Episode 180: Local Anesthetics

On this episode: Dr. Jed Wolpaw with Dr. Gillian Isaac

In this 180th episode I welcome back Dr. Gillian Isaac for another ABA keyword episode. We review local anesthetics.

All keywords covered

Questions & Notes

Click → jump to answers/notes.

KEY POINT 1: LOCAL ANESTHETIC PROVIDES ANESTHESIA AND ANALGESIA BY BLOCKING PAIN TRANSMISSION ALONG NERVE FIBERS

KEY POINT 2: KEY TARGET IS VOLTAGE-GATED NA CHANNELS (INTRACELLULAR) MEDIATED BY HYDROPHOBIC INTERACTIONS

LOCAL ANESTHETICS BLOCK NERVE CONDUCTION BY?

- **a.** **Closing calcium channels**
- **b.** **Decreasing intracellular sodium concentration**
- **c.** **Decreasing K conductance**
- **d.** **Causing extrusion of intracellular K**
- **e.** **Inhibiting cellular influx of sodium**

IN NORMAL TISSUE, WHICH PROPERTY OF DRUG HAS GREATEST EFFECT ON SPEED OF ONSET?

- **a.** **Amide**
- **b.** **Protein binding**
- **c.** **Intrinsic vasoconstrictor activity**
- **d.** **pKa**
- **e.** **potency**

WHICH OF THE FOLLOWING IS RESPONSIBLE FOR DURATION OF ACTION OF LA?

- **a.** **Concentration**
- **b.** **Metabolism**
- **c.** **Molecular Weight (MW)**
- **d.** **Tissue protein binding**
- **e.** **Volume injected**

WHICH OF FOLLOWING CHARACTERISTICS ASSOCIATED W/ LONGER DURATION OF ACTION?

- **a.** **High degree of lipid solubility**
- **b.** **High degree of protein binding**
- **c.** **High MW**
- **d.** **High pKa**
- **e.** **Presence of ester linkage**

WHICH HAS LONGEST ELIMINATION HALF-TIME?

a. **Bupivacaine**

b. **Lidocaine**

c. **Mepivacaine**

d. **Ropivacaine**

KEY POINT 3: DEGREE OF NERVE BLOCKADE DEPENDS ON CONCENTRATION AND VOLUME

KEY POINT 4: MOST LIPID SOLUBLE AGENTS CONTAIN BENZENE RINGS W/ AMIDE GROUP; CATEGORIZED AS AMINO ESTERS OR AMIDES

PARA-AMINOBENZOIC ACID (PABA) IS A METABOLITE OF?

a. **Mepivacaine**

b. **Ropi**

c. **Bupi**

d. **Procaine**

WHICH LOCAL ANESTHETIC UNDERGOES LEAST HEPATIC CLEARANCE?

a. **Chloroprocaine**

b. **Bupivacaine**

c. **Ropivacaine**

d. **Lidocaine**

BENZOCAINE HAS ALL OF FOLLOWING PROPERTIES EXCEPT

a. **Weak alkaline**

b. **Used only topically**

c. **Metabolized by esterase in blood**

d. **Formation of methemoglobin**

KEY POINT 5: POTENCY RELATED TO LIPID SOLUBILITY; MORE LIPID SOLUBLE ~ MORE POTENT

WHICH OF FOLLOWING STATEMENT CONCERNING PK IS TRUE:

a. **↓ MW ~ ↓ incidence of allergic reaction**

b. **↓ protein bind ~ ↓ sys tox**

c. **↑ ionization ~ ↑ placental transfer**

d. **↓ lipid sol ~ faster onset**

e. **Presence of ester linkage ~ ↑ dur of action**

KEY POINT 6: CLINICAL USE OF LA MAY BE "ENRICHED" W/ USE OF EPINEPHRINE, OPIOIDS, A-2 AGONISTS, BUT VALUE OF ALKALIZATION USE IS DEBATABLE

