



# Peri-operative Pain Blocks

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# Objective

- ▶ Discuss the most common causes of postoperative pain
- ▶ Identify the types of blocks used for prevention of postoperative pain
- ▶ Review the medications used in perioperative blocks

# What is Postoperative Pain Prevention?

- AKA preventive analgesia or preemptive analgesia
- Use of analgesics to reduce postoperative pain:
  - Incidence is underreported
  - Undertreated
- Use of preventive analgesia:
  - Hastens functional recovery
  - Improves speed of hospital discharge
  - Decreases acute morbidity
  - Reduces probability of developing chronic postoperative pain



# Preventive Analgesia Rationale

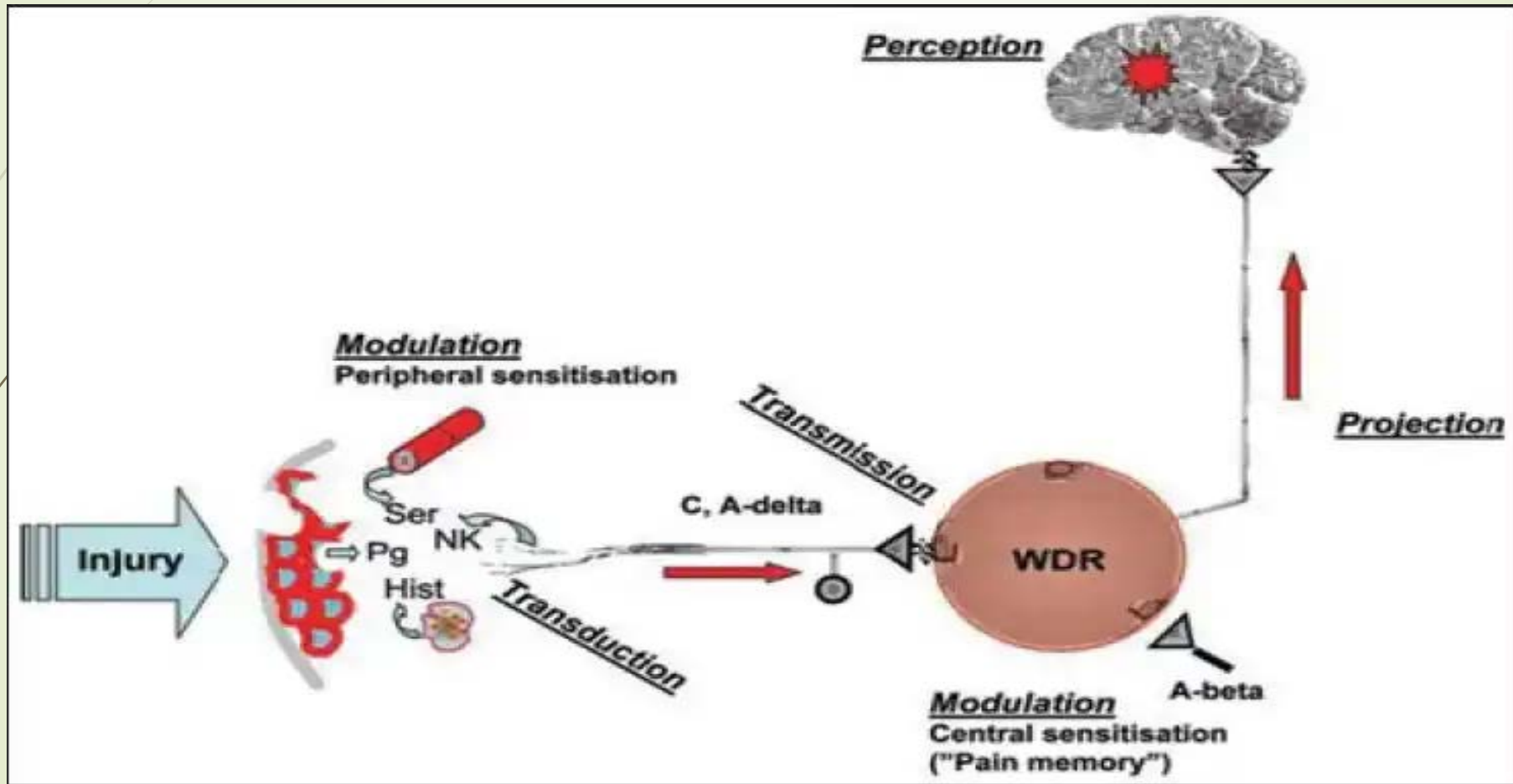
- Noxious stimuli are detected by nociceptors
- Peripheral terminals of nociceptors convert energy at the stimulus site to electrical activity then transferred to the dorsal horn of the CNS
- Transmission of nociceptive signals in the dorsal horn, aspartate & glutamate (neuroexcitatory), substance P (acts on NMDA) & AMPA receptors
- Nociceptors are divided based on location & response
  - 'First pain' myelinated A  $\delta$  nociceptors are specialized for detecting mechanical & thermal injury & for triggering a rapid sharp pain response
  - 'Second pain' unmyelinated C nociceptors respond to strong mechanical, thermal, chemical stimuli, & more delayed burning pain response

# Preventive Analgesia Rationale Cont.

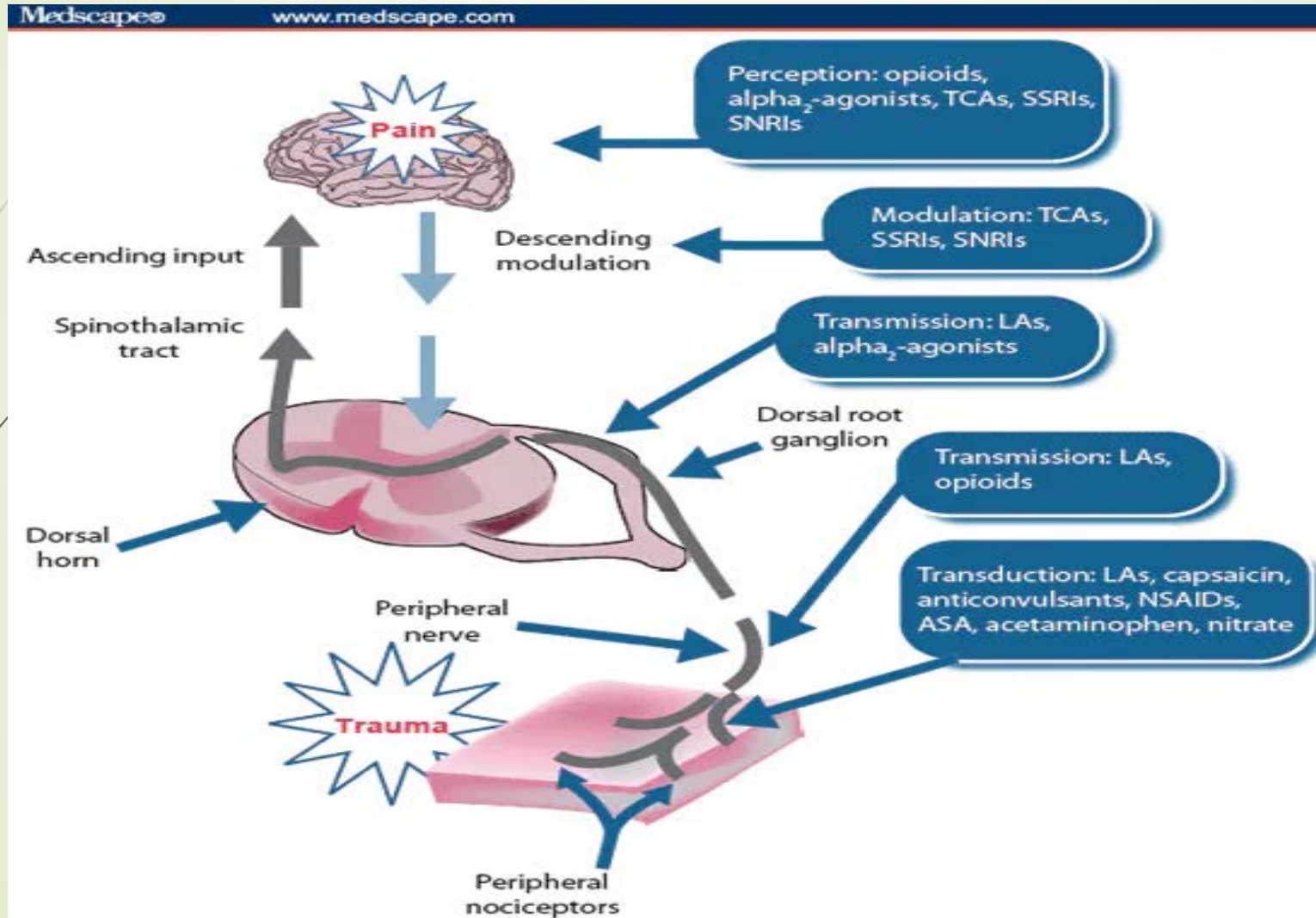
- ▶ External stimuli that activate nociceptors & induce pain may or may not result in overt tissue damage
- ▶ Stimuli associated with actual tissue damage initiate several alterations of both the peripheral & central pain pathways (local inflammatory response with substance P, prostaglandins, serotonin, bradykinin, & histamine)
  - ▶ Mediators lead to peripheral sensitization of the nociceptors, resulting in altered transduction & increased conduction of nociceptive impulses towards the CNS
  - ▶ Pain signals from the nociceptors to in the dorsal horn lead to prolonged alterations in the responsiveness of these neurons
  - ▶ Signals from A $\delta$  & C fibers will be amplified (hyperalgesia) resulting in sensation not being interpreted as touch but as pain
  - ▶ Central sensitization may outlast the stimuli that triggered the alterations & become a 'pain memory'



