Opioids

Clinical uses:
- Analgesia
- Decrease MAC
- Smooth anesthetic
- Antitussive

As a single agent, opioids yield inferior sedation!

Disadvantages:
- Respiratory Depression
- Nausea/Vomiting
- Bradycardia
- Hypotension
- Urinary retention
- Dysphoria/Euphoria
- Prolonged emergence
- Trunchal rigidity

Fentanyl

- Potency: 75-125x more potent than morphine as an analgesic
- More rapid onset and shorter duration
- Speed of onset: 3.5-6 minutes
- Duration: 30-60 minutes
- Low dose (1-2ug/kg) causes analgesia
- Higher doses (2-20ug/kg) blunt responses to intubation/surgery
- Recurrent respiratory depression
**Remifentanil**
- Ultra short acting opioid - mu agonist
- Ester linkage renders it susceptible to hydrolysis by plasma and tissue esterases
- **Rapid speed of onset:** 1-2 minutes
- **Context sensitive T<sub>1/2</sub>:** 3-10 minutes – regardless of duration
- Intense levels of analgesia of short duration
- No residual opioid effects
- More rapid recovery

**Remifentanil Complications**

**Common**
- Bradypnea (<8 bpm) – minutes
- Nausea / Vomiting
- Pruritis

**Rare**
- Hypotension
- Bradycardia
- Chest Wall Rigidity

**Remifentanil**
- Often used in a Propofol admixture
- 100mcg remifentanil + 200mg Propofol
- Used in a continuous infusion pump
  - Loading bolus or micro boluses of 150mcg/kg/min
  - Initial infusion 70mcg/kg/min
- Works to countereffect the lack of propofol analgesic effects
- Utilizes significantly less Propofol
OPIOIDS

Patient Management
1. Acute intoxication
2. Chronic administration due to recognized medical indication
3. Use of long-acting opioid antagonists
4. Use of long-acting opioid antagonists & agonist/antagonist combinations

OPIOIDS
1. Management – Acute Intoxication
2. Chronic Medical Administration
Patient likely not forthcoming
Must respect patient tolerance
*Awareness of synergistic effects with other anesthetic agents – benzodiazepines
Preparation to immediately provide airway management
*Avoid antagonists and agonist/antagonists
*Anesthetic administration – ‘Start Low & Go Slow’

Management of the Medically Dependent
3. Use of long-acting opioid antagonists
Naltrexone – T1/2 – 4-10 hours
Reduces euphoria, craving, withdrawal
Methadone – T1/2 – 24+ hours
Also inhibits serotonin reuptake
Also inhibits norepinephrine reuptake
Also antagonizes NMDA receptors
Eg. Ketamine, Nitrous Oxide, Tramadol
Physical dependence persists
OPIOIDS
Management of the Medically Dependent
4. Use of long-acting opioid antagonists & agonist/antagonist combinations

AT-121
EXPERIMENTAL ANALGESIC
ACTS AT OPIOID MU AND NOCICEPTION RECEPTORS
100X BETTER AT REDUCING PAIN IN MONKEYS THAN MORPHINE
NOCICEPTION RECEPTORS COUNTERACT THE EXPERIENCE OF PLEASURE
ABUSE & DEPENDENCE RELATED EFFECTS BLOCKED
NO RESPIRATORY DEPRESSION
2-3 YEARS – DOSE RESPONSE & CLINICAL STUDIES

Ketamine
Phencyclidine derivative producing ‘dissociative’ anesthesia
- Dissociation between thalamus and limbic system
Cataleptic state
- Eyes open
- Slow nystagmic gaze
- Noncommunicative
- Amnesia present
- Dose dependent analgesia
**Ketamine**

**Mechanisms of Action**
- Antagonist NMDA Receptor
- Agonist Adrenergic Receptors
- Antagonist Muscarinic Receptors CNS
- Blocks Reuptake of Catecholamines
- Agonist at opioid Sigma Receptor