70 KG PT C/O PAIN OF THIGH ABSCESS, WHICH HAS BEEN INFILTRATED W/ 30 ML OF 1% LIDOCAINE AND 1:200,000 EPI. EFFECT OF LA INEFFECTIVE MOST LIKELY BC:

a. **Acidosis at site of injection**

b. **Epi-induced limitation of duration**

c. **Insufficient dose**

d. **Low ionization of lidocaine**

e. **Protein binding ligand**

KEY POINT7: RATE OF LOCAL ANESTHETIC SYSTEMIC ABSORPTION DEPENDS ON SITE OF INJECTION, DOSE, SITE, PK PROPS, VASOACTIVE AGENTS

WHICH OF FOLLOWING STATEMENTS CONCERNING INTERCOSTAL BLOCKS AND POSTOP PAIN IS TRUE?

a. **Block at mid-axillary line provides analgesia to anterior and lateral ab walls**

b. **Blood levels of LA higher than axillary block**

c. **Intervascular injection unlikely**

d. **Loss of resistance insures proper needle placement**

e. **Paravertebral spread prevented by adding epi to solution**

PLASMA CONCENTRATION OF EQUAL DOSES OF LA HIGHEST AT SITE OF ADMIN AT

a. **Axillary brachial plexus**

b. **Caudal**

c. **Intercostal**

d. **Lumbar epidural**

e. **Subcutaneous**

KEY POINT 8: SYSTEMIC TOXICITY FROM CLINICAL USE OF LA IS UNCOMMON OCCURRENCE. PTS W/ CARDIOVASCULAR COLLAPSE W/ ROPI/BUPI/MEPI MAY BE ESPECIALLY DIFFICULT TO RESUSCITATE, HOWEVER LIPID EMULSION IS EFFECTIVE THERAPY.

REFRACTORY CARDIAC ARREST MOST LIKELY AFTER RAPID UNINTENTIONAL INJECTION OF WHICH OF FOLLOWING?

a. **Lidocaine**

b. **Bupivacaine**

c. **Ropivacaine**

d. **Chloroprocaine**

ASRA GUIDELINES FOR TREATMENT OF LAST AND CARDIAC ARRHYTHMIAS INCLUDE USE OF INTRALIPID AND AVOIDANCE OF ALL OF THE FOLLOWING DRUGS EXCEPT:

a. **Vasopressin**

b. **Beta blockers**

c. **Calcium channel blockers**

d. **Low dose epi (<= 1mcg/kg)**

WHICH OF FOLLOWING IS SIGN OF LIDO TOX FROM A HIGH BLOOD LEVEL?

a. **Shivering**

b. **Nystagmus**

c. **Lightheadedness**

d. **Tonic clonic seizures**

18 M HAS SEIZURES DURING PLACEMENT OF INTERSCALENE BRACHIAL PLEXUS BLOCK USING 0.5% BUPIVACAINE. ANESTHESIOLOGIST BEGINS TO HYPERVENTILATE W/ 100% O2. RATIONALE FOR THIS THERAPY INCLUDE ALL OF FOLLOWING EXCEPT?

a. **Therapy helps prevent hypoxia**

b. Hyperventilation decrease blood flow and delivery of LA to brain

c. Hyperventilation elevates seizure threshold

d. Hyperventilation induce LA to ionized form

KEY POINT 9: DIRECT APPLICATION OF LA CAN RESULT IN CHANGES CONSISTENT WITH NEURONAL INJURY. LIDOCAINE CAN CAUSE TNS

TNS AFTER SPINAL ANESTHESIA ASSOCIATED W/ EACH OF FOLLOWING EXCEPT:

a. Lidocaine

b. Lithotomy position

c. Ambulatory anesthesia

d. Concentration of local anesthetic injected

TNS MOST COMMONLY SEEN AFTER SPINAL INJECTION OF WHICH LOCAL ANESTHETIC?

