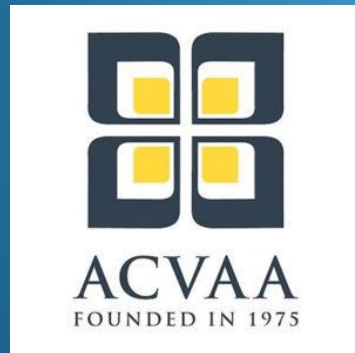


Preventive Analgesia for the High Volume Spay Neuter Environment



Lydia Love DVM DACVAA

May 2018

A few definitions

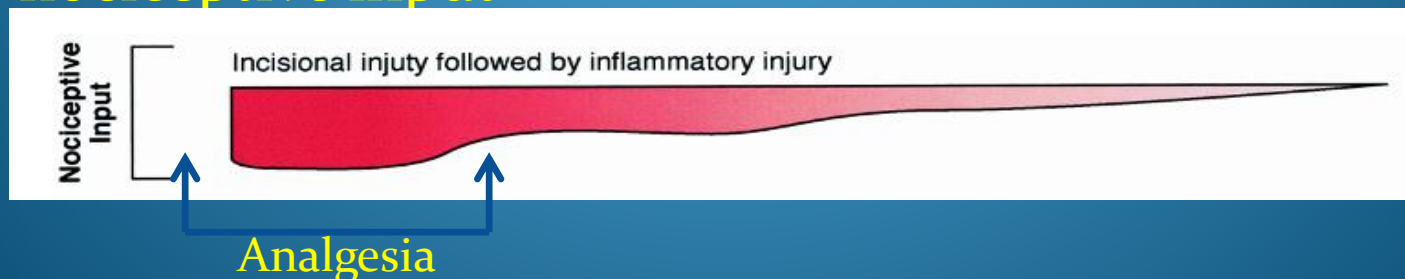
- Pain
 - An unpleasant sensory and emotional response to actual or potential tissue damage
 - Subjective experience
- Nociception
 - Neural encoding of actual or potential tissue damage
 - Does not imply conscious awareness
- Central sensitization
 - Amplification of the excitability and efficiency of central nociceptive neural pathways
 - CNS activity-dependent plasticity



A few definitions



- Multimodal analgesia
 - The use of different classes of analgesics that interrupt the pain pathway at various locations
 - Allows for lower doses of any one drug
- Pre-emptive analgesia
 - Limited to administration of analgesic prior to nociceptive input

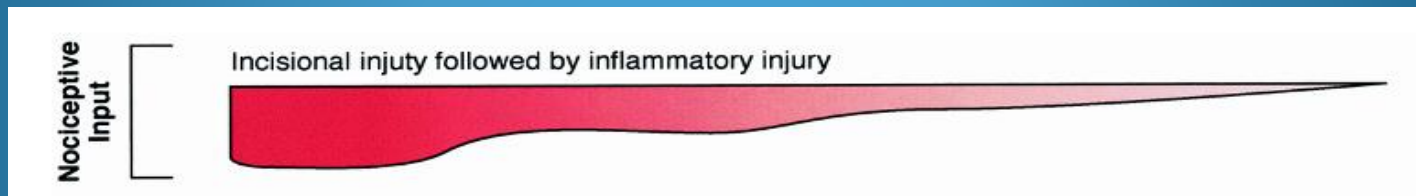


Preventive Analgesia

- A comprehensive analgesic strategy designed to minimize the deleterious immediate and long-term effects of nociceptive perioperative input
 - Pre-emptive
 - Multimodal
 - Efficacious
 - Of adequate duration