# Preventive Analgesia Rationale

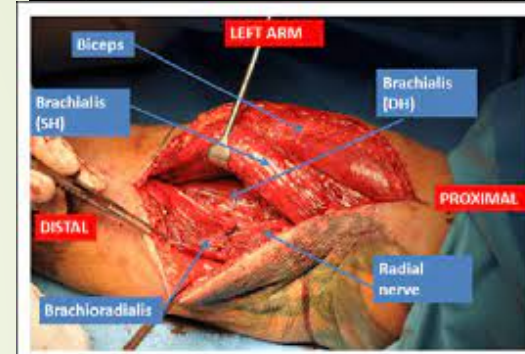
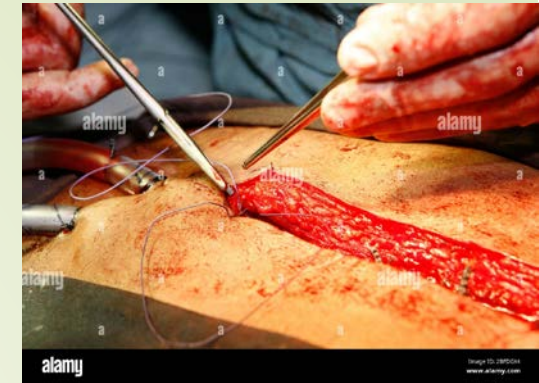


# Acute pain



# Causes of Perioperative Pain

- Tissue trauma
  - Surgical incision
  - Dissection
  - Burns
- Direct nerve injury
  - Nerve Transection
  - Stretching
  - Compression



- Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia I: physiological pathways and pharmacological modalities. Can J Anaesth. 2001;48(10):1000.

-Alamy. Surgical Incision. Accessed at <https://www.alamy.com/surgeons-stitch-close-a-surgical-wound-image353725852.html?imageid=DD9F69DF-CF24-4062-B2DB-54C43EB5BD4D&p=1446279&pn=1&searchId=152d0a64a0fc9ea4ce4ce28721dd7db5&searchtype=0> on 1/12/2023

-[https://www.researchgate.net/figure/Surgical-dissection-demonstrating-the-superficial-SH-and-deep-head-DH-of-brachialis\\_fig3\\_335236577](https://www.researchgate.net/figure/Surgical-dissection-demonstrating-the-superficial-SH-and-deep-head-DH-of-brachialis_fig3_335236577) accessed on 1/13/23

-Burn Wound Management. Plastic Surgery Key. <https://plasticsurgerykey.com/burn-wound-management/> accessed on 1/13/23



# Meme break

Don't think of it  
as surgery.

Think of it as  
being recalled to  
the factory for an  
adjustment!!

someecards  
user card



# Definition of Local Anesthesia

## Local

- Temporary loss of feeling in one small area of the body
- May be injected , applied or both
- Utilized in medical, surgical, or dental procedures
- Due to vasodilation of local anesthetic, utilization of epinephrine may decrease blood loss, delay absorption, and prolong anesthesia
  - True for lidocaine, but does not prolong anesthesia for mepivacaine or bupivacaine

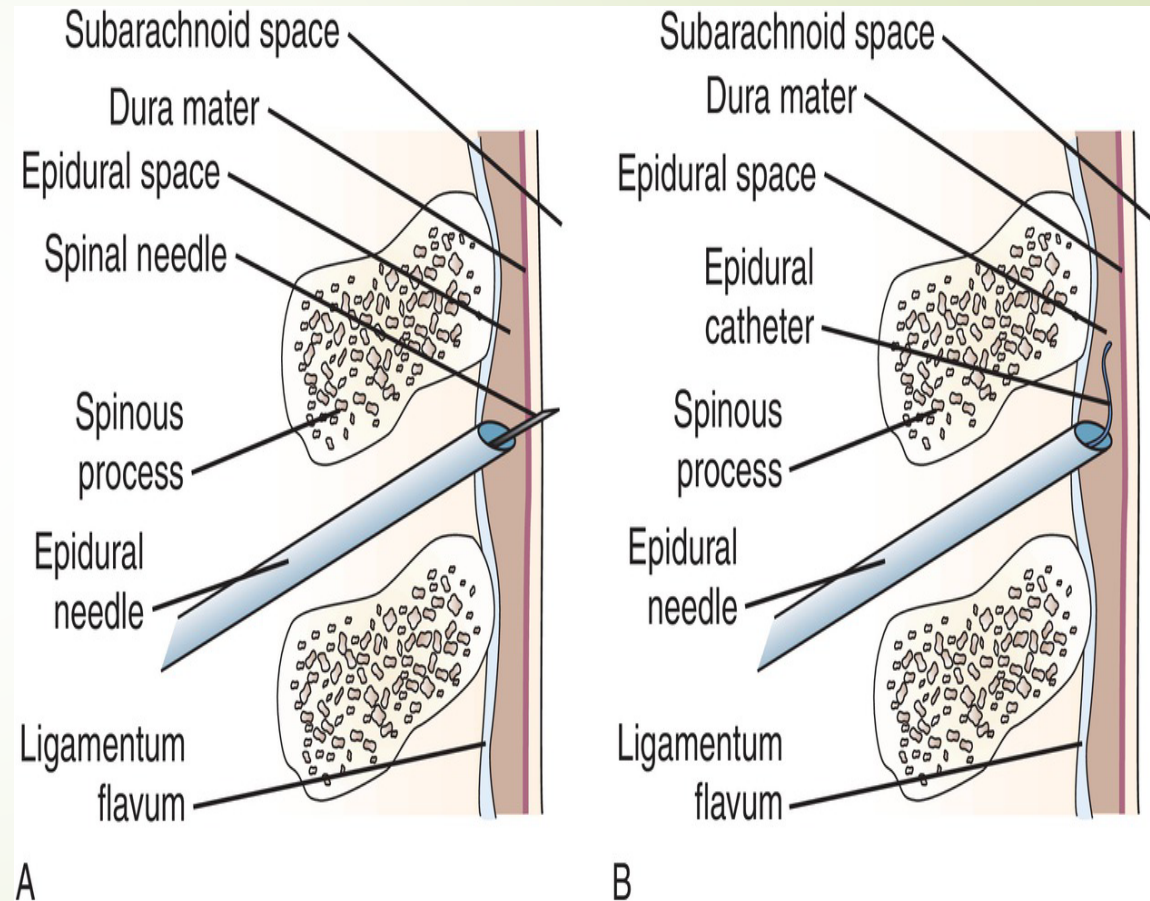
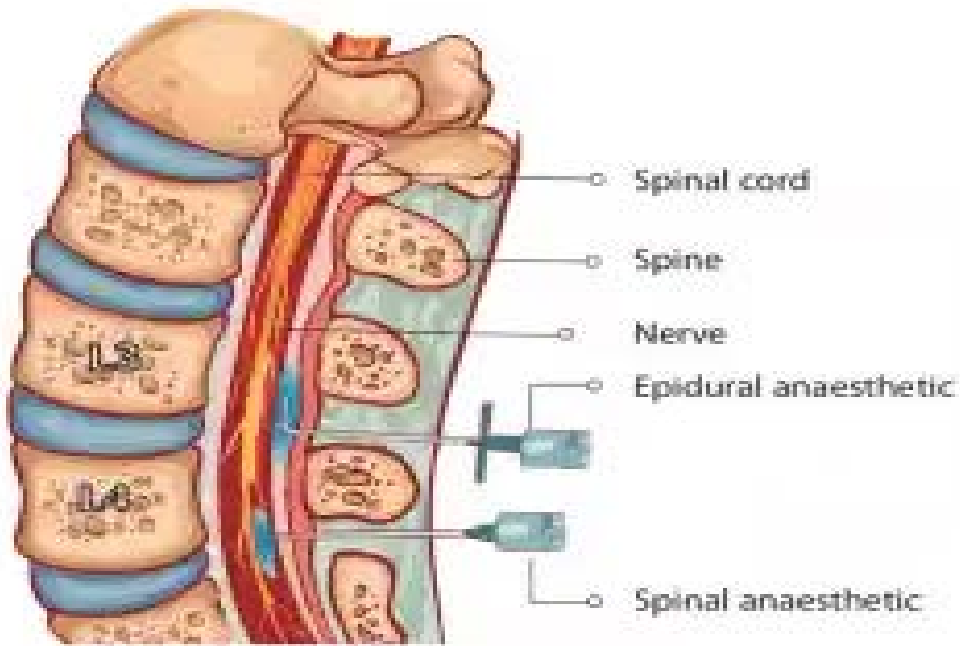
# Definition of Regional Anesthesia