a. Lidocaine

b. Bupivacaine

c. Prilocaine

d. Tetracaine

KEY POINT 10: UNTOWARD REACTION TO LA RELATIVELY COMMON; TRUE ALLERGY RELATIVE RARE

PRILOCAINE NOT REC FOR OB ANESTHESIA BECAUSE:

a. Cause metHb

b. Very short DOA

c. Not metabolized by newborn

d. Most toxic of local amides

e. Produce longer motor than sensory block

PATIENT HAS PALPITATION, FLUSHING, LIGHT HEADEDNESS AFTER GINGIVAL INJECTION OF LOCAL ANESTHETIC. THIS REACTION MOST LIKELY CAUSED BY?

a. Epi in local

b. Local allergy

c. PABA allergy

d. Methyl-paraben reaction

e. Vasovagal reaction

COMMON ELEMENT THOUGHT TO BE PRESENT IN CAUDA EQUINA SYNDROME AFTER SPINAL ANESTHESIA IS

a. Use of microcatheter

b. Maldistribution of local anesthetic

c. Administration of lidocaine

d. Addition of epinephrine

WHICH OF FOLLOWING CAN CAUSE RIGHTWARD SHIFT OF OXY-HB DISSOCIATION CURVE?

a. Met-Hb

b. Carboxy-Hb

c. Hypothermia

d. Pregnancy

WHICH OF FOLLOWING LA INAPPROPRIATELY PAIRED W/ PROPERTIES OF TOXICITY?

a. Tetracaine-topical anesthesia

b. Bupivacaine-IV anesthesia

c. Prilocaine-infiltrative

d. Chloroprocaine-epidural

WHAT ARE YOU DOING TO TAKE MIND OFF STRESSFUL TIME?

Also check out Episode 41 for an in-depth episode on local anesthetics

Basic:

- mechanism, uptake, compare, prolongation of action
- side effects: seizures, cauda equina, transient neurologic syndrome/symptom (TNS), cardiotoxicity
- allergies, preservatives/additives
- met-Hemoglobinemia (met-Hb)
- local anesthetic systemic toxicity (LAST), American Society of Regional Anesthesia (ASRA) checklist, intralipid

Advanced:

- LAST, ASRA, intralipid

Tested:

- 2-chloprocaine onset, metabolism
- calculating concentration
- factors affecting onset, metabolism
- placental transfer

Key point 1: Local anesthetic provides anesthesia and analgesia by blocking pain transmission along nerve fibers

Key point 2: Key target is voltage-gated Na channels (intracellular) mediated by hydrophobic interactions

4:44

Local anesthetics block nerve conduction by?

a. Closing calcium channels
b. Decreasing intracellular sodium concentration
c. Decreasing K conductance
d. Causing extrusion of intracellular K
e. Inhibiting cellular influx of sodium
    - Answer: E – basic physiology. Must be non-ionized to cross

05:50

In normal tissue, which property of drug has greatest effect on speed of onset?

a. Amide
b. Protein binding
c. Intrinsic vasoconstrictor activity
d. pKa
e. potency

- Answer: D. Guaranteed to see this! Memorize (or know mechanism), either way.
- Speed = pKa bc affects ionization; needs to be non-ionized to cross bilayer membrane.
- Greater non-ionized = greater concentration gradient
- Note that most of local anesthetic is basic so the minority of it actually crosses

7:29

Which of the following is responsible for duration of action of LA?

a. Concentration
b. Metabolism
c. Molecular Weight (MW)
d. Tissue protein binding
e. Volume injected

- Answer: D. if binds locally, won't get washed away

8:07

Which of following characteristics associated w/ longer duration of action?

a. High degree of lipid solubility
b. High degree of protein binding
c. High MW
d. High pKa
e. Presence of ester linkage

- Answer: B. similar question to above.
- Lipid solubility ~ potency ~ cross bilayer quicker

8:55

Which has longest elimination half-time?

a. Bupivacaine
b. Lidocaine
c. Mepivacaine
d. Ropivacaine

- Answer: A. more protein bound (to receptor), thus also most associated w/ (cardiac) toxicity

Key point 3: Degree of nerve blockade depends on concentration and volume

Key point 4: Most lipid soluble agents contain benzene rings w/ amide group; categorized as amino esters or amides