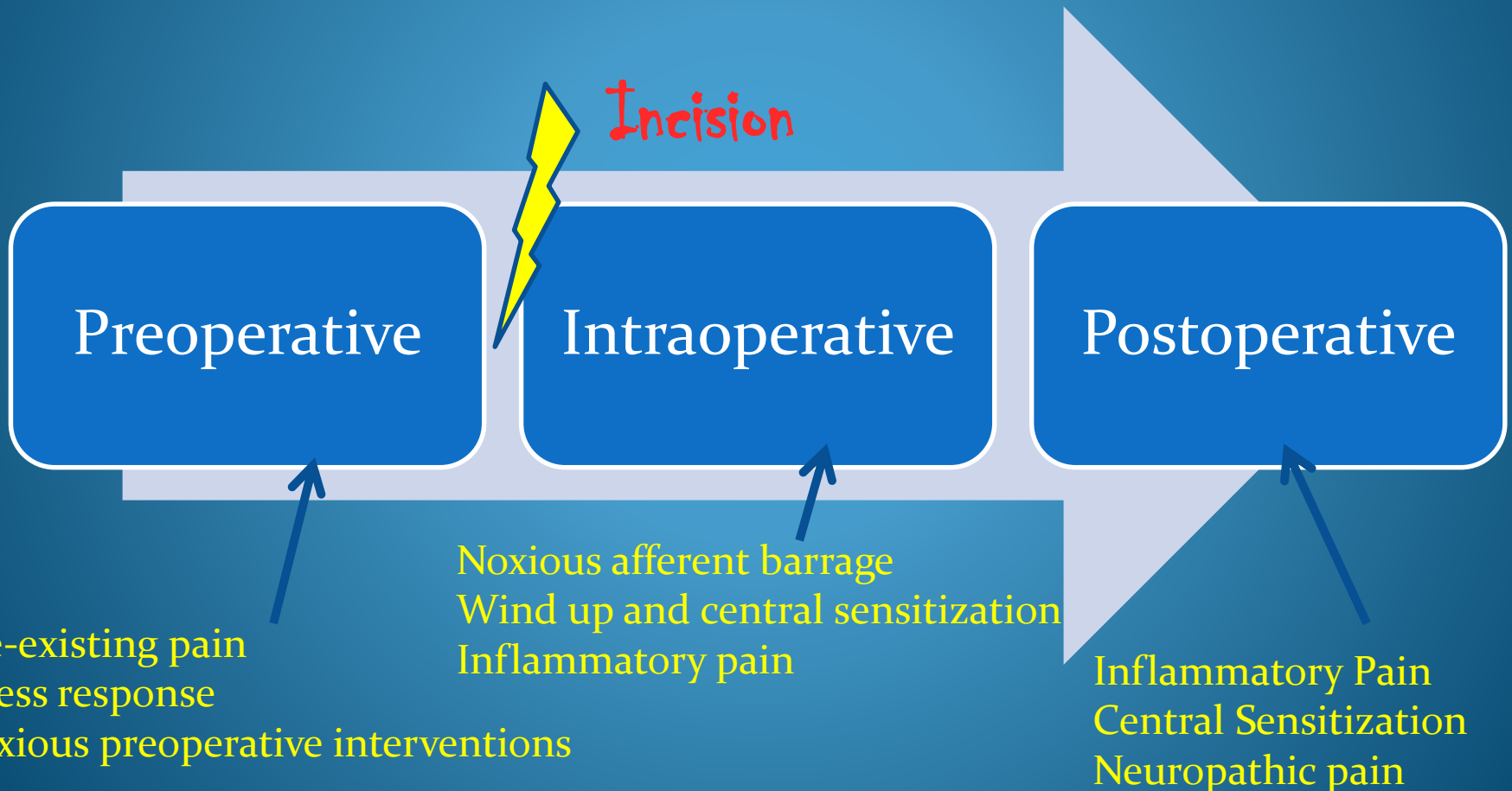
Preventive Analgesia

- Recognizes that afferent nociceptive barrage at time of incision is not the only factor

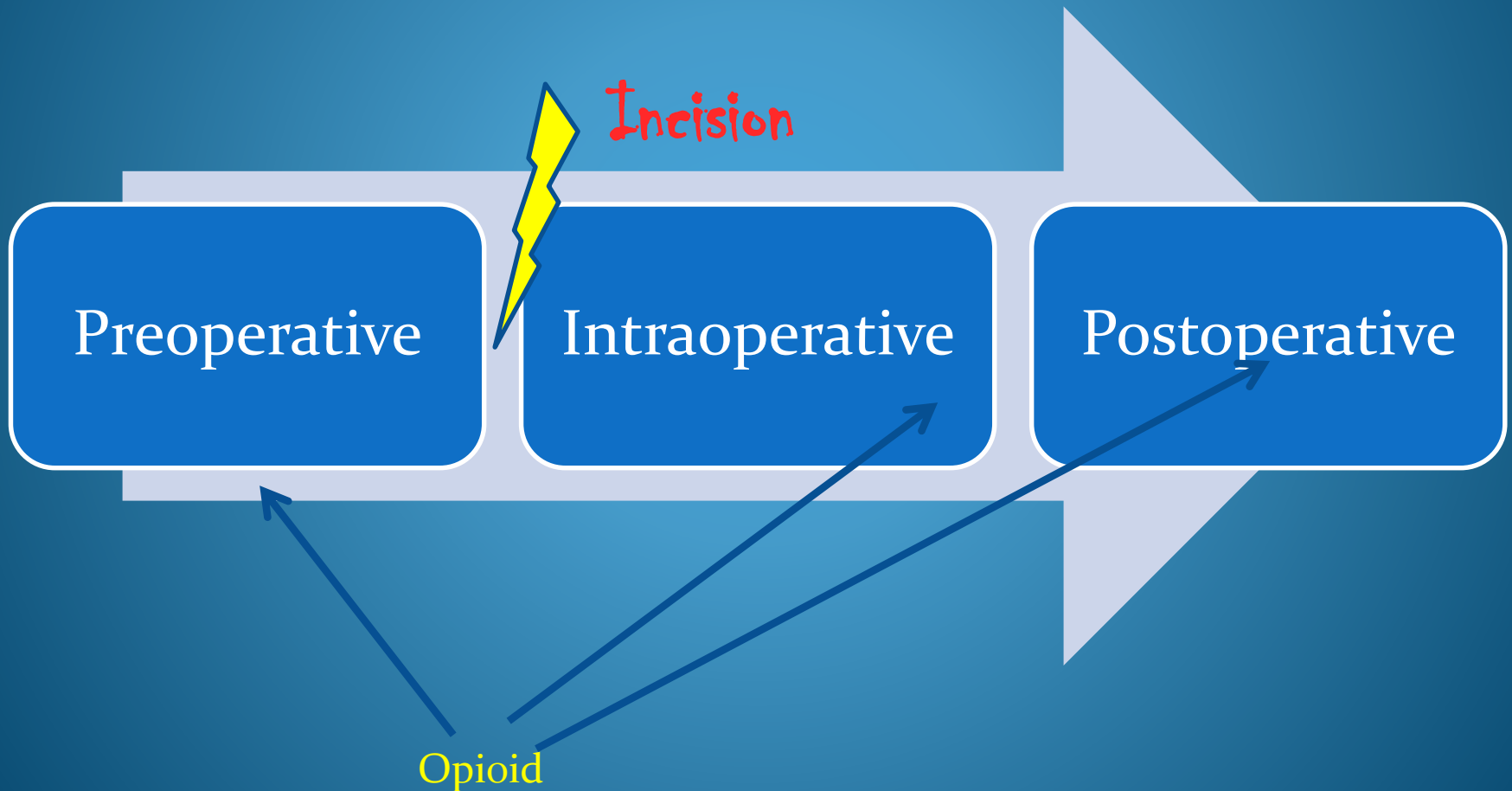


- Aims to cover pre-, intra-, and post-operative noxious events
- Reducing immediate analgesic needs
- Reducing central sensitization & chronic pain