- ▶ Regional: injection around a cluster of nerves to numb a larger area of the body
  - ▶ Neuraxial: Injection into the subarachnoid/epidural space
    - ▶ Spinal (subarachnoid): Injection into the dural sac that contains CSF- complete block
    - ▶ Epidural: Utilizes a Tuohy needles to access the epidural space-partial block
  - ▶ Peripheral nerve block
    - ▶ Upper extremity blocks (interscalene, suprascapular, infraclavicular, axillary, intercostobrachial, wrist, and digital nerve blocks)
    - ▶ Lower extremity blocks (lumbar plexus (psoas compartment), femoral nerve block, fascia iliaca, obturator nerve, popliteal, saphenous, ankle, and digital nerve block)
    - ▶ Scalp block
    - ▶ Cervical plexus block
    - ▶ Thoracic nerve blocks (intercostal, paravertebral, interfascial plane blocks)
    - ▶ Abdominal nerve blocks (transversus abdominis plane, subcostal, rectus, ilioinguinal and iliohypogastric, transversalis fascia plane, and quadratus lumborum block)
    - ▶ Pudendal and paracervical blocks

# Difference in Neuraxial Anesthesia

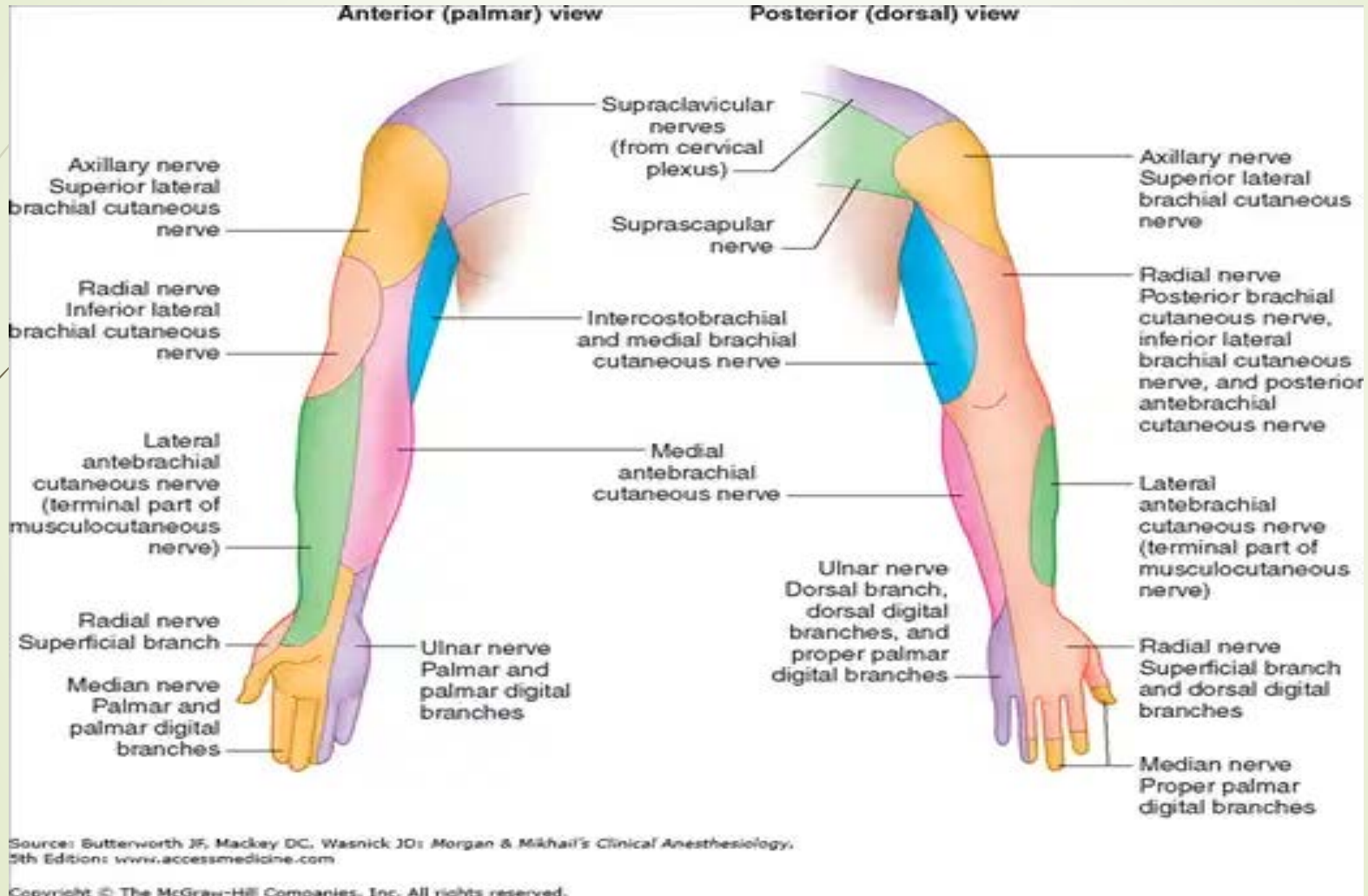
## Spinal vs. epidural administration

As illustrated below, a spinal anesthetic is injected into the subarachnoid space and an epidural is injected into the epidural space.