**Water Soluble, Permits Administration**
- IV, IM, Intranasal, Oral, Rectal

**Respiratory Effects**
- Intact Reflexes
- Maintenance FRC
- Response to Hypercarbia Maintained
- Bronchodilator

**Cardiovascular Effects**
- Increased HR
- Increased BP
- Increased CO
- Direct Myocardial Depressant

**KETAMINE – INFLUENCE ON THE EFFECTS OF ASTHMA**
- Blocks NMDA receptor-induced bronchoconstriction
- Reduces nitric oxide production in pulmonary tissues
- Suppresses macrophage function and oxidative ability
- Reduces inflammatory cytokine production (reduces interleukin-4 concentration)
KETAMINE – INFLUENCE ON THE EFFECTS OF ASTHMA

• REVERSES HISTAMINE-INDUCED BRONCHOCONSTRICTION
• INCREASES SYNAPTIC CATECHOLAMINE LEVELS BY BLOCKING REUPTAKE OF NOREPINEPHRINE CAUSING Bронchodilation
• DECREASES CALCIUM INFLUX AND RELAXES SMOOTH MUSCLE
• INHIBITS VAGAL OUTFLOW, CAUSING SPASMOLYTIC EFFECTS OF AIRWAY SMOOTH MUSCLE

Ketamine – Modifying Adverse Effects

Emergence Phenomenon
- Reducing Incidence --
  - Benzodiazepines
  - Environmental Factors
- Potentiating Incidence --
  - Atropine / Scopalamine
  - Droperidol

Hypersalivation
- Reducing Incidence – Glycopyrrolate

Analgesia IV 0.3mg/kg = 0.1mg/kg morphine
- Partial reversal by Naloxone

Propofol

1% Isopropyl Phenol
Very Lipophilic
Delivery in oil-in-water emulsion
  - 10% Soybean Oil
  - 2.25% Glycerol
  - 1.2% Egg Phosphatide - Lecithin not Albumin
**Not contraindicated in most egg allergies
  ‘Yolk not the egg White’
*Overall the prevalence of allergy to propofol is 2.3% - not associated with egg allergy
Applications of Propofol

▪ Hypnosis
▪ Sedation
▪ Amnesia
▪ Muscle Relaxation
▪ Antiemetic
▪ Mood Alteration
▪ Anticonvulsant

Propofol

Clinical Effects

- Hypotension (20-30% decrease BP)
- Exaggerated in Hypovolemia, Elderly
- No change in heart rate
- Dose dependent depression ventilation
- Rapid, smooth emergence

Adverse Effects

- Pain on Injection
- Hypotension
- Post-Sedation Neuroexcitation
- Sepsis

Benzodiazepines for IV Sedation

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Midazolam</th>
<th>Diazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolites</td>
<td>Insignificant</td>
<td>Yes</td>
</tr>
<tr>
<td>T₁/₂ (hr)</td>
<td>1.5-2.6</td>
<td>20-80</td>
</tr>
<tr>
<td>Unique Effects</td>
<td>Greater amnesia &amp; BP decline</td>
<td>Vein irritation</td>
</tr>
<tr>
<td>Formulations</td>
<td>1mg and 5 mg/mL</td>
<td>5 mg/mL</td>
</tr>
<tr>
<td>IV Increment</td>
<td>1-2 mg</td>
<td>2.5-5 mg</td>
</tr>
<tr>
<td>Duration *</td>
<td>15-30</td>
<td>15-30</td>
</tr>
<tr>
<td>PO Doses</td>
<td>0.5-0.75mg/kg</td>
<td>10-20mg</td>
</tr>
</tbody>
</table>

* Estimates – patient may require additional doses more often
### Benzodiazepines for PO Sedation