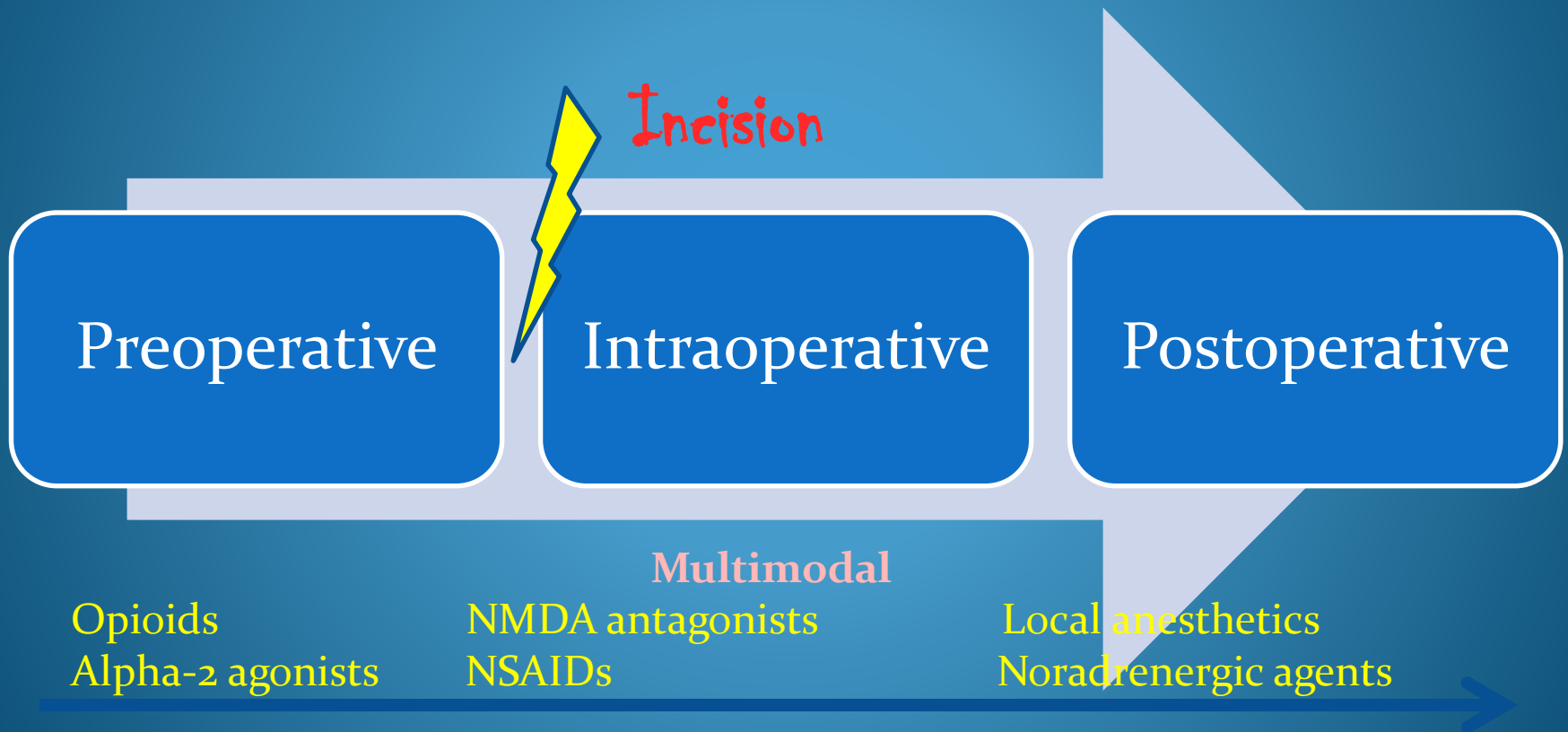
Pre-emptive Analgesia



Pre-emptive Analgesia



Preventive Analgesia



Duration of analgesic action covers **entire perioperative time period**

Preventative Analgesia

- Drug options
 - Opioids
 - Alpha-2 agonists
 - NMDA antagonists
 - Local Anesthetics
 - NSAIDs
 - Oral adjuncts