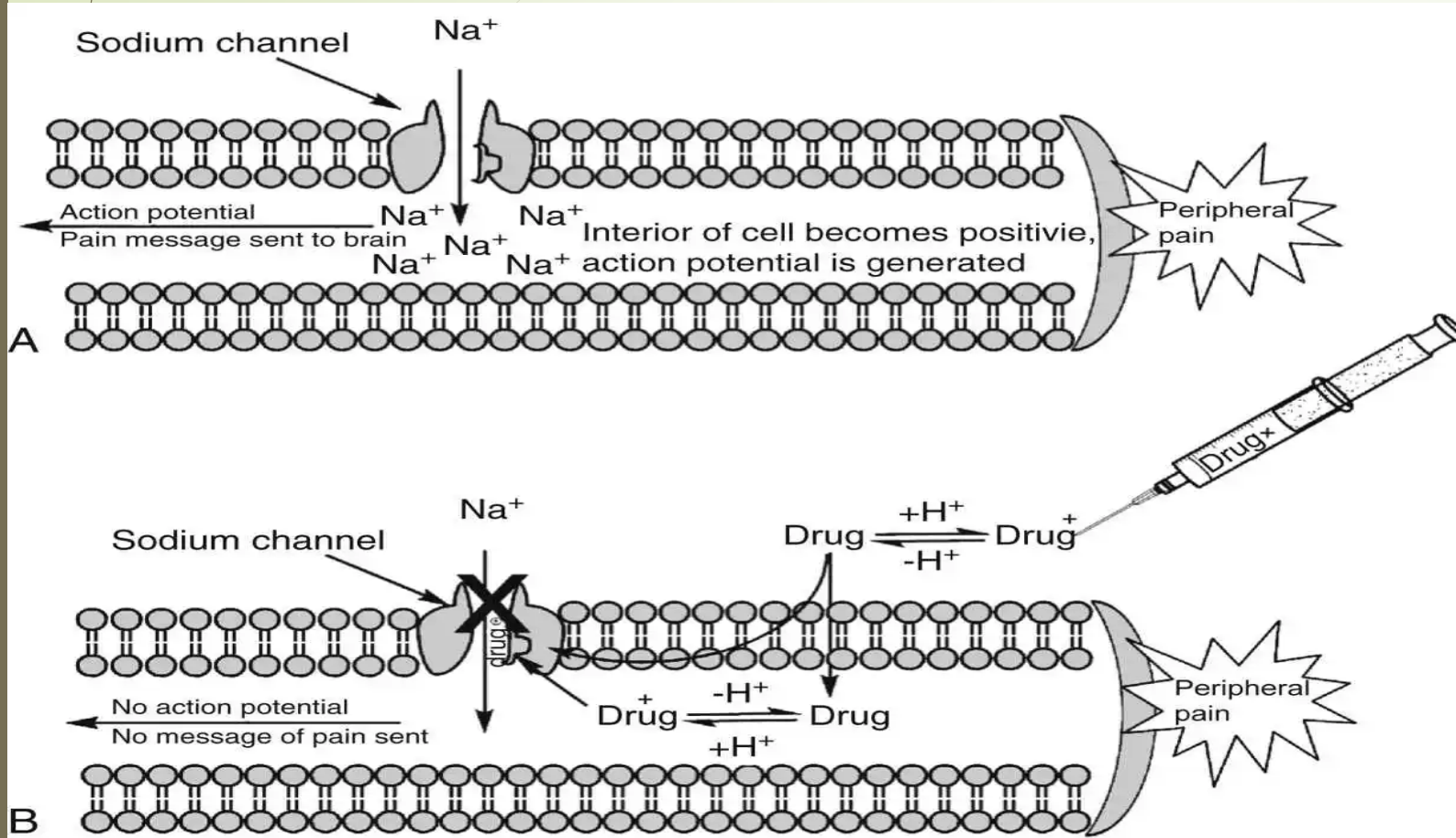




# Peripheral Nerve block



# Mechanism of Nerve Block



## Sequence of Nerve Blockade

Vasomotor block, dilation of skin vessel, increased cutaneous flow

Blockade of cold temp fibers

Temperature discrimination lost

Slow and fast pain

Tactile sense lost

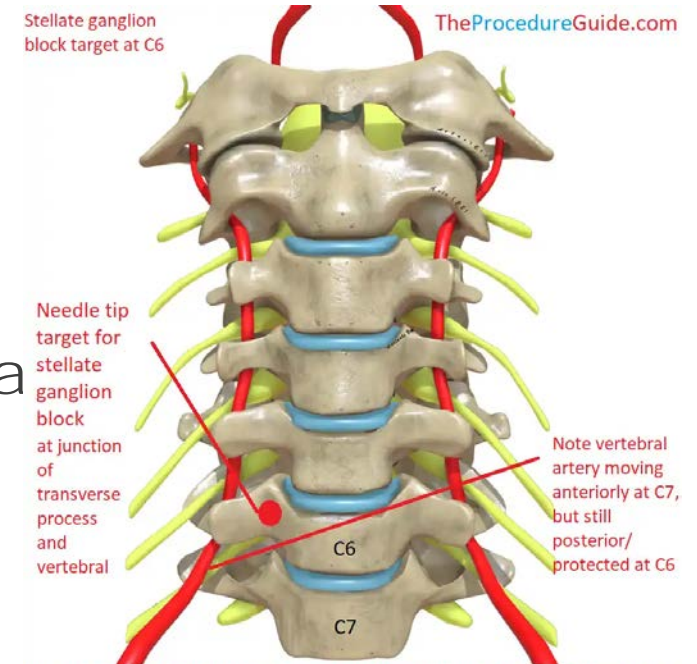
Pressure sense lost

Proprioception lost

Motor Paralysis

# Specific Nerve Blocks

- Sympathetic Nerve block
  - Blocks pain from sympathetic nervous system to one area
  - Example: stellate ganglion block
- Neurectomy:
  - Destroying a damaged peripheral nerve
  - Example: double axonal crush, transection & cap
- Rhizotomy
  - Destroying a nerve root that extends from the spine
  - Destruction by surgical instrument or burning them with a chemical or electrical current



Modified of an original from Wikipedia ([https://en.wikipedia.org/wiki/File:Cervical\\_Spine\\_Anterior\\_View.png](https://en.wikipedia.org/wiki/File:Cervical_Spine_Anterior_View.png)). Licensed under a



# Four Categories of Nerve Blocks

## ➤ Therapeutic

- Used for acute & chronic pain treatment
- Examples include:
  - Lumbar Epidural Steroid Injection

## ➤ Diagnostic

- Source identification of pain
  - Zygapophysial blockade (facet joint)
  - Stellate ganglion block

## ➤ Prognostic

- Utilization to determine if permanent solution, ie surgery, would be successful

## ➤ Preemptive

- Prevention of subsequent pain



# Contraindication to Regional Anesthesia

## ➤ Absolute

- Patient refusal
- Allergy to local anesthetics\*\*\*\*\*

## ➤ Relative

- Active infection at the site of the injection
- Patients with coagulopathies
- Preexisting neurologic deficit
- Inability to cooperate

# Complications of Regional Anesthesia

- ▶ The main complications seen in regional anesthesia are:
  - ▶ Block failure
  - ▶ Local anesthetic toxicity
    - ▶ Rare (0.01%)
    - ▶ Most associated with regional nerve block
  - ▶ Permanent neurological injury in central neural blockades is rare
  - ▶ Allergic reactions to local anesthetics may occur but rare
  - ▶ Post-dural puncture headache is a common (<1%) complication related to epidural and spinal anesthesia
  - ▶ Backache is a frequent complaint of neuraxial anesthesia
  - ▶ Central neural blockade may cause hypotension and severe bradycardia
  - ▶ Epidural or spinal hematoma is rare but can cause irreversible damage if it is not diagnosed promptly: BBW for anticoagulants
  - ▶ Epidural abscess is a serious but not frequent (0.07%) complication after neuraxial block

# History of Local Anesthetics

- It all started with cocaine & Freud
- 1850: Von Scherzer brought Coca leaves to Europe from Peru
- 1884: Koller performed first eye operation on a glaucoma patient using cocaine 10-30%
- 1891: Pure cocaine synthesized
- 1895: Freud- "I need a lot of cocaine, I am overflowing with new ideas, theoretical ones as well."
- 1891-1930: amino ester local anesthetics synthesized
- 1898-1996: amino amide local anesthetics prepared
- 1905: Novocaine found to be safe and effective for use
- 1965: Bupivacaine on the scene
- 1996: Ropivacaine appears

# Preservative or not preservative

- Preservatives added to inhibit bacteria growth
- Preservatives such as benzoyl alcohol, methyl & propyl paraben
- Usually added to multi-dose vials (MDV) & rarely to single-dose vials (SDV)
- Spinal injection: Documented adverse effects following injection of preservatives via blind injection, but no reported adverse consequences of preservative injection via properly guided injections
- Theoretical concern associated with epidural d/t continuous exposure to preservatives





# Local Anesthetics

## ▶ Esters

- ▶ Cocaine
- ▶ Benzocaine
- ▶ Procaine (Novocaine)-Bicillin C-R
- ▶ Tetracaine
- ▶ Chlorprocaine

## ▶ Amide

- ▶ Lidocaine
- ▶ Mepivacaine
- ▶ Bupivacaine
- ▶ Ropivacaine
- ▶ Levobupivacaine
- ▶ Prilocaine: Only used for dental
- ▶ Articaine: Only used for dental

# Ester Anesthetics

- Cocaine (Goprelto, Numbrino) 40mg/ml
  - Onset of action: 1 min
  - Duration:  $\geq 30$  mins
  - $T_{1/2}$  1-1.7 hours
- Only approved for intranasal anesthesia
- Cocaine 4% discontinued >1 year ago
- Adverse effects
  - HTN: 78%
- Concerns:
  - Lowering of seizure threshold
  - CV disease
  - Cocaine abuse



-Topical cocaine: Drug information. Hudson, OH: Lexicomp, 1978-2023. <http://online.lexi.com/>. Updated date. Accessed 1/6/23.