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Triazolam</th>
<th>Diazepam</th>
<th>Lorazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolites</td>
<td>Insignificant</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>$T_{1/2}$ (hr)</td>
<td>1.5-5.5</td>
<td>20-80</td>
<td>10-20</td>
</tr>
<tr>
<td>Onset PO (min)</td>
<td>30-45</td>
<td>60-90</td>
<td>90-120</td>
</tr>
<tr>
<td>Duration (hr)</td>
<td>1-2</td>
<td>2-4</td>
<td>3-6</td>
</tr>
<tr>
<td>Anxiolyis Dose (mg)</td>
<td>0.125-0.25</td>
<td>5-10</td>
<td>2-4</td>
</tr>
<tr>
<td>Sedation Dose (mg)</td>
<td>0.5-0.75</td>
<td>10-20</td>
<td>4-6</td>
</tr>
</tbody>
</table>

### Geriatric Drug Clearance

**Drugs subject to hepatic metabolism or renal excretion are metabolized at 1/2 to 1/3 the rate of younger adults**

- Fentanyl = 50% less for 85 yr old
- Midazolam = 30% less for 60yr old
  - 60% less for 80 yr old
- Diazepam = 66% less for the geriatric patient
- Propofol = 15% less for 65 yr old
- More pronounced hypotension

### $\alpha_2$-agonists

- Medications act at the $\alpha_2$ adrenergic receptor which exist in the central and peripheral nervous system resulting in...
  - Sedation
  - Analgesia
  - Muscle Relaxation
  - Stable respiratory rates
  - Predictable cardiovascular responses
Selectivity of $\alpha_2$-agonists

- **Selective...**
  - **Clonidine** - $\alpha_1$:$\alpha_2$ specificity 1:220
    - More vascular sympatholytic effect
    - Normotensive
    - Avoids tachycardia
  - **Highly Selective...**
  - ‘Dex’ - $\alpha_1$:$\alpha_2$ specificity 1:1620
    - Decrease sympathetic activity without paralysis of compensatory homeostatic reflexes

Oral Clonidine - Premedicant

**Dosing (4mcg/kg)**
- Adults: 0.2mg oral or sublingual
- Elderly: 0.1mg

**Effects**
- Sedation
- Does not cause amnesia
- Postoperative analgesia
- Reduces anesthetic requirements
- Reduces postoperative nausea/vomiting

Oral Clonidine - Premedicant

**Contraindications**
- Pre-Procedure Hypotension
- Autonomic Dysfunction
- Pre-Procedure Bradycardia
- Severe Coronary Artery Disease
- Cardiac Conduction Abnormalities
- Chronic Renal Failure
- Cerebrovascular Disease
**Dexmedetomidine**
- Utilized Oral, Intranasal, IV Infusion
- Tasteless, Non-Irritating to Mucosa
- Now available as a generic
- Produces ‘rousable sedation’ – exhibiting many properties similar to natural sleep
- Pregnancy category C
- Complete biotransformation in liver
- IV terminal elimination half-life 2 hours

**Dental-specific Studies**
- Dexmedetomidine sedation with and without midazolam for third molar surgery
  - Smiley MK, Prior SR 61:3;2014
- A comparison of Dexmedetomidine sedation with and without midazolam for dental implant surgery

*IV Dex alone showed a slower onset and unpredictable sedative and amnestic response than more common anesthesia alternatives*
Rationale for Continuous Infusion

- Enhanced cardiovascular stability
- Enhanced respiratory stability
- Minimize fluctuations in drug serum concentration
- Smoother intraoperative course
- Less patient movement
- Utilize less drug
- More rapid recovery

Bennett JOMFS 1998

Continuous Infusion
What Works Well?
Propofol – Ideal Pharmacokinetics

GA
- Induction
  - Adult 1.25 mg/kg
  - Peds 2.5-3.5 mg/kg
- Maintenance
  - Adult 100-200 mcg/kg/min
  - Peds 125-300 mcg/kg/min

MAC
- Induction
  - Injection 0.5 mg/kg
  - or 50-100 mcg/kg/min
- Maintenance
  - 25-150 mcg/kg/min

*Minimize infusion dose to optimize recovery times*
Continuous Infusion
Less Ideal!