Pain Pathway

Opioids
Alpha₂ agonists
NMDA antagonists

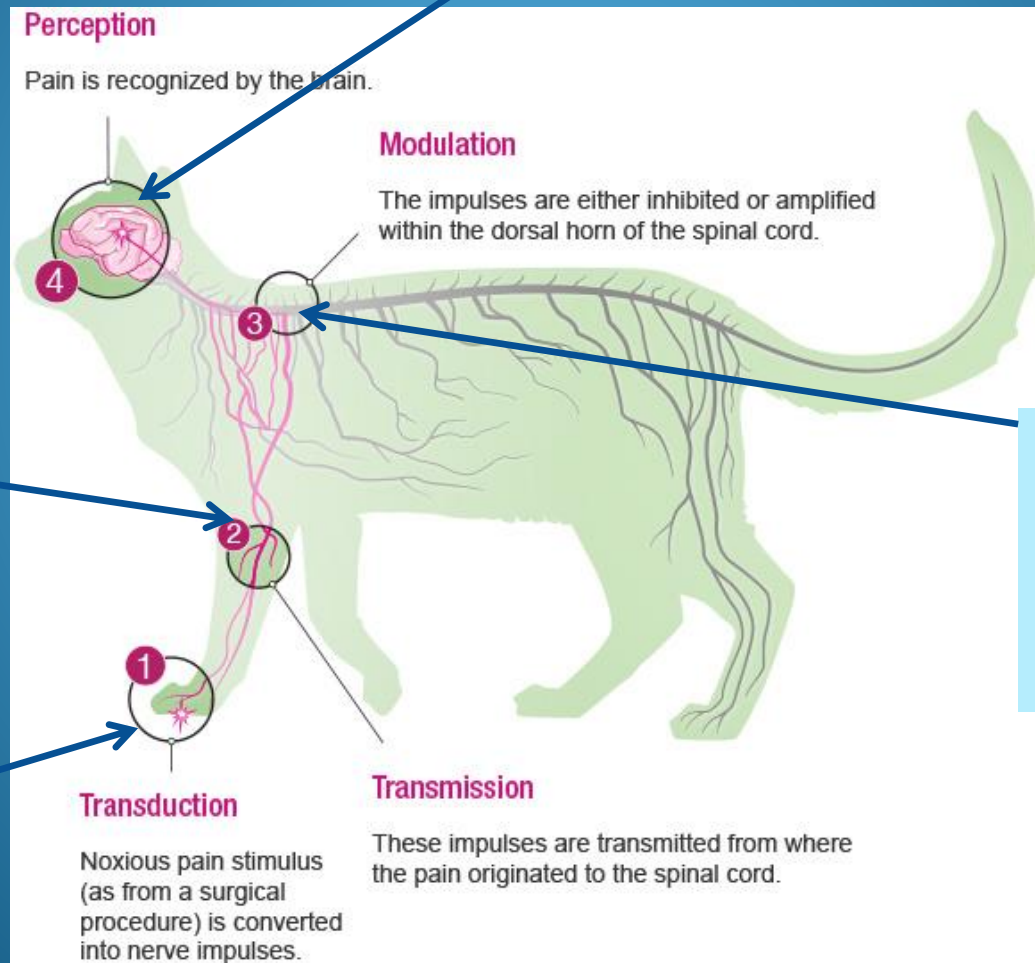
Local anesthetics

Local anesthetics

NSAIDs

Opioids

Alpha-2 agonists

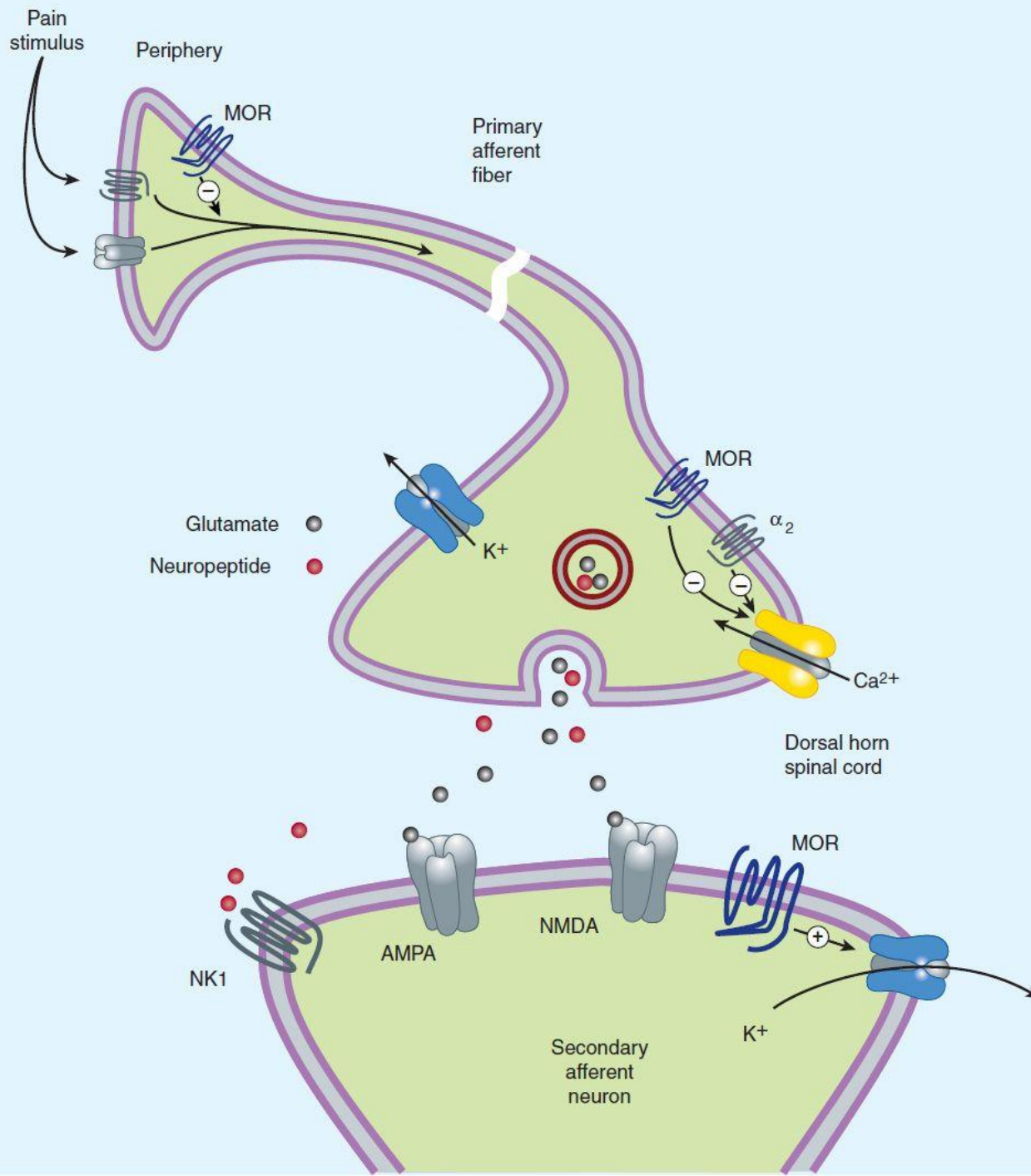


Opioids
Local anesthetics
Alpha₂ agonists
NMDA antagonists
NSAIDs

Opioids

- Foundational analgesics
- Opioid receptors highly conserved across species
 - Important for maintenance of homeostasis
 - Pharmacogenetic differences exist
- Mu, kappa, delta, ORL-1 receptors
- Endorphins, enkephalins, dynorphin, nociceptin





