

## Local Anesthetics (Regional Analgesics)

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A mom brings her son to the ER with two nasty gashes on his head from a soccer game. They need to be sutured. The MD says she's going to "numb" the areas so it doesn't hurt when she repairs the wounds.

The mom asks "is it NOVOCAIN?" The MD replies "we don't use NOVOCAIN anymore, but something like it, and better and safer."

The MD injects the drug into the tissues surrounding the wounds and repairs them in about 30 minutes.

## Local Anesthetics

- Drugs used to prevent or reduce/eliminate "unpleasant sensations" – usually, but not only, pain – in or on a relatively localized area of the body, without altering the patient's level of consciousness.
- Sometimes called "regional analgesics" -- because they are used to relieve/prevent pain (analgesic effect) in a region of the body.

## Some Administration Routes Used to Induce Local Anesthesia

- Topical
  - » on mucous membranes
  - » on skin (not very effective if skin is intact)
- *Infiltration*
- Regional nerve block
- Spinal/Epidural
- IV regional anesthesia (see next page)

### Can/Should LAs Be Given IV?

- Lidocaine, IV, is commonly given for certain cardiac arrhythmias: this involves rather low doses, given very slowly, but this doesn't fit the concept of using an LA to cause "anesthesia"
- IV LAs for "IV regional anesthesia" — a specialized technique to provide anesthesia to an entire limb: don't do it unless you're an anesthesiologist (or CRNA) trained in this technique... it's DANGEROUS
- Bottom line: If you don't want to give an LA into a vein (you almost certainly don't, unless you're an anesthesiologist or nurse anesthetist), be SURE you don't.

### Can LAs Be Used To Provide General Anesthesia (i.e., putting the patient to sleep for major surgery)?

- LAs cannot be used as general anesthetics, whether for induction or maintenance: the doses that might theoretically achieve the goals of general anesthesia would lead to toxic, if not lethal, systemic effects.
- Lidocaine is often given IV during surgery to maintain or prevent or treat arrhythmias.
- Take home message: LAs cannot be used in lieu of suitable inhaled or parenteral general anesthetics.

### Two Main Chemical Classes

Amides

Esters

Name recognition: If the drug's generic name ends in "caine" it's a local anesthetic!

### Amides

- Prototype = lidocaine (XYLOCAINE)
- Most widely used, overall, of all LAs
- Lidocaine is closest to "ideal" in terms of most properties desired in a LA
  - » Fast onset, relatively good duration, relatively low toxicity or risk of allergic reactions
- Metabolically inactivated in the liver.

Name recognition: If a drug's generic name ends in 'caine' and the letter "i" appears twice in the generic name, it's an amide-type local anesthetic.

## Some Other Amides

- Bupivacaine (MARCAINE)
- Mepivacaine (CARBOCAINE)
- Prilocaine (CITANEST)

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Differ from prototype mainly in terms of pharmacokinetics, potency; you don't need to "know" these individually.

## Esters — Prototype: Procaine (NOVOCAINE)

- Procaine itself seldom used\*... properties are *far* from "ideal," especially if used without supplemental vasoconstrictor:
  - » Not very potent — large amounts/doses needed
  - » Slow onset of action, very short duration of action due to rather rapid metabolic inactivation by plasma esterases
- Other esters — still used relatively less than amides, mainly because amides less likely to → allergic responses

\*This is why if your patient is NOT getting procaine you shouldn't tell them "we're giving you NOVOCAINE"; and why you should be skeptical if your patient, especially < about 40 years old, says, e.g., "I've gotten NOVOCAINE before... had a bad reaction to it," etc.

## Some Other Esters

- Chlorprocaine\* (NESACAINE)
- Tetracaine\* (PONTOCAINE)
- Benzocaine } see
- Cocaine } later

\*Differ from prototype mainly in terms of pharmacokinetics, potency; you don't need to "know" anything specific about chlorprocaine, tetracaine, for the exam.

Note: esters end in "caine" and the letter "i" appears only once in the generic name.

See later slides about benzocaine, cocaine, however.

## General Principles I.

- LA molecules work inside sensory nerves to prevent depolarization and generation of action potentials necessary for the nerve(s) to send sensory signals to the brain
- LAs are injected or otherwise administered outside the nerves and so must diffuse into nerve to get to site of action — and must be in *nonionized* form to do that

## General Principles - II

- Function of all *excitable tissues* can be depressed if LA dose (blood level) is too high (i.e., toxic levels):
  - » all nerves, including ANS, somatic, and in brain
  - » all muscle (smooth, cardiac, skeletal)
- Sensation of pain first to go as LA effects develop, last to return as they wear-off

The lidocaine that the MD selected, and injected, contained a tiny amount of vasoconstrictor, epinephrine.