**Ketamine**
- Metabolism to norketamine, an active metabolite
- Norketamine - 1/3-1/5 as potent and contributes to prolonged effects, especially with intravenous infusion

- No statistical significance in respiratory stability, satisfaction, PONV
- Ketamine group – prolonged recovery

Characteristics of an ‘Ideal’ anesthetic Agent
- Sufficient Potency
- Non-Flammable
- Non-pungent - Bronchodilator
- No Adverse Respiratory Complication
- No Adverse Cardiac Complications
- Provide Muscle Relaxation
- Minimal Metabolism
- No Postemergence Side Effects (EA)
- Reliable and Simple Delivery System
- Economical

VOLATILE ANESTHETICS
Low Blood Gas Solubility Confers Many Clinical Advantages!

Rapid Onset
Greater Control & Precision of Depth
Rapid Recovery
Rapid Return of Airway Reflexes
McKay: Anesth Analg 2005
Desflurane > Sevoflurane > Isoflurane > Halothane
VOLATILE ANESTHETICS

MAC: MINIMUM ALVEOLAR CONCENTRATION

‘Concentration of inhaled anesthetic agent that prevents movement in response to skin incision in 50% of subjects at sea level in 100% oxygen’

- Alveolar concentration can be easily measured
- Weight & Anesthetic duration do not alter MAC
- Doses of anesthetics in MACs are additive
- MAC highest at age 6 months, then declines

FACTORS AFFECTING MAC

<table>
<thead>
<tr>
<th>INCREASES MAC</th>
<th>DECREASES MAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEDIATRICS</td>
<td>NITROUS OXIDE</td>
</tr>
<tr>
<td>HYPERCAPNEA</td>
<td>CNS DEPRESSANTS</td>
</tr>
<tr>
<td>HYPERTHERMIA</td>
<td>HYPOCAPNEA</td>
</tr>
<tr>
<td>ALTITUDE</td>
<td>HYPOTHERMIA</td>
</tr>
</tbody>
</table>
VOLATILE ANESTHETICS

<table>
<thead>
<tr>
<th>Properties</th>
<th>Halothane</th>
<th>Isoflurane</th>
<th>Desflurane</th>
<th>Sevoflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boiling Point</td>
<td>50</td>
<td>48.6</td>
<td>22.8</td>
<td>58.6</td>
</tr>
<tr>
<td>Pungency</td>
<td>Excellent</td>
<td>Poor</td>
<td>Marked</td>
<td>Excellent</td>
</tr>
<tr>
<td>Blood Gas Solubility</td>
<td>2.3</td>
<td>1.4</td>
<td>0.42</td>
<td>0.66</td>
</tr>
<tr>
<td>MAC 100% O₂</td>
<td>0.77</td>
<td>1.15</td>
<td>6</td>
<td>2.05</td>
</tr>
<tr>
<td>MAC 70% N₂O</td>
<td>0.29</td>
<td>0.56</td>
<td>2.5</td>
<td>0.66</td>
</tr>
<tr>
<td>Metabolism</td>
<td>20%</td>
<td>2.4%</td>
<td>0.02%</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

VOLATILE ANESTHETICS

Respiratory Depressant Effect
Sevoflurane
Isoflurane
Desflurane
*Least to Greatest

Bronchodilating Effect
Sevoflurane
Isoflurane
Desflurane
*Greatest to Least

SEVOFLURANE INDUCTION PROCEDURE:
COMPARISON between FIXED 8% vs INCREMENTAL TECHNIQUE in PEDIATRIC PATIENTS

100 children
Both groups premedicated with midazolam 0.5mg/kg
1. Sevo at 1% N₂O 50%-increased sevo by 1%
every 3 breaths for induction
2. Sevo 8% N₂O 50% induction
Time to LOC lower using 8% method
Incremental method cost almost half of fixed 8% induction method

Singh PM
AANA Journal 82:2014
SEVOFLURANE vs PROPOFOL for ANESTHETIC INDUCTION: A META-ANALYSIS