Opioids

Full mu agonists

Morphine

Hydromorphone

Oxymorphone

Meperidine

Methadone

Fentanyl

Remifentanyl

Mixed agonist-antagonists

Buprenorphine

Butorphanol

Nalbuphine

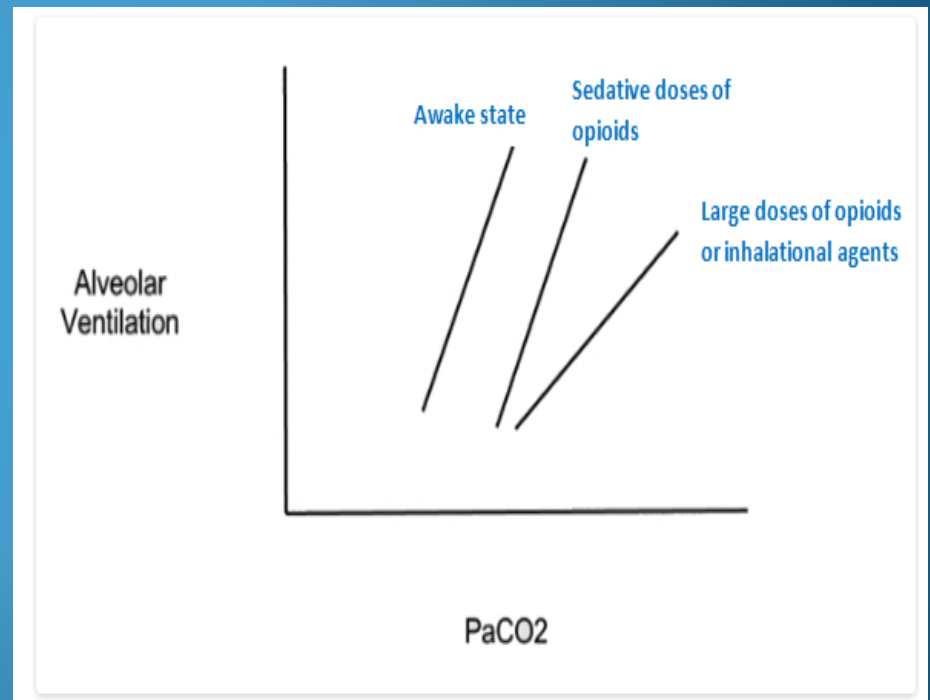
Antagonists

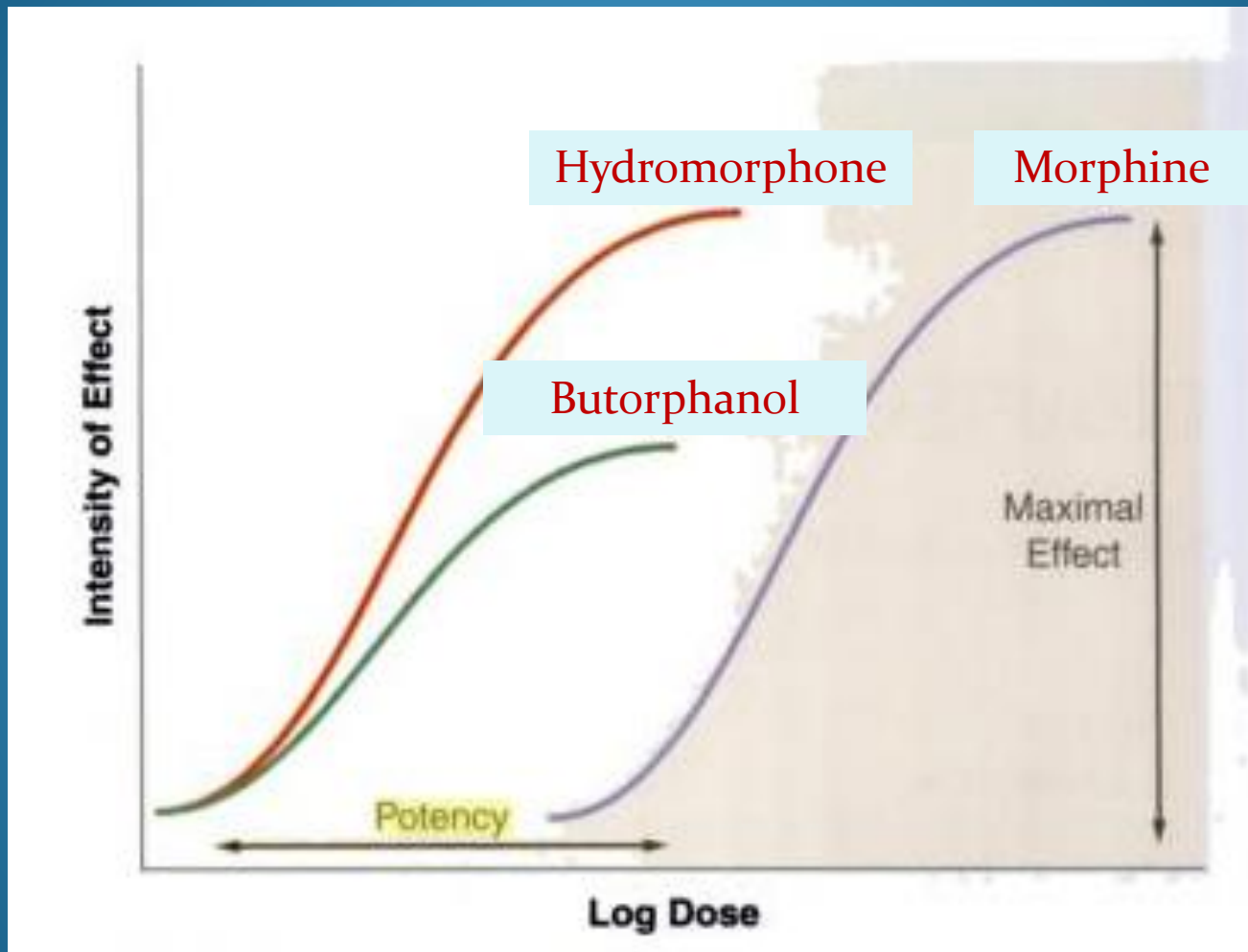
Naloxone

Naltrexone

Adverse Effects of Opioids

- Cardiovascular
- Respiratory
- Thermoregulation
- Gastrointestinal
- Urinary tract
- Immune system