8:54

Para-aminobenzoic acid (PABA) is a metabolite of?

a. Mepivacaine
b. Ropi
c. Bupi
d. Procaine

- Recognize that one is not like the others! 3 are amides (2 l's in name) , 1 is ester (1 I in name).
- Answer: D

11:27

Which local anesthetic undergoes least hepatic clearance?

a. Chloroprocaine
b. Bupivacaine
c. Ropivacaine
d. Lidocaine

- Answer: A. one is not like the others. Broken down by esterases

12:52

Benzocaine has all of following properties except

a. Weak alkaline
b. Used only topically
c. Metabolized by esterase in blood
d. Formation of methemoglobin

- Answer: A - note that these types of questions are being phased out.
- B: Benzocaine spray, probably never injected.
- C: one I, so ester → metabolized by esterase
- D: fact that it can cause metHb
- A: pka 2.5, very unusual for locals we use

Key point 5: Potency related to lipid solubility; more lipid soluble ~ more potent

14:41

Which of following statement concerning PK is true:

a. ↓ MW ~ ↓ incidence of allergic reaction
b. ↓ protein bind ~ ↓ sys tox
c. ↑ ionization ~ ↑ placental transfer
d. ↓ lipid sol ~ faster onset
e. Presence of ester linkage ~ ↑ dur of action

- Lipid sol ~ potency; onset ~ pKa
- D: Lipid sol ~ onset bc crosses quicker, but classically associated w/ potency
- E: associated w/ ↓ dur of action bc esterase
- C: less transfer
- B: not necessarily
- Answer: D primary determinant of onset of action is A) pKa, B) MW, c) lipid solubility, d) protein binding

Key point 6: Clinical use of LA may be "enriched" w/ use of epinephrine, opioids, α-2 agonists, but value of alkalization use is debatable

17:38

70 kg pt c/o pain of thigh abscess, which has been infiltrated w/ 30 mL of 1% lidocaine and 1:200,000 epi. Effect of LA ineffective most likely bc:

a. Acidosis at site of injection
b. Epi-induced limitation of duration
c. Insufficient dose
d. Low ionization of lidocaine
e. Protein binding ligand

- Answer: A. basic pKa in acidic environment → ionized and can't cross.
- B: opposite is true
- C: is actually reasonable
- D: opposite is true
- E: would cause increased duration
- Of note, 300mg lido in 70kg pt (70 x 7 = 490mg max dose)

Key point 7: Rate of local anesthetic systemic absorption depends on site of injection, dose, site, pk props, vasoactive agents

IV > intercostal > caudal > epidural > brachial plexus > subcutaneous

20:43

Which of following statements concerning intercostal blocks and postop pain is true?

a. Block at mid-axillary line provides analgesia to anterior and lateral ab walls
b. Blood levels of LA higher than axillary block
c. Intervascular injection unlikely
d. Loss of resistance insures proper needle placement
e. Paravertebral spread prevented by adding epi to solution

- Answer: B - Memorize the order!!

21:36

Plasma concentration of equal doses of LA highest at site of admin at

a. Axillary brachial plexus
b. Caudal
c. Intercostal
d. Lumbar epidural
e. Subcutaneous

- Answer: C as above

Key point 8: Systemic toxicity from clinical use of LA is uncommon occurrence. Pts w/ cardiovascular collapse w/ ropi/bupi/mepi may be especially difficult to resuscitate, however lipid emulsion is effective therapy.

22:41

Refractory cardiac arrest most likely after rapid unintentional injection of which of following?