- 12 included studies
- Time to LOC was similar
- More frequent apnea in propofol group
- Induction complications similar
- Time to successful LMA insertion similar
- Success with LMA first attempt higher in sevoflurane group
- PONV more significant in sevoflurane group

Joo H
Anesth Analg
91:2000

SEVOFLURANE vs PROPOFOL for INDUCTION and MAINTENANCE of ANAESTHESIA with the LARYNGEAL MASK AIRWAY in CHILDREN

Study of 120 children
Propofol 3mg/kg induction
5mg/kg/hr maintenance group
Sevoflurane 7% induction
1.7% maintenance group
LMA insertion time shorter with sevoflurane group
Heart rate higher in the sevo group
Emergence more rapid with sevo group
Emergence agitation increased with sevoflurane group

Lopez Gil M
Ped Anes
9:1999

WHAT is EMERGENCE AGITATION?

Children aroused from anesthesia enter a state of excitation...
- Irritable, uncompromising, uncooperative, incoherent, crying
- Do not recognize familiar people, objects
- Combative behavior
- Occurs within 30 min of recovery
- Often resolves spontaneously
EMERGENCE AGITATION RISK FACTORS

- Preschool age: 2-6
- Boys > girls
- Preoperative anxiety
- Distress during induction
- Previous traumatic experience at dentist
- Poor pain control
- Head & neck procedures

CHILDREN...
- More emotional
- Less social
- More impulsive
- Less adaptable

PARENTS...
- High anxiety

EFFECTS OF EMERGENCE AGITATION

- Injury to the child
- Injury to the surgical site
- Inability to control bleeding
- Accidental removal of dressings
- Accidental removal of IV catheters
- May require additional nursing care
- May require supplemental sedatives/analgesics
- Raises questions about anesthetic ‘quality’
- Causes anxiety in parents witnessing EA

PHARMACOLOGICAL PREVENTION of SEVOFLURANE and DESFLURANE RELATED EMERGENCE AGITATION in CHILDREN: A META-ANALYSIS of PUBLISHED STUDIES

- 324 studies identified
- 58 relevant articles
- 37 studies included
- 3172 total patients
- Randomized studies
- Double-blinded studies
- Control group
- Standardized definition of EA

Dahmani S
Brit J Anaes
104:2010
TREATMENTS STUDIED for PROPHYLACTIC PREVENTION of EA

Midazolam
Propofol
Fentanyl
Ketamine
α₂-Agonist
Local anesthesia
Ondansetron

PROPHYLACTIC TREATMENT of EA DAHMANI 2010

Midazolam
Premedication – not protective against EA
Bolus after induction – not protective against EA

Propofol
Continuous infusion – protective against EA
Bolus at end of case – protective against EA
Bolus after induction – not protective against EA

Ketamine
Premedication – protective against EA
Bolus after induction – protective against EA
Bolus at end of case – protective against EA

Fentanyl
Intranasal – protective against EA
Bolus after induction – not protective against EA

α₂-Agonist – Dexmedetomidine/Clonidine
All routes/timing – protective against EA

Local anesthesia
Protective against EA

Ondansetron
Not protective against EA
Only 2 studies – more research needed

Only 2 studies – more research needed
EVIDENCE-BASED CONCLUSIONS

Reduce/Eliminate Emergence Agitation & Prevalence of Nausea/Vomiting to attain Ideal Pediatric Anesthetic Experience

**Premedication:** Midazolam 0.5mg/kg

**Dexmedetomidine:** 3-4mcg/kg

**Induction:** Sevoflurane: Incremental to 8%

**Maintenance:** Sevoflurane 1.5-3%

**Emergence:** Propofol 0.5-1mg/kg

---

**Xenon Anesthesia**

- Originally discovered in 1939 by Behnke and Yarborough of the US Navy
- Lawrence published experiments in 1946
- Lachmann, Erdmann and rediscovered it in 1990
- Multi-center clinical trials have been completed in the European Union
- Noble gas found in very small concentrations (0.0000087) in the air
- Manufactured by fractional distillation of liquified air - expensive

---

**Xenon Anesthetic Gas**

Fulfills many of the ideals of an anesthetic gas...