## Principles III. LA Metabolism

For either LA class (amide or ester), the slower the rate of metabolism\* the...

- ...faster the onset of action
- ...longer the duration
- ...greater the potency
- ...greater the risk of toxicity

*\*because it is the unmetabolized LA that is responsible for both the desired and adverse effects of these drugs*

## Vasoconstrictors (almost always EPI) in LAs

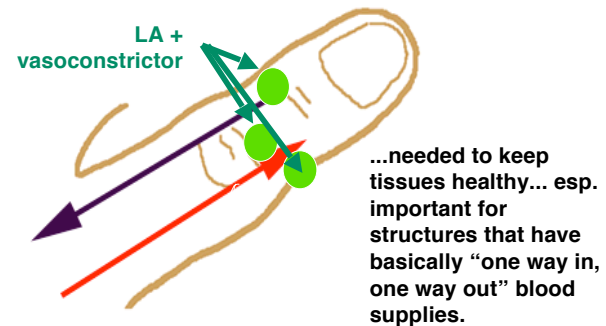
- Including a tiny amount of EPI in an injected LA causes LOCAL vasoconstriction, keeping blood flow from “washing” the LA away from its intended site of action as quickly as otherwise.
- This...
  - » shortens onset of LA action (works faster)
  - » prolongs duration of LA action
  - » increases intensity of response to LA (“better”/bigger effect for a given dose of LA)
  - » not indicated/safe for all LA routes/sites
- *Vasoconstrictors in LAs don't ↓ risk or severity of allergic reactions to LA, nor raise BP or prevent a fall of BP... there's simply not enough EPI in LAs to do that.*

### Units of “Strength” of LAs and Vasoconstrictors In Them: How the Various Products are Labeled\*

- **LAs themselves:**
  - **% solution**, e.g., 2% lidocaine (= 2 g of drug/100 mL = 20 mg/mL)
- **Vasoconstrictors in the LA:**
  - **Dilution**, e.g., 1:1,000 (= 1 mg/mL)

\*Not testable; for info only

Since vasoconstrictors in an LA ↓ local blood flow to the injection site, they may also ↓ blood flow...



### Allergic Reactions to LAs

- Variable incidence, severity [can be mild... or fatal (anaphylaxis)]
- More common with esters than amides
- Cross-reactivity within a class, not between: if one ester caused allergic response before, ANY ester is likely to do so in the same patient, but an amide poses no problem
- History of prior allergic reactions may be unreliable (did the pt. *really* have a “bad reaction” to NOVOCAIN, or did the doc/nurse simply call whatever LA he/she used “Novocain”?)

### LA Toxicity From *Overdose* (not from allergic reactions!)

- Depends on blood concentration of LA (mainly depends on dose)
- Risk ↑ whenever enough LA enters blood faster than liver (amides) or esterases (esters) can metabolically inactivate it
- Risk ↓ by vasoconstrictor (EPI slows entry of LA into bloodstream)
- S/Sx
  - » CV depression (↓↓↓ HR and contractility, ↓↓↓ BP)
  - » ↓↓↓ of brain’s ventilatory control center
  - » Seizures / convulsions... if the patient receiving an LA starts becoming irritable, anxious, or generally “hyper” this should be a warning that LA blood levels are getting too high... and full-blown seizures may soon follow
- Ventilatory failure during convulsions is main cause of death, may be accompanied by “cardiovascular collapse” (hypotension, cardiac depression)
- No specific antidote... treat seizures with anticonvulsants, normalize BP and cardiac function with proper drugs (e.g., alpha agonists to ↑ BP), support ventilation, etc.

## Cocaine

- Ester, used as topical LA (e.g., on eye, mucous membranes of nose) during surgery
- Powerful cerebral cortical stimulant (contributes to abuse)
- Has sympathomimetic activity on its own (review Exam 1 notes for mechanism)
- *Never* used + vasoconstrictor (cocaine is a powerful vasoconstrictor)

## Benzocaine\*

- Main ingredient in OTC local anesthetic products, esp. for use on skin (for rashes, etc.) and mucous membranes
- Properties
  - » ester
  - » structure, properties, prevent good diffusion into nerves
- Uses, limitations, concerns:
  - » OTC preparations often contain subtherapeutic amounts of the drug
  - » Indicated for short-term use on small areas of “intact” skin or mucous membranes -- but...
  - » Efficacy on intact skin often isn’t very good
  - » Prolonged use may → drug-induced dermatitis (allergic reaction?)

\*If you’ve ever been to the dentist and he/she swabbed some “numbing agent” on your gums to reduce pain that would occur when they inject a LA a few minutes later, that “numbing agent” was benzocaine.