-Juergens Jeffrey. Cocaine: A Historical Perspective. March 19, 2016. Accessed at <https://www.addictioncenter.com/community/tbt-brief-history-cocaine/> on 1/13/2023.

-Cocaine. Accessed at <https://en.wikipedia.org/wiki/Cocaine> on 1/13/2023

# Ester Anesthetics

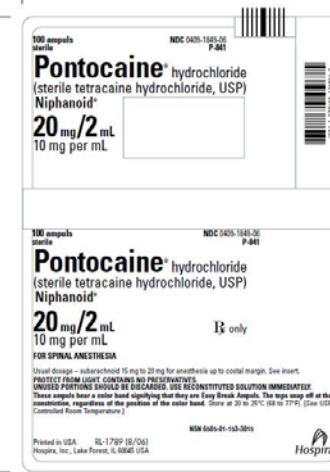
- Benzocaine (Anbesol) 20%
  - Onset of action: 15-30 seconds
  - Absorption: poor through intact skin, well absorbed through broken skin and mucous membranes
  - Duration: 5-10 mins
- Adverse effects
  - Contact dermatitis
- Concerns
  - Methemoglobinemia: increased risk with spray formulation in the mouth or mucous membranes especially in higher risk population





# Ester Anesthetics

- Tetracaine (Pontocaine, Dicaine) 1%
  - 1st synthesized in 1928 (chemist also discovered meperidine)
  - Onset of action: up to 15 mins
  - Duration: 1.5-3 hours
- Only approved for spinal anesthesia & eye stuff
- Adverse effects
  - Hypotension
- Concerns
  - Hyperthyroidism
  - Decreased plasma esterases
  - CV disease



-Tetracaine spinal: Drug information. Hudson, OH: Lexicomp, 1978-2023. <http://online.lexi.com/>. Updated date. Accessed 1/15/23.

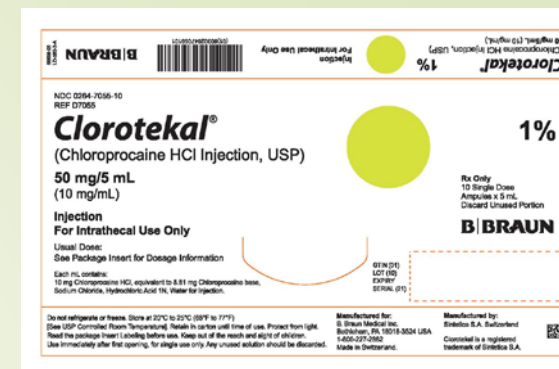
Tetracaine. Sigma Pharmaceutical accessed at <https://www.sigmapharmaceuticals.com/anesthetics/709-tetracaine-05-solution-5-ml-exp-722.html> on 1/28/23.

-Pontocaine. Wood Library. Accessed at <https://www.woodlibrarymuseum.org/museum/pontocaine/> on 1/28/23.



# Ester Anesthetics

- Chloroprocaine (Chloroketal, Nesacaine) regular & MFP: 1%, 2%, 3%
  - Approved for use in the USA since 1955
  - Onset of action: 6-12 min
  - Duration: up to 60 mins
- Use for local & regional anesthesia lasting less than 60 mins
- Manufacturer does not recommend for subarachnoid use (spinal) but Nesacaine MPF has been safely used off-label for spinal anesthesia
- Adverse effects
  - Procedural pain: 16%
  - Hypotension: 5%
- Concerns:
  - Contraindications related to spinal anesthesia:
    - Decompensated heart failure, hypovolemic shock coagulopathy
  - CV disease d/t hypotension & bradycardia (inadvertent intravascular administration)
  - Methemoglobinemia: Closely monitor G6PD, hx of methemoglobinemia, cardiac/pulmonary compromise, exposure to oxidizing agents, or infants <6 months



# Amide Anesthetics

- ▶ Lidocaine (Xylocaine) regular & MFP: 0.5%, 1%, 1.5%, 2%, 4%
  - ▶ Discovered in 1943, marketed in 1949
  - ▶ Onset of action: 3-20 mins
  - ▶ Duration: 2-2.5 hours
- ▶ Use for local & regional anesthesia
- ▶ Adverse effects
  - ▶ Procedural pain: 16%
  - ▶ Hypotension: 5%
- ▶ Concerns:
  - ▶ CV disease d/t hypotension & bradycardia (inadvertent intravascular)
  - ▶ Methemoglobinemia: Closely monitor G6PD, hx of methemoglobinemia, cardiac/pulmonary compromise, exposure to oxidizing agents, or infants <6 months



# Amide Anesthetics

- Mepivacaine (Carbocaine) regular & MPF: 1%, 1.5%, 2%
  - Available since 1960s
  - Onset of action: 2-4 mins
  - Duration: 3-3.5 hours
- Use for local & regional anesthesia
- Avoid intravascular or subarachnoid injection
- Aspiration should be performed to ensure no intravascular administration
- Adverse effects
  - Bradycardia, anxiety, chills confusion
- Concerns:
  - CV disease d/t hypotension and bradycardia (inadvertent intravascular administration)
  - Methemoglobinemia: Closely monitor G6PD, hx of methemoglobinemia, cardiac/pulmonary compromise, exposure to oxidizing agents, or infants <6 months
  - Concern if family history of familial malignant hyperthermia



# Amide Anesthetics

- ▶ Bupivacaine (Marcaine & Sensorcaine) regular and PF: 0.25%, 0.5%, 0.75%, Xaracoll Implant
  - ▶ Discovered in 1957
  - ▶ Onset of action: <15 mins
  - ▶ Duration: 2-8 hours
  - ▶  $T_{1/2}$ : 3.5 hours
- ▶ Use for local and regional anesthesia
- ▶ Xaracoll ® implant only for inguinal hernia repair
- ▶ Adverse effects
  - ▶ Nausea: 39-60%
  - ▶ Vomiting: 10-29%
  - ▶ Constipation: 7-42%
  - ▶ Headache: 6-32%
  - ▶ Parasthesia: 4-18%
  - ▶ Pruritis: 3-19%
  - ▶ Dysgeusia: 15-18%





# Amide Anesthetics

## ➤ Bupivacaine

### ➤ BBW:

- There have been reports of cardiac arrest with difficult resuscitation or death with use of bupivacaine for epidural anesthesia in OB patients using 0.75% concentration
- Resuscitation has been difficult or impossible despite apparently adequate preparation & appropriate management
- Cardiac arrest has occurred after convulsions resulting from systemic toxicity, presumably following unintentional intravascular injection
- 0.75% (7.5 mg/mL) concentration of bupivacaine is not recommended for OB anesthesia & should be reserved for surgical procedures where a high degree of muscle relaxation & prolonged effect are necessary
- Inadvertent intravascular injection could cause bupivacaine droplets to be deposited in the pulmonary or other capillary beds
- Administer bupivacaine into the subacromial space at the end of arthroscopic shoulder surgery
- Direct arthroscopic visualization must be used to confirm proper placement of the needle tip before injecting bupivacaine
- CV disease d/t hypotension & bradycardia (inadvertent intravascular administration)
- Methemoglobinemia: Closely monitor G6PD, hx of methemoglobinemia, cardiac/pulmonary compromise, exposure to oxidizing agents, or infants <6 months