a. Lidocaine
b. Bupivacaine
c. Ropivacaine
d. Chloroprocaine

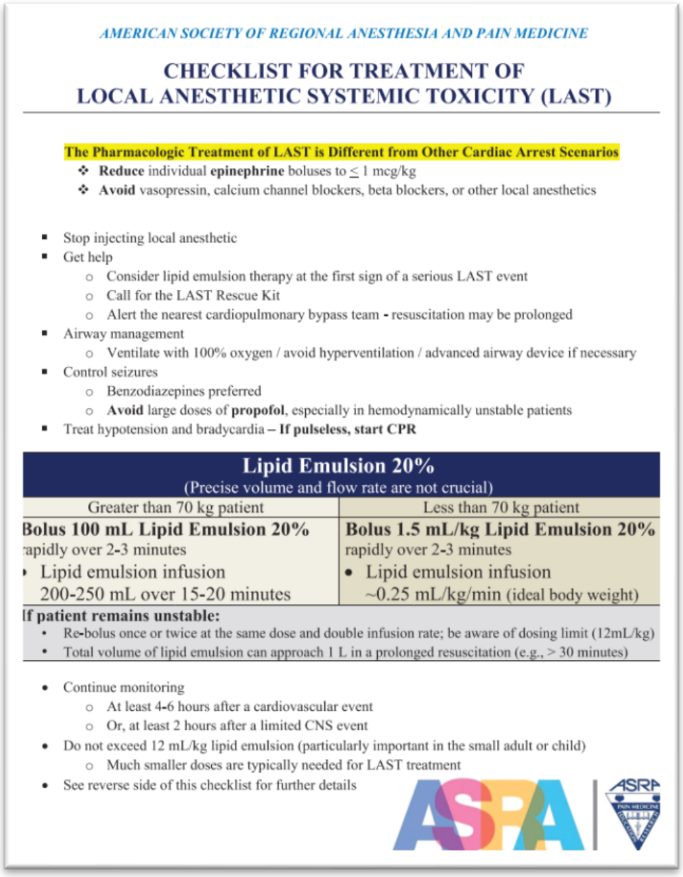
- Answer: B – knowing this is highly protein bound

23:29

ASRA guidelines for treatment of LAST and cardiac arrhythmias include use of intralipid and avoidance of all of the following drugs except:

a. Vasopressin
b. Beta blockers
c. Calcium channel blockers
d. Low dose epi (<= 1mcg/kg)

- Answer: D
- ASRA checklist
  - Stop injection, get help, call for intralipid,
  - Airway mgt, control seizure, avoid large doses of propofol especially if hemodynamically unstable; stabilize hemodynamics
  - Lipid emulsion: > 70kg, bolus 100ml intralipid, then run 200-250ml over 15
  - <70kg, 1.5ml/kg then 0.25 ml/kg/min based on IBW.
  - Don't exceed 12ml/kg of intralipid
  - Continue monitoring at least 4-6 hrs after event



AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

CHECKLIST FOR TREATMENT OF LOCAL ANESTHETIC SYSTEMIC TOXICITY (LAST)

The Pharmacologic Treatment of LAST is Different from Other Cardiac Arrest Scenarios

- **Reduce** individual **epinephrine** boluses to ≤ 1 mcg/kg
- **Avoid** vasopressin, calcium channel blockers, beta blockers, or other local anesthetics

- Stop injecting local anesthetic
- Get help
  - Consider lipid emulsion therapy at the first sign of a serious LAST event
  - Call for the LAST Rescue Kit
  - Alert the nearest cardiopulmonary bypass team - resuscitation may be prolonged
- Airway management
  - Ventilate with 100% oxygen / avoid hyperventilation / advanced airway device if necessary
- Control seizures
  - Benzodiazepines preferred
  - **Avoid** large doses of **propofol**, especially in hemodynamically unstable patients
- Treat hypotension and bradycardia – **If pulseless, start CPR**

Lipid Emulsion 20%
(Precise volume and flow rate are not crucial)

Greater than 70 kg patient	Less than 70 kg patient
Bolus 100 mL Lipid Emulsion 20% rapidly over 2-3 minutes	**Bolus 1.5 mL/kg Lipid Emulsion 20%** rapidly over 2-3 minutes
• Lipid emulsion infusion 200-250 mL over 15-20 minutes	• Lipid emulsion infusion ~0.25 mL/kg/min (ideal body weight)

If patient remains unstable:
- Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (12mL/kg)
- Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g., > 30 minutes)

