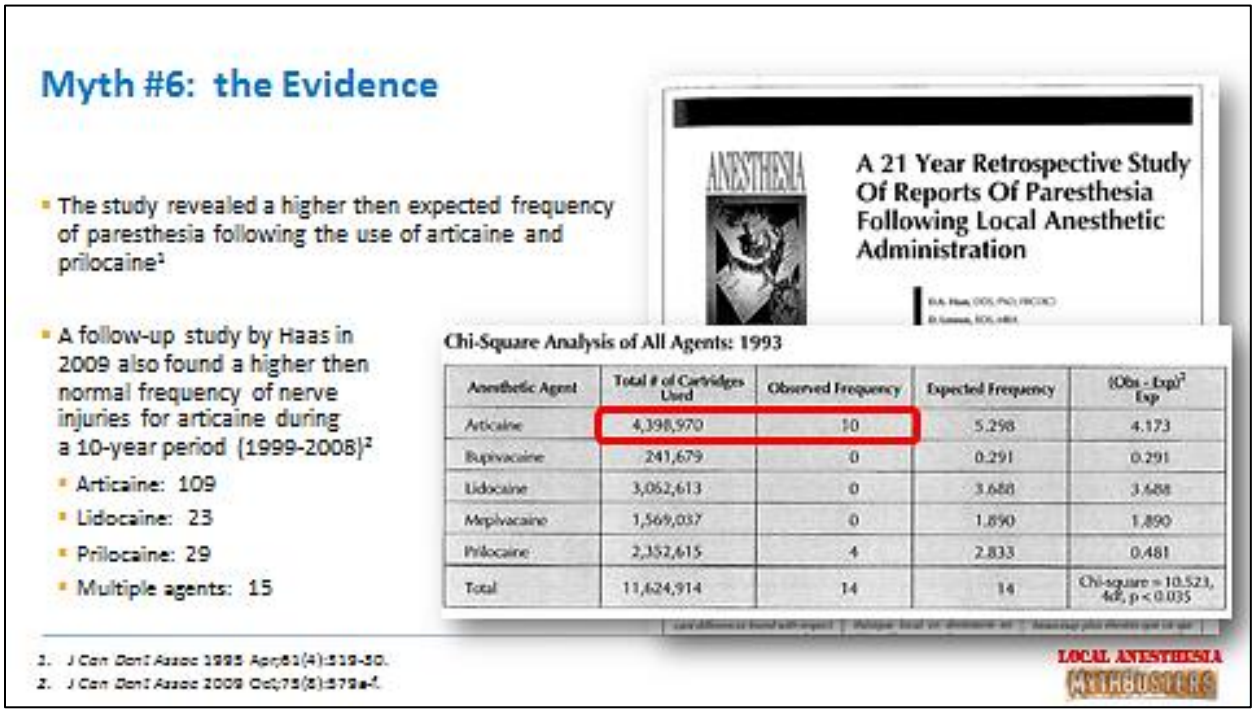
Lidocaine with or without EPI
Prilocaine with or without EPI

Myth #6: "I don't use articaine for blocks because it causes paresthesia."

- A paresthesia as an abnormal sensation, such as of burning, pricking, tickling, or tingling
- Paresthesias are one of the more general groupings of nerve disorders known as neuropathies
- Paresthesias may manifest as total loss of sensation (ie, anesthesia), burning or tingling feelings (ie, dysesthesia), pain in response to a normally nonnoxious stimulus (ie, allodynia), or increased pain in response to all stimuli (ie, hyperesthesia)

Articaine important dates: (Malamed SF. Articaine 30 years later. Oral Health. Feb 2016)

- 1969: Developed in Germany
- Entered clinical use
  - 1976: Germany
  - 1983: Canada
  - 1998: United Kingdom
  - 2000: United States
  - 2005: Australia



Myth #6: The Evidence

- Examined nerve injuries in Denmark from 1997-2004
- 56 total
- Highlighted the lingual nerve as a high risk area for nerve injury

Clinical Paper
Oral Medicine

Nerve injury caused by mandibular block analgesia

	Inferior alveolar nerve	Lingual nerve	Sum *N* (%)
Articaine 4%	5	24	29 (54%)
Prilocaine 3%	4	6	10 (19%)
Lidocaine 2%	3	7	10 (19%)
Mepivacaine 3%	0	4	4 (7%)
Mepivacaine 3% + Articaine 4%	0	1	1 (2%)
Number of nerve injuries	12	42	54 (100%)