# Amide Anesthetics

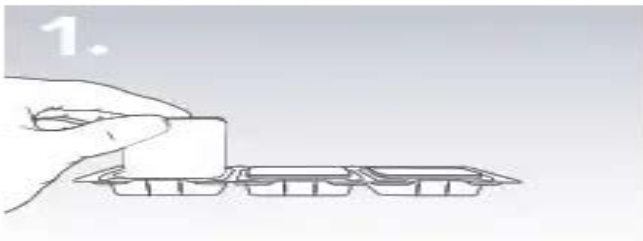
- ▶ Bupivacaine: Xaracoll® implant



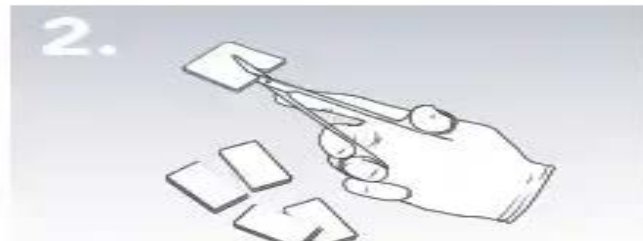
## PLACEMENT INSTRUCTIONS

Three fully resorbable collagen implants, each containing 100 mg bupivacaine HCl, for a total dose of 300 mg for open inguinal hernia repair.

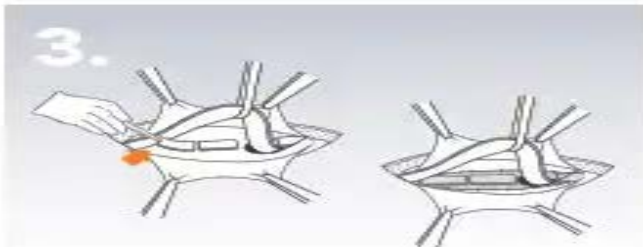
Intended for single-dose administration:



1. From package to procedure with no need for special preparation



2. 3 collagen implants should be cut in half and placed into surgical site dry



3. 3 halves should be placed into the inguinal hernia repair site below the site of mesh placement



4. 3 remaining halves should be placed between the muscle/fascia layer and skin closure

## ADDITIONAL PLACEMENT INSTRUCTIONS

- Supplied as a sterile product that should be handled using aseptic technique
- Inspect packaging and implants; do not use if damaged
- Outer pouch and inner blister should be peeled open aseptically
- Avoid excessive handling and compression of the collagen implants

# Liposomal Bupivacaine (Exparel) 1.3%



- ▶ Onset: Rapid
- ▶ Duration: Local: Up to 72 hours; Systemic: Plasma levels can persist for 96 hours after local administration or 120 hours after interscalene brachial plexus nerve block.
- ▶ Absorption: Systemic absorption varies; dependent on dose, route of administration, & vascularity of administration site
- ▶ Protein binding: 95%
- ▶  $T_{1/2}$ : 13 to 34 hours
- ▶ Note: Bupivacaine (liposomal) is not bioequivalent to bupivacaine HCl;
  - ▶ Dosing conversion from bupivacaine HCl to bupivacaine (liposomal) or vice versa is not available
  - ▶ Non-bupivacaine-based LA may cause an immediate release of bupivacaine (liposomal) if administered together locally
  - ▶ **Bupivacaine** should NOT be administered sooner than 20 minutes after injection of **lidocaine**
  - ▶ Do not administer other LA or other formulations of bupivacaine within 96 hours of bupivacaine (liposomal) administration
  - ▶ Bupivacaine HCl may be administered simultaneously in the same syringe or injected immediately before bupivacaine (liposomal) if the mg ratio of bupivacaine HCl to bupivacaine (liposomal) does not exceed 1:2
- ▶ **However, Cochrane reviews have commented on the 'low quality and volume of evidence' and the lack of benefits of liposomal bupivacaine over bupivacaine for infiltration and peripheral nerve blockade to treat postsurgical pain**



# Amide Anesthetics

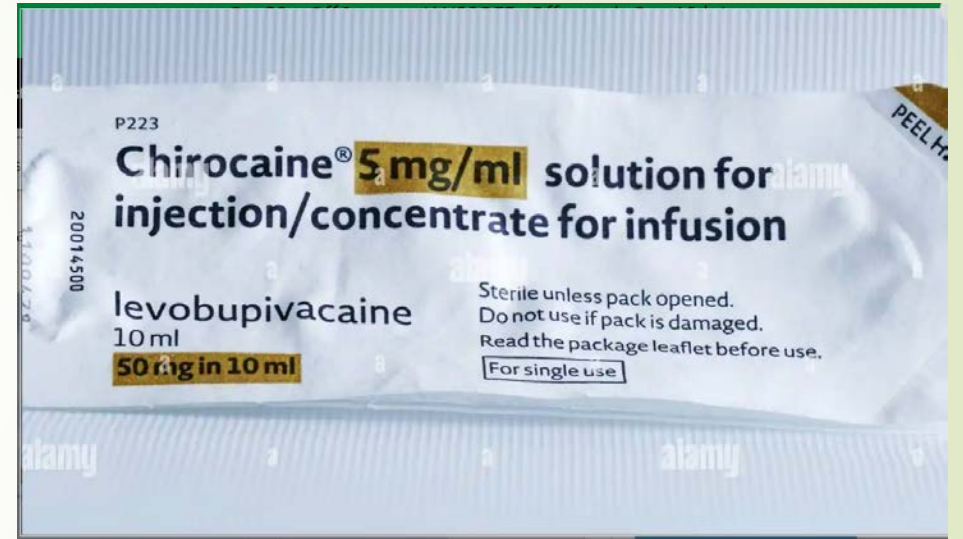
- Ropivacaine (Naropin) regular & preservative free 2mg/ml, 5mg/ml, 7.5mg/ml, 10mg/ml
  - FDA approved in 1996
  - Onset of action: 3-15 mins dependent on route
  - Duration: 3-15 hours dependent on route
  - $T_{1/2}$ : 5-7 hours
  - S-enantiomer of mepivacaine
- Use for local & regional anesthesia
- Adverse effects
  - Bradycardia: 6-20%
  - Hypotension: 32-69%
  - Nausea: 13-25%
- Concerns
  - CV disease d/t hypotension & bradycardia (inadvertent intravascular administration)
  - Methemoglobinemia: Closely monitor G6PD, hx of methemoglobinemia, cardiac/pulmonary compromise, exposure to oxidizing agents, or infants <6 months





# Amide Anesthetics

- ▶ Levobupivacaine (Chirocaine)
  - ▶ FDA approved in 1999.
  - ▶ Single isomer form of bupivacaine
- ▶ Removed from U.S. market, still available in Europe



# Metabolism and Elimination

- ▶ Amide LA (e.g., lidocaine, mepivacaine, bupivacaine, ropivacaine) are used most & are metabolized primarily by the liver
- ▶ Most ester LA are metabolized by plasma cholinesterases in the blood
- ▶ Very little medication is renally eliminated unchanged <1%
  - ▶ Renal failure rarely causes an increase in serum concentrations of active medication

# Opioids

- ▶ MOA for Nerve Block
  - ▶ Act by boosting the antinociception of LA
  - ▶ It causes hyperpolarization of the afferent sensory neuron through G-coupled receptor mechanism
- ▶ Buprenorphine
  - ▶ Lipophilic partial opioid receptor agonist that acts by blocking voltage-gated Na<sup>+</sup> channels & acts as LA
  - ▶ The metabolic intermediate is norbuprenorphine, which acts on MOR, KOR, & DOR
  - ▶ Potential anti-hyperalgesic effects
  - ▶ Application of perineural buprenorphine along with levobupivacaine interscalene in shoulder arthroscopy doubles the length of time for analgesia
  - ▶ Bupivacaine supraclavicular blocks with perineural buprenorphine are superior (analgesia prolonged by 6 h) to bupivacaine with IM buprenorphine
  - ▶ Almost no studies showed any difference in the occurrence of PONV or respiratory depression as adverse effects in patients receiving opioids with anesthetics & not receiving anesthetics