Clinical Anesthesia by Paul Barash

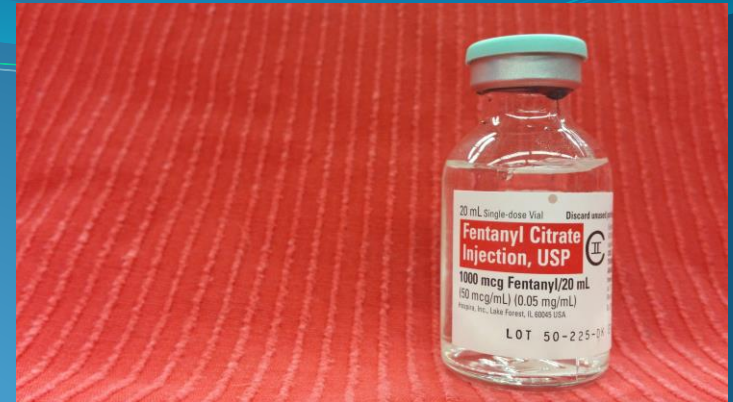
Full mu agonists

- Morphine
 - Inexpensive, can release histamine
 - Likely to cause vomiting
- Hydromorphone
 - Still rather inexpensive
 - A little less vomiting, minimal histamine release
- Methadone
 - Expensive
 - Still less vomiting, SNRI & NMDA antagonist



Full mu agonists

- Fentanyl and its congeners
 - Short-acting
 - IM administration lasts ~ 30 min
 - Infusion must be set up for ongoing analgesia
 - Relatively expensive
 - Good choice for hemodynamically unstable patients
 - Not likely to be used in HVSN clinics



Mixed agonist/antagonists

- Buprenorphine
 - Partial mu agonist, kappa antagonist
 - Good analgesic for moderate pain
 - Higher doses last longer
 - Not absorbed well SQ in cats
 - Can be given OTM
 - Relatively expensive
 - Could consider Simbadol as cheaper on a per mg basis

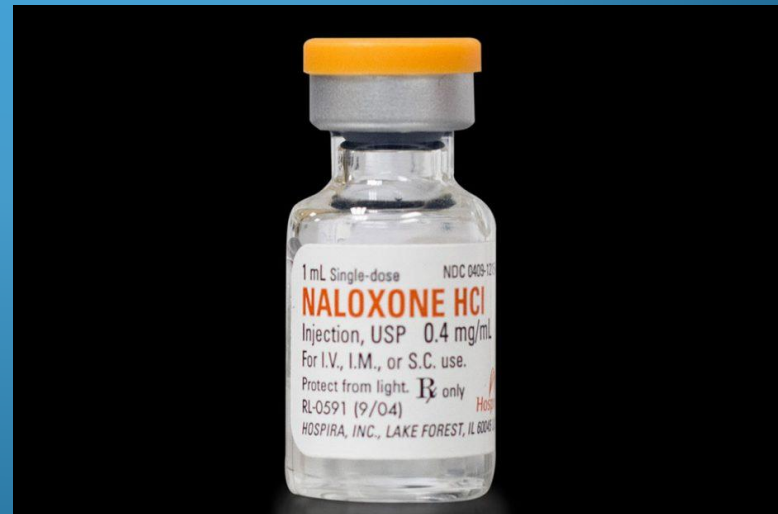


Mixed agonist/antagonists

- Butorphanol & Nalbuphine
 - Good sedative
 - Mild analgesic activity
 - Ineffective analgesic for abdominal procedures
- Combine with local anesthetics and NSAIDs for minor procedures

Opioid Antagonists

- Naloxone
 - Antagonistic at all opioid receptors
 - Should have available for anesthesia-related CPR
 - Also, can titrate to reverse unwanted opioid effects
 - Dysphoria
 - Hyperthermia



Alpha₂ Agonists

- Presynaptic alpha₂ receptors
 - Inhibit norepinephrine release
 - Increase descending inhibition
- Co-localize with opioid receptors on primary afferents and in the dorsal horn
- Profound analgesia
 - Sedative effects outlast analgesic effects



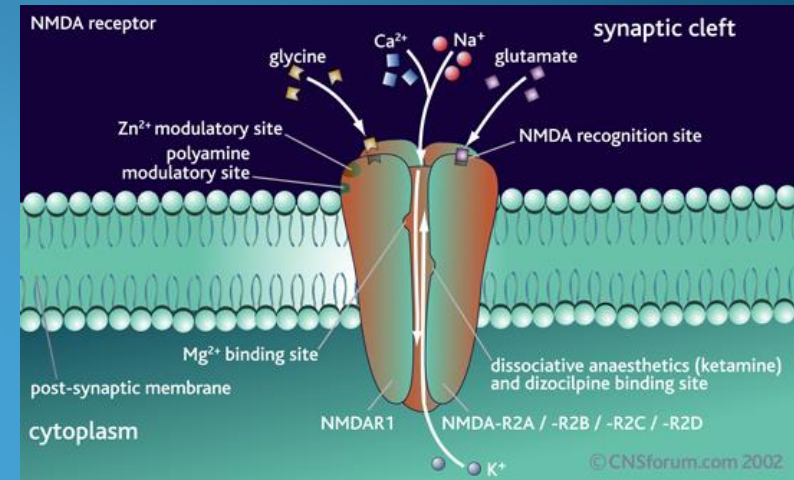
Alpha₂ Agonists

- Profound cardiovascular effects
- Profound sedative qualities
- Profound anxiolysis
- Only partially dose-dependent
- Reversible