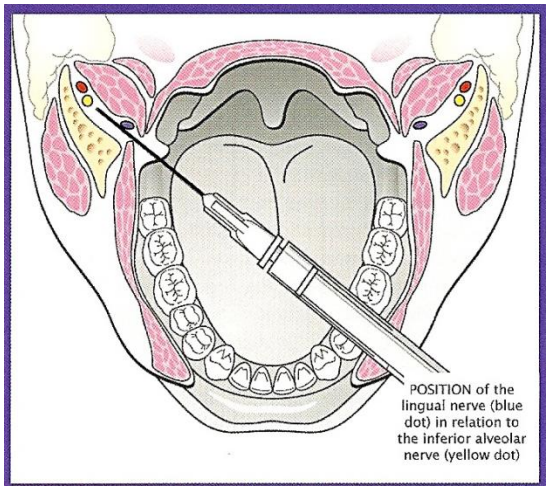
Int J Oral Maxillofac Surg 2006;35:437-443.

LOCAL ANESTHESIA MYTHBUSTERS

A 2003 study showed a range in the number of fascicles present within the lingual nerve, being anywhere from 1 to 8. Of the 12 nerves studied, 4 (33%) had only 1 fascicle

The investigators speculated that a unifascicular nerve may be injured more easily than a multifascicular one

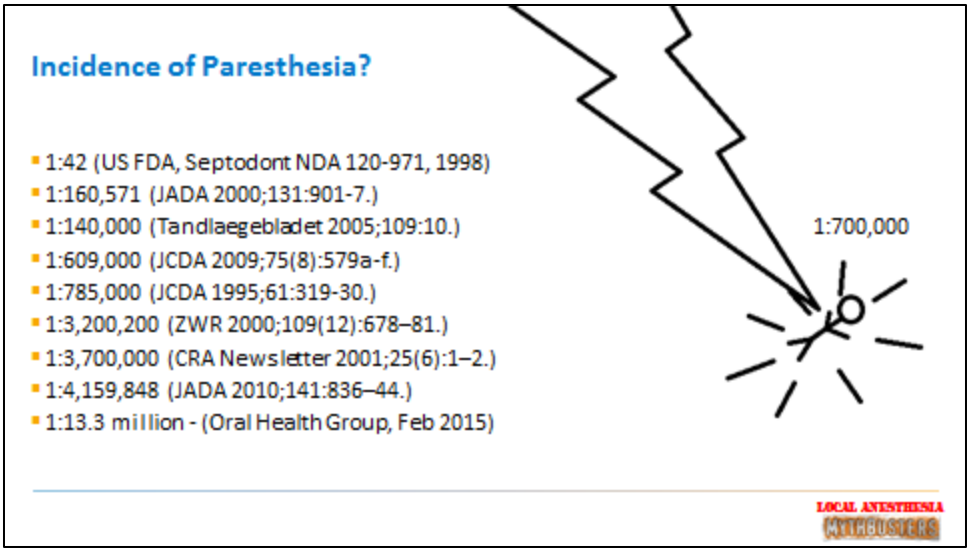
To date, this seems to be the most plausible explanation for the finding of the predilection of the lingual nerve for permanent paresthesia



POSITION of the lingual nerve (blue dot) in relation to the inferior alveolar nerve (yellow dot)

References:

- *JADA* 2003;134(2):195–199.
- *Team Work* 2009;2(2):28-34.

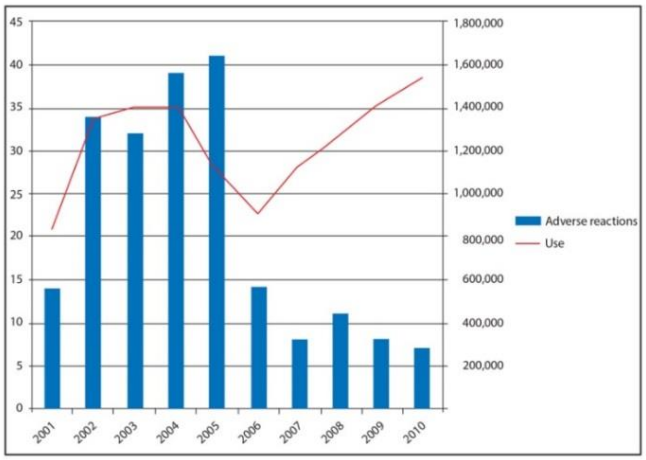


- Let's keep it real… PARESTHESIA IS A RARE EVENT!
- The mechanism is UNCLEAR
- Factors thought to be involved with Paresthesia:
    - Direct needle trauma
    - Intra-neural hematoma
    - Extra-neural hematoma
    - Edema (extra- and intra-neural)
    - Chemical neurotoxicity of articaine