# Opioids

## ▶ Fentanyl

- ▶ Compared to morphine, intrathecal fentanyl (10–25 µg dose) has exhibited a prolonged & higher extent of the sensory block with less adverse effect
  - ▶ Epidural fentanyl with a higher occurrence of adverse effects
- ▶ **Low benefit for the use of fentanyl with other local anesthetics, such as ropivacaine or lidocaine plus epinephrine, mepivacaine plus epinephrine (in supraclavicular blocks), ropivacaine (in sciatic/femoral blocks), and lidocaine (interscalene blocks)**
- ▶ Studies have shown that the combination of fentanyl with 0.25% bupivacaine and epinephrine prolonged the anesthesia by 18 h in paravertebral blocks
- ▶ Fentanyl boosted the efficacy of bupivacaine & lidocaine mixture in cervical plexus blocks

## ▶ Sufentanil

- ▶ A lower dose range (1.5 µg) of sufentanil is recommended for less adverse effect
- ▶ Epidural administration of 0.75–1 µg /mL sufentanil showed excellent potential in alleviating pain in various patients when combined with ropivacaine 0.1% (total hip replacement)



# Opioids

## ▶ Tramadol: Not available in the U.S.

- ▶ It is a weak opioid that acts by blocking Na<sup>+</sup> & K<sup>+</sup> channels as well as acting as a weak serotonin/norepinephrine reuptake inhibitor
- ▶ Tramadol used through intrathecal route at a dose of 10–50 mg has been used with varying degree of success
- ▶ Epidural dose of 1–2 mg/kg of tramadol has been used in varied types of surgeries such as obstetric, pediatric abdominal surgeries, & lower abdominal surgeries
- ▶ Tramadol as an adjuvant to LA in PNB has yielded with contradictory results with uncertain safety profile
- ▶ Use of this agent is recommended only in postoperative epidural infusion, not as an adjuvant to local anesthetics in PNB

## ▶ Morphine

- ▶ Intrathecal morphine (100–200 mg) & epidural morphine (1–5 mg) have shown good analgesic effect in obstetric, orthopedic surgery, & diverse subsets of the population
- ▶ Use of morphine as an adjuvant in PNB exhibits contradictory results in different studies
  - ▶ Some showing prolongation of analgesia, but many showed no benefit
  - ▶ Use of morphine in PNB is not recommended
  - ▶ Studies have failed to show any advantage of PNB aided by morphine over IV & IM routes

# Vasoconstrictors

- Addition of a vasoconstrictor to a LA:
  - Decrease in the peak plasma concentration of the LA
  - Increase in the duration & the quality of anesthesia
  - Reduction of the minimum concentration of anesthetic needed for nerve block
  - Decrease of blood loss during surgical procedures
- Addition of vasoconstrictor to regional anesthesia:
  - Should not be used in nerve blocks because many nerves run immediately adjacent to arterial vessels
  - Inadvertent intravascular injection could cause ischemia
  - Epinephrine administration also should be avoided near the terminal arterial branches in the digits, tip of the nose, ear lobes, or tip of the penis
  - Some providers will add epinephrine to epidural injection to identify intravascular injection- no more than 5ml & monitor for 2 mins to detect change in HR

-Sisk AL. Vasoconstrictors in local anesthesia for dentistry. *Anesth Prog.* 1992;39(6):187-93. PMID: 8250339; PMCID: PMC214861

-Salam GA. Regional anesthesia for office procedures: part I. Head and neck surgeries. *Am Fam Physician.* 2004 Feb 1;69(3):585-90. PMID: 14971840

-Rom A. Stevens M.D., Nigel E. Sharrock M.B., Ch.B, [Epidural Anesthesia. Essentials of Pain Medicine and Regional Anesthesia \(Second Edition\)](#), 2005. Accessed at

<https://www.sciencedirect.com/topics/medicine-and-dentistry/epidural-anesthesia#:~:text=Bupivacaine%20or%20levobupivacaine%200.5%20to,of%20sensory%20and%20motor%20block>. On 1/15/2023

# Vasoactive/alpha-2 agonist

## ► Clonidine

- Imidazole derivative used for PNB
- Acts through hyperpolarization of nucleotide-gated ion channels for *in vivo* elongation of nerve blockade by LA
- **Meta-analysis showed that clonidine can extend the duration of nerve blockade by ~ 2 hours**
- Doses ranging from 30-300 µg of clonidine prolong the time of request for first analgesic by 2-2.5 h
- 70% of the trial studies, clonidine 150mcg is the effective dose
- Bupivacaine/clonidine was shown to prolong the popliteal fossa nerve blockade but failed to show the same effect with 0.5% levobupivacaine
- High dose clonidine has systemic side effects including hypotension & bradycardia which should be avoided

## ► Dexmedetomidine

- May also causes hypotension & bradycardia
- Dexmedetomidine prolongs the motor & sensory blockade effect of intrathecal bupivacaine
- Can prolong the blockade of the peripheral nerve by 200 min in a dose of 1 µg/kg
- Systematic review & meta-analysis by Abdallah & Brull have shown that dexmedetomidine can further extend the action of long-acting LA used in spinal blocks
- Peripheral application of dexmedetomidine may exceed the effect of clonidine
- Different doses ranging from 1 µg/kg, 30 µg, 100 µg to 0.75 µg/kg of additive were used in different studies
- Perineural dosages >60mcg can significantly increase the risk of reversable bradycardia/hypotension

# Anesthetic Allergy

- ▶ Most idiosyncratic reactions are nonallergic
- ▶ 2 distinct types
  - ▶ Allergic contact dermatitis & delayed swelling at site of administration
    - ▶ Uncommon, but well established
    - ▶ Begin hours after injection
    - ▶ Peak around 72 hours
    - ▶ Type IV hypersensitivity reaction
  - ▶ Generalized urticaria or anaphylaxis
    - ▶ Rare & data is limited to case reports
    - ▶ Sxms usually begin within an hour
    - ▶ Some reaction (Ig)E mediated type I hypersensitivity reaction



# Anesthetic Allergy

- ▶ Suspected local anesthetic allergy should be referred for evaluation by allergist or dermatology
- ▶ Limited evidence in cross-reactivity based on structural group
- ▶ Possible allergens that could also be involved
  - ▶ Latex
  - ▶ Chlorhexidine
  - ▶ Parabens
  - ▶ Ethylenediaminetetraacetic acid (EDTA)
  - ▶ Sulfites-antioxidant but no relation to immunogenicity

# Special Populations

## Morbid Obesity (BMI >40)

- High risk for:
  - Difficult airway management
  - Cardiopulmonary dysfunction
  - Acid aspiration
  - Increased perioperative morbidity and mortality
- Difficulty of regional anesthesia due to:
  - Patient positioning
  - Identifying usual bony landmarks
  - Needle penetration

# Special Populations

## Morbid Obesity (BMI >40)

- ▶ Duke University Medical Center performed an analysis of 9,038 procedural blocks performed in an ambulatory center
- ▶ Block failure per BMI
  - ▶ BMI <25: 9.5%
  - ▶ BMI 25-29: 10.7%
  - ▶ BMI >30: 12.7%
  - ▶ BMI >35: 12.9%
- ▶ Review of risk adjusted outcomes show that the only statistically significant change in block failure was in BMI >30
- ▶ **BUT**
- ▶ Overall rate of complications was low 0.3%



# Special Populations Breast Feeding Persons


- Worrisome due to transfer of meds into breast milk
- Most recommendations are “pump & dump” for 24 hours after receiving anesthesia to avoid passing meds to the child
- Transfer of meds into breast milk depends on pharmacological properties such as:
  - Protein binding: less enters breast milk
  - Lipid solubility: increased enters breast milk
  - Molecular weight: less enters breast milk
  - Maternal plasma level: increased enters breast milk