NMDA Antagonists

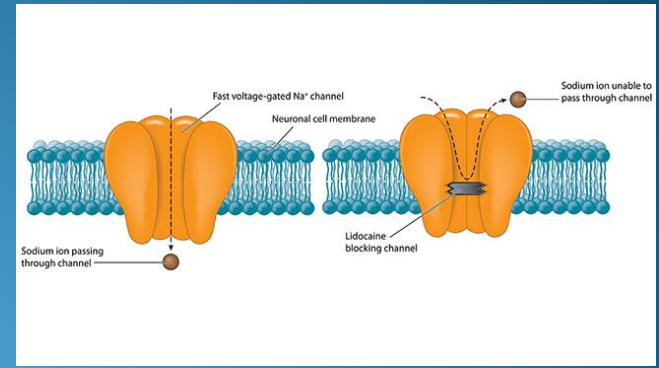
- Ketamine/Tiletamine
 - Block glutamate activation of NMDA channels
 - Voltage- and ligand-gated
 - Partial depolarization kicks Mg^{2+} blockade out
 - Basis for windup and central sensitization
 - Dissociatives binding site in the pore
- Ketamine provides analgesia and anti-hyperalgesia



www.cnsforum.com

Local Anesthetics

- Block voltage-gated Na^+ channels
- Weak bases must be in uncharged form to cross the lipid bilayer
- Prevent afferent nociceptive traffic
- Decrease inhalant & opioid requirements
- Reduce the stress response, reduce windup and central sensitization
- Improve GI function, decrease hospital stays, improve patient satisfaction, reduces the incidence of chronic pain



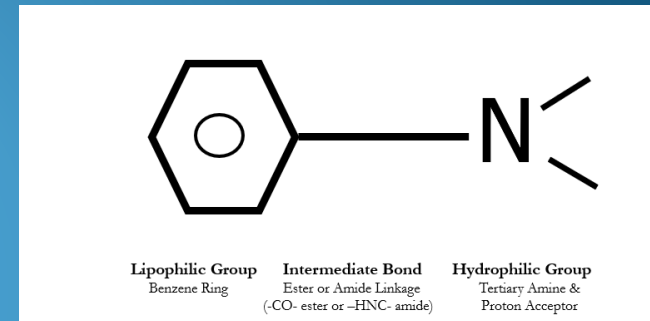
www.brainfacts.org

Incorporating Local Anesthetics

- Pre-incisional infiltration
- Wound infiltration
- Body wall splash
- Intratesticular/spermatic cord blocks
- Intraperitoneal blocks
- Soaker catheters
- Epidural

Short-acting Local Anesthetics


- Lidocaine
 - Fast onset
 - Duration 45 – 90 minutes
 - Keep total dose under ~5 mg/kg
- Mepivacaine
 - Lowest pKa, fast onset
 - Duration 45 – 90 minutes
 - Dosing as for lidocaine



Long-acting Local Anesthetics

- Bupivacaine
 - Slightly slower onset
 - Duration up to ~240 minutes
 - Differential blockade can be pronounced
 - CNS and CV toxicity closer than with lidocaine
 - Maximum dose ~2 mg/kg
- Ropivacaine
 - S-enantiomer
 - Safer cardiovascular profile
 - Maximum dose 2-3 mg/kg

Local Anesthetic Adjuncts

- Duration of action influenced by:
 - Lipophilicity
 - Vascularity of tissue
 - Protein binding
 - Adjuncts
 - Epinephrine, alpha-2 agonists, buprenorphine
 - Steroids, tramadol, neostigmine
-  Mixing short- and long-acting drugs
 - Does not provide onset benefit
 - Shortens duration of action

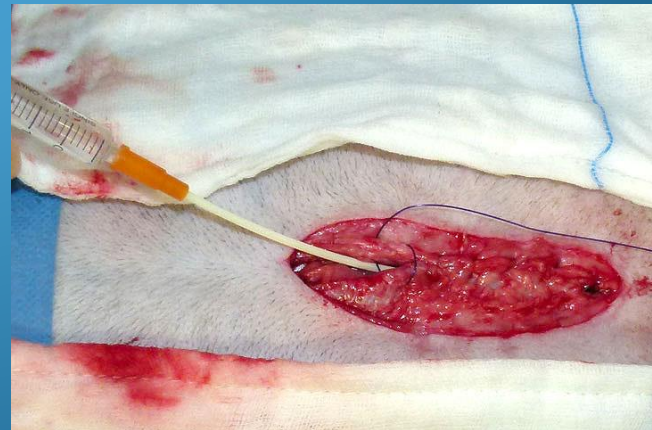
Intratesticular Blocks

- Aspirate first
- Inject until testicle feels turgid
- Hematoma on testicle may result
- Cats
 - 0.25 mL local anesthetic injected into each testicle
- Dogs
 - Depends on size of dog
 - Usually a maximum of 2 mL/testicle will suffice



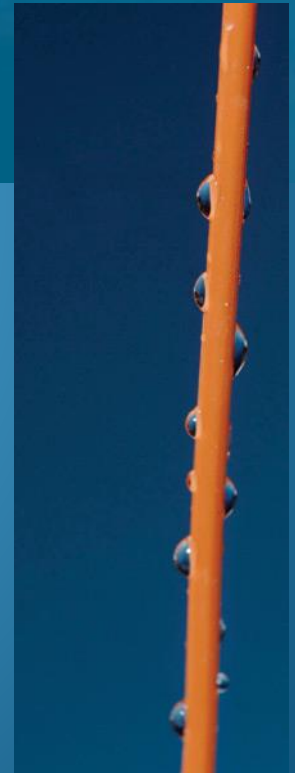
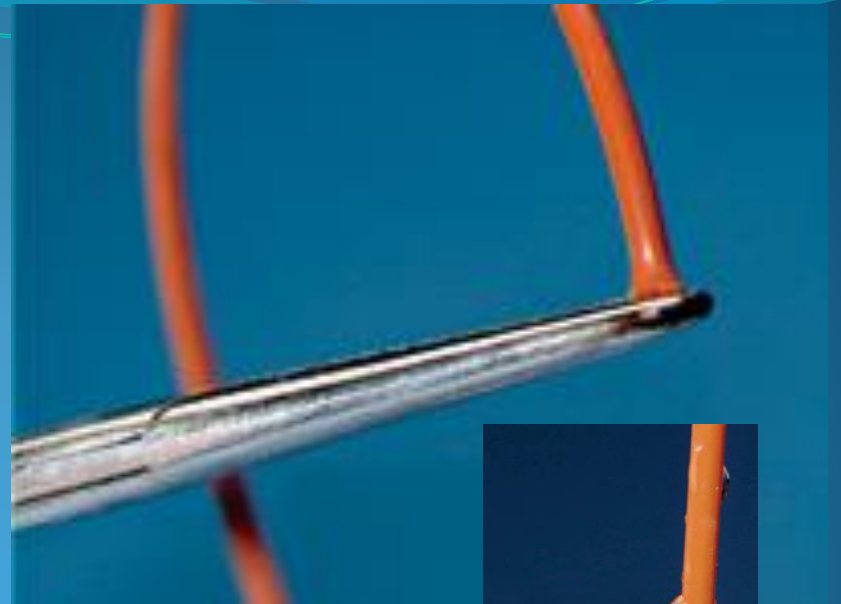
Intraperitoneal blocks