"Weber Effect":

where a new product when introduced to the marketplace is subject to a closer level of scrutiny by users than more traditional, well-known products

At some point you see… fewer reports of adverse events despite increased use

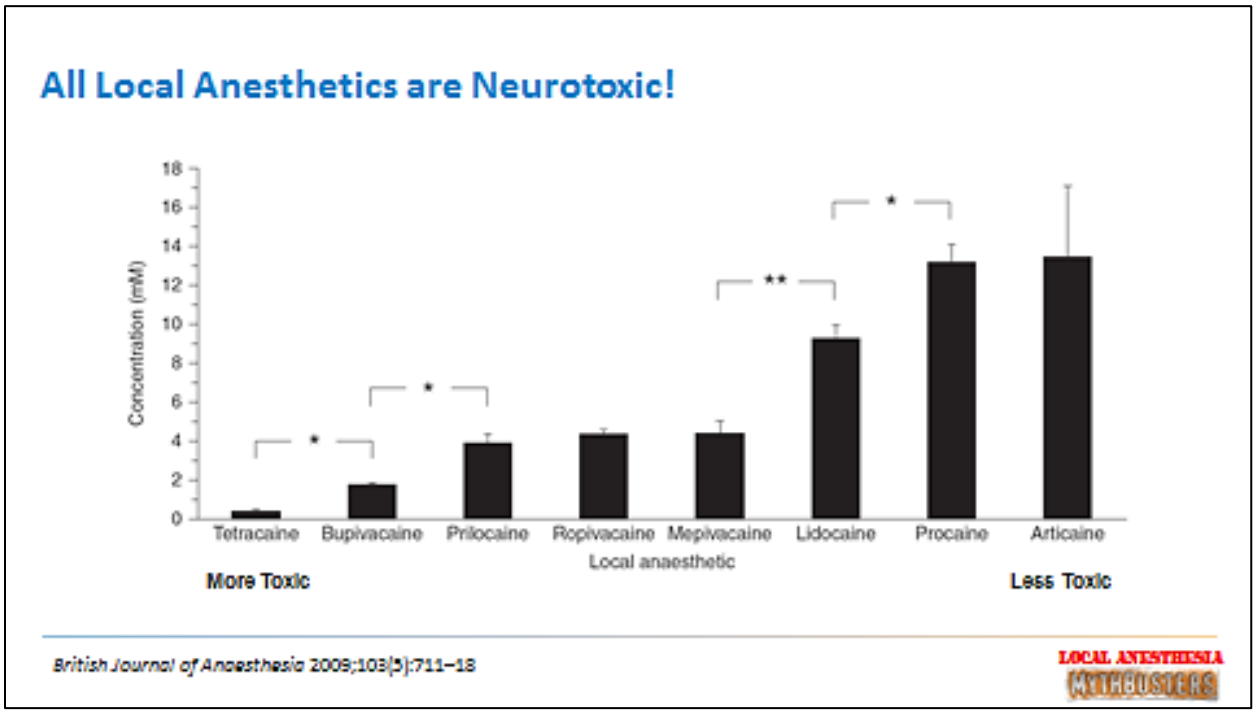


Reference:

- *Dent Update* 2015; 42: 88–93.
- *JADA* 2010;141(7):836-844.
- www.OralHealthGroup.com

Neurotoxicity?

- Articaine may be less neurotoxic then other local anesthetics
- 4% versus 2%?



The Verdict… UNCLEAR

- Despite reports about paresthesias and articaine – the data linking the two is largely anecdotal and of insufficient quality to make clinical guidelines - retrospective and biased
- Controlled studies are needed!
- Clinical neurotoxicity of 2% vs. 4% solutions is unclear and unproven
- The risks ratios are all over the map!
- Change technique rather than local anesthetic?

So what should I do?

- Use articaine for IANB injections
- If not convinced, use lidocaine (buffered?)
- Or, use lidocaine for IANB, use articaine via buccal infiltration
- Or, use articaine only on the maxilla or not at all