# Special Populations

## Breast Feeding Persons

- ▶ Neuraxial anesthesia considered the gold standard
  - ▶ Site of LA is major determinant of systemic levels of LA
  - ▶ Intercostal & epidural space is considered highly vascular=higher absorption
  - ▶ Femoral/sciatic & brachial plexus region considered less vascular=lower absorption
- ▶ No studies evaluate the absorption rate of LA for different regional nerve blocks in breastfeeding mothers
- ▶ Case report demonstrated the use of bupivacaine 0.25% at 10ml/hr for 5 days in a breastfeeding mother showed no detectable quantities in the infant's blood
  - ▶ This is due to low oral bioavailability of bupivacaine
  - ▶ Cessation of breastfeeding with LA is not needed



# Special Populations: Substance Use Disorder (SUD)

- ▶ Not an absolute contraindication to anesthesia & opioids
- ▶ Mitigation or exposure avoidance is important to prevent relapse
- ▶ SUD increases likelihood of:
  - ▶ Aspiration
  - ▶ Generalized edema
  - ▶ Compromised airway
  - ▶ Venous thrombosis
  - ▶ SQ abscess
  - ▶ Lymphadenopathy
  - ▶ Hepatomegaly
  - ▶ Hemodynamic instability
  - ▶ Encephalopathy
  - ▶ Increased tolerance to opioids

# Local Anesthetic Systemic Toxicity (LAST)

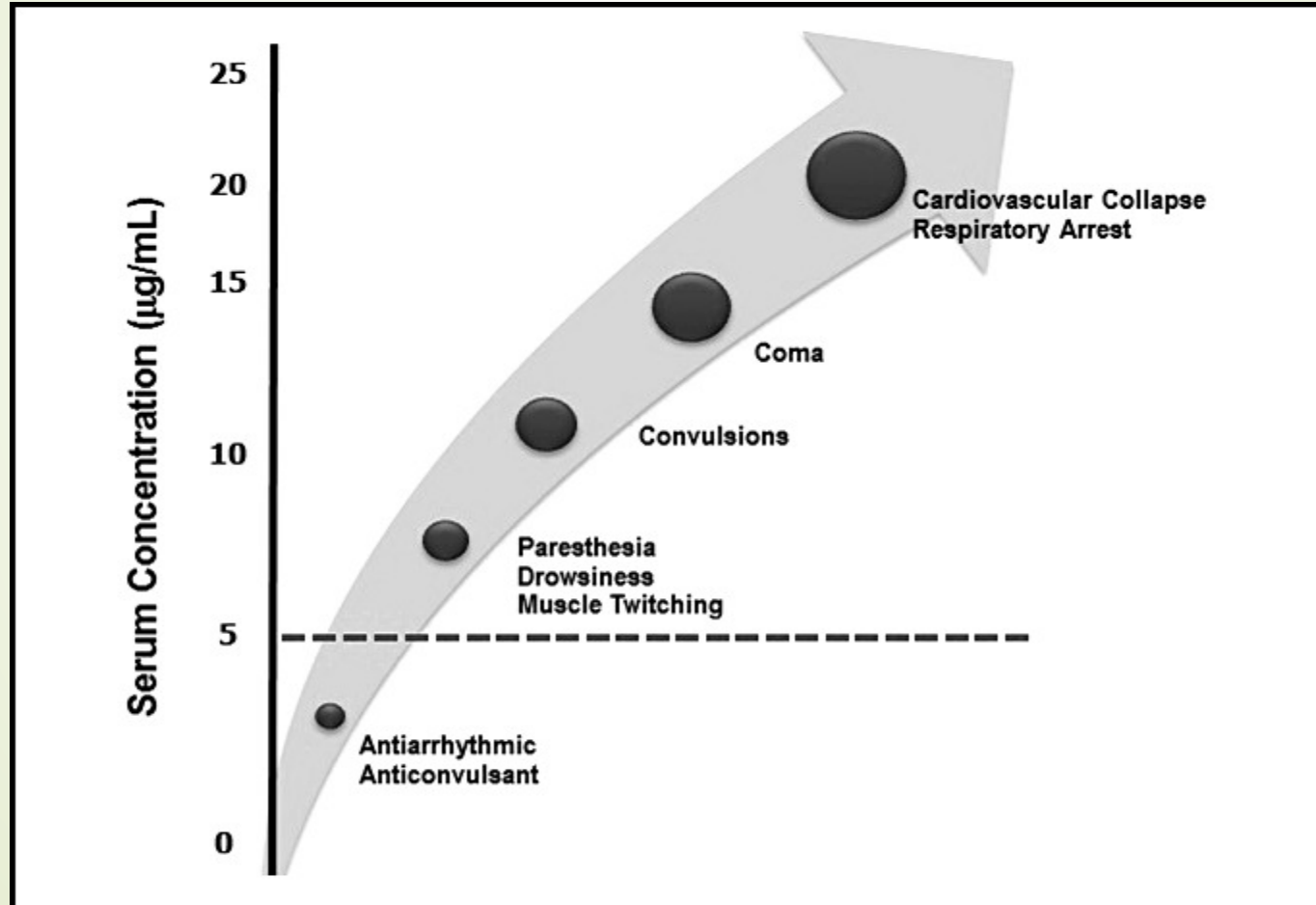
- ▶ 1st discovered in the 1970s as cardiac effects associated with bupivacaine & fatal cardiac arrest
- ▶ Rising use of LA in practice has increased the incidence of LA toxicity
- ▶ Sxms range from minor to cardiac arrhythmias and seizure
- ▶ Reports are highly variable
  - ▶ 0/12,000 nerve blocks in some reports
  - ▶ 25/10,000 reported in others
  - ▶ 79/10,000 brachial plexus blocks resulted in seizures

# Local Anesthetic Systemic Toxicity (LAST)

- Usually occurs from accidental intravascular administration
- Comorbidities may increase the likelihood
  - Hepatic dysfunction
  - Cardiac disease
  - Pregnancy
  - Metabolic syndrome
  - Older adults
  - Infants <4 months of age
- Normally presents within 50 seconds in 50% of cases & within 5 minutes of 75% of cases



# Serum Concentration and Adverse Effects



# Local Anesthetic Systemic Toxicity (LAST)

## ➤ Recognition

### ➤ Initial

- Agitation, confusion, dizziness, drowsiness, dysphoria, auditory changes, tinnitus, perioral numbness, metallic taste, dysarthria

### ➤ Progression

- Seizures, respiratory arrest, coma, cardiac toxicity (bradycardia, hypotension, hypertension, wide complex ST segment changes, asystole, ventricular ectopy/tachycardia/fibrillation)

# Local Anesthetic Systemic Toxicity (LAST)

## ► Treatment:

- Airway-immediate ventilation and oxygenation
- Seizures- benzodiazepines
  - Consider propofol or thiopental but they increase the risk of hypotension and cardiac depression
- Hypotension & decreased cardiac output:
  - Standard ACLS guidelines BUT:
    - Epinephrine: use < 1mcg/kg instead of 1mg
    - NO vasopressin: increase risk of pulmonary hemorrhage
    - NO calcium channel blocker (diltiazem/verapamil) or beta blockers (esmolol, metoprolol)
    - NO procainamide: will exacerbate the condition
    - Amiodarone for arrhythmias

# Local Anesthetic Systemic Toxicity (LAST)

## ► Treatment:

### ► Possible use of lipid emulsion therapy

- Utilized in case studies
- 1.5ml/kg of 20% lipid emulsion and subsequent infusion of 0.25ml/kg/min x 10 mins after hemodynamic stability attained
- Not to exceed 10ml/kg for 30 minutes

### ► Worst Case Scenario

- Cardiopulmonary bypass recommended until the LA is cleared



-Mahajan A, Derian A. Local Anesthetic Toxicity. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from:

<https://www.ncbi.nlm.nih.gov/books/NBK499964/>

-[https://www.msoca.org/angell\\_services/intravenous-lipids/](https://www.msoca.org/angell_services/intravenous-lipids/) accessed on 1/15/2023.

-First cardiopulmonary bypass machine. [https://en.wikipedia.org/wiki/File:Cardiopulmonary\\_bypass\\_machine.png](https://en.wikipedia.org/wiki/File:Cardiopulmonary_bypass_machine.png) accessed on 1/15/2023





# Questions