- Continue monitoring
  - At least 4-6 hours after a cardiovascular event
  - Or, at least 2 hours after a limited CNS event
- Do not exceed 12 mL/kg lipid emulsion (particularly important in the small adult or child)
  - Much smaller doses are typically needed for LAST treatment
- See reverse side of this checklist for further details

26:40

Which of following is sign of lido tox from a high blood level?

a. Shivering
b. Nystagmus
c. Lightheadedness
d. Tonic clonic seizures
   - Note that in OR when you give lido, pts may c/o C.
   - May clinically see perioral numbness, nystagmus, then seizure
   - Answer: A

28:11

18 M has seizures during placement of interscalene brachial plexus block using 0.5% bupivacaine. Anesthesiologist begins to hyperventilate w/ 100% O2. Rationale for this therapy include all of following except?

a. Therapy helps prevent hypoxia
b. Hyperventilation decrease blood flow and delivery of LA to brain
c. Hyperventilation elevates seizure threshold
d. Hyperventilation induce LA to ionized form
   - A: yes
   - B: yes
   - C: incorrect (CORRECTION: At 28:58 I state that hyperventilation increases the seizure threshold. This is incorrect, it DECREASES the seizure threshold.
   - D: incorrect alkalosis should convert to unionized form

Key point 9: Direct application of LA can result in changes consistent with neuronal injury. Lidocaine can cause TNS

- Symptoms include back pain after block resolves, and radiates to buttocks and legs
- Not associated w/ motor or sensory loss, or EMG changes
- Can be severe to require hospitalization
- Clears < 1-4 days
- Most common in lithotomy; less likely w/ pregnancy

30:28

TNS after spinal anesthesia associated w/ each of following except:

a. Lidocaine
b. Lithotomy position
c. Ambulatory anesthesia
d. Concentration of local anesthetic injected
   - Answer: D

31:09

TNS most commonly seen after spinal injection of which local anesthetic?

a. Lidocaine
b. Bupivacaine
c. Prilocaine
d. Tetracaine
   - Answer: A

Key point 10: Untoward reaction to LA relatively common; true allergy relative rare

32:32

Prilocaine not rec for OB anesthesia because:

a. Cause met-Hb
b. Very short DOA
c. Not metabolized by newborn
d. Most toxic of local amides
e. Produce longer motor than sensory block
   - Answer: A (also benzocaine)

33:17

Patient has palpitation, flushing, light headedness after gingival injection of local anesthetic. This reaction most likely caused by?

a. Epi in local
b. Local allergy
c. PABA allergy
d. Methyl-paraben reaction
e. Vasovagal reaction

- Answer: A. Symptoms in context of highly vascular area, think related to epi.
- B: not injecting much, so less likely
- E: not likely
- Actual allergies are rare, so more likely to be epi
- Why important to note if local injected by surgeon has epi? Not uncommon to see some vascular absorption of the epi.

35:18

Common element thought to be present in cauda equina syndrome after spinal anesthesia is

a. Use of microcatheter
b. Maldistribution of local anesthetic
c. Administration of lidocaine
d. Addition of epinephrine

- Idea of TNS, if concentrated, then maldistributed
- C and D: false
- A: microcatheter associated w/ TNS, not CES
- CES: similar backpain but also has motor (bilateral leg weakness), autonomic (bowel/bladder control)

37:00

Which of following can cause rightward shift of oxy-Hb dissociation curve?

a. Met-Hb
b. Carboxy-Hb
c. Hypothermia
d. Pregnancy

- Answer: D

- A-C cause left shift

37:33

Which of following LA inappropriately paired w/ properties of toxicity?

a. Tetracaine-topical anesthesia
b. Bupivacaine-IV anesthesia
c. Prilocaine-infiltrative
d. Chloroprocaine-epidural

- Answer: B: as discussed, this is false

What are you doing to take mind off stressful time?

Random Recs:

Genius on the edge: The bizarre double life of Dr. William Stewart Halsted

Killer Angels

The Powder Mage Trilogy

References:

Barash Clinical Anesthesia 8th edition: Chapter on Local Anesthetics