- Standard method for laparoscopic procedures
- Diluted and sprayed in the peritoneal cavity
- Assistant drips bupivacaine onto body wall while the abdominal cavity is still open



Wound Soaker Catheters

- A catheter with many holes placed in the lowest layer of wound closure
- Particularly helpful for amputations and large wounds
- Instill bupivacaine 2 mg/kg q 4-6 hours

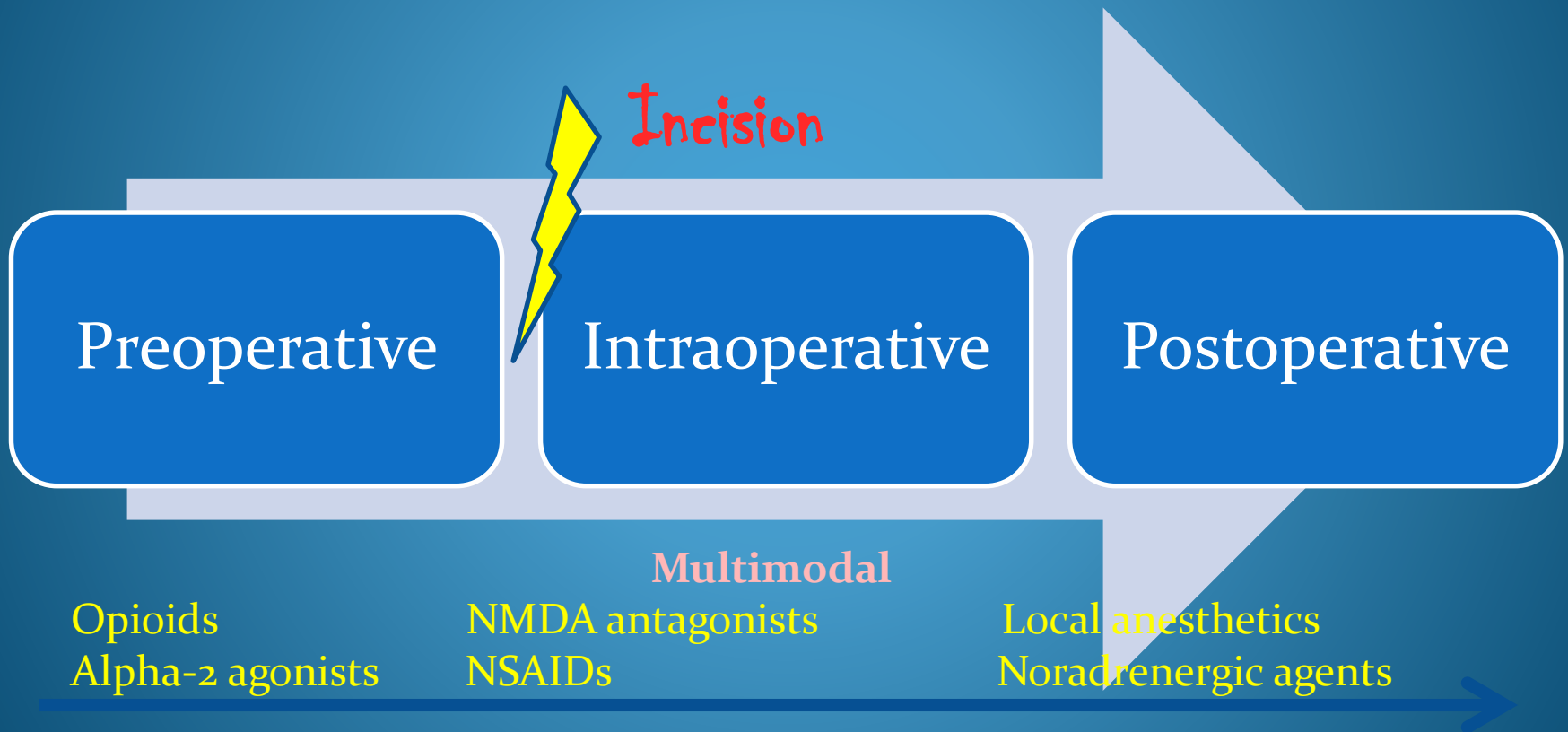




NSAIDs

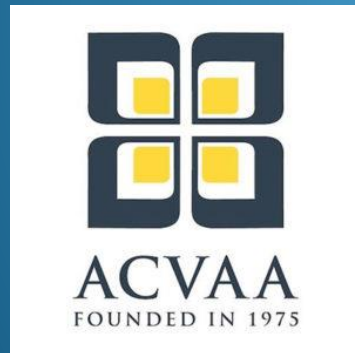
- Important part of multimodal analgesia
- Pre op vs post op administration
 - Avoid administering NSAIDs when renal blood flow is prostaglandin dependent:
 - Hypotension
 - Hypovolemia
 - Hyponatremia
 - Pre-existing renal disease
 - If not monitoring blood pressure, consider waiting until recovery
- Cats – patient and dose-selection is key to safety

Preventive Analgesia



Duration of analgesic action covers **entire perioperative time period**

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