- Lowest blood gas solubility (0.12)
- MAC = 0.63, 1.5x more potent than N2O
- Non-flammable
- Absence of metabolism
- Low toxicity
- Devoid of teratogenicity
- Produces highest regional flow in the brain, liver, kidney and intestine
- No cardiovascular depression
Xenon and the Global Environment

- Volatile anesthetics and N₂O contribute to the greenhouse effect
- N₂O is 230x more potent as a greenhouse gas than CO₂
  - N₂O as a waste anesthetic contributes 0.1% of global warming
- Xenon adds no atmospheric pollution
- Xenon does not deplete the ozone layer

Xenon Anesthetic Gas

- Because of its rarity and expense, waste must be reduced to an absolute minimum
- Given via a rebreathing system using the lowest possible gas flow
- Closed loop feedback control mechanism delivers only the amount needed to maintain constant gas concentration and volume

Muscle Relaxants

**Depolarizing** – Mimics action of Ach
- Succinylcholine

**Nondepolarizing** – Interferes with Ach
- Long Acting
  - Pancuronium
- Intermediate Acting
  - Vecuronium
  - Rocuronium
  - Cisatracurium
- Short Acting
  - Atracurium
  - Rocuronium
  - Mivacurium
### Muscle Relaxants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset (min)</th>
<th>Duration (min)</th>
<th>Intubating Dose mg/kg</th>
<th>Infusion mcg/kg/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Succinylcholine</td>
<td>1</td>
<td>4</td>
<td>2-3</td>
<td>2</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>1-2</td>
<td>20-35</td>
<td>0.6-1.2</td>
<td>--</td>
</tr>
<tr>
<td>Mivacurium</td>
<td>2-3</td>
<td>12-20</td>
<td>0.25</td>
<td>5-6</td>
</tr>
<tr>
<td>Atracurium</td>
<td>3-5</td>
<td>20-35</td>
<td>0.4-0.5</td>
<td>6-8</td>
</tr>
<tr>
<td>Cisatracurium</td>
<td>3-5</td>
<td>20-35</td>
<td>0.1</td>
<td>1-1.5</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>3-5</td>
<td>20-35</td>
<td>0.08-0.1</td>
<td>1</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>3-5</td>
<td>60-90</td>
<td>0.1</td>
<td>--</td>
</tr>
</tbody>
</table>

### Succinylcholine: Pros & Cons

- Trigger for Malignant Hyperthermia
- Only Emergencies for peds, not elective use
- Bradycardia with first dose
- Hyperkalemia possible
- Fasiculations and Masseter Spasm
- Consider Defasculation Dose of tubocurarine
- Postop Myalgias
- Bronchospasm / Histamine release
- Increased Intraocular / Intragastric Pressure
- Redosing can result in dysrhythmias

### Sugammadex (Bridion)

- Gamma-cyclodextrin ring shaped molecule which reverses the effects of neuromuscular blocking agents rocuronium and vecuronium by encapsulation in the plasma not at the neuromuscular junction
- Lack of cardiovascular side effects
- Reduces effectiveness of BCPs for 7 days
Sugammadex

Use after immediate administration of rocuronium:
- 16mg/kg – Cost: $114 per 200mg
- Recovery 3 times faster than neostigmine

---

Sugammadex

**Precautions**

**Side Effects**
- Hypersensitivity
- Malignant hyperthermia
- Intra-abdominal pressure monitoring

**Additional Information**
- Recovery from neuromuscular block may be less rapid in children or elderly patients
- Sugammadex intoxication can be managed with supportive care

**Contraindications**
- Known hypersensitivity to sugammadex or its components
- Use with extreme caution in patients with a history of malignant hyperthermia
- Use with caution in patients with severe hypotension

---

Kovanaze Nasal Spray

- 3% tetracaine hydrochloride
- 0.05% oxymetazoline hydrochloride intranasal spray
- Used for regional maxillary pulp anesthesia of incisors, canines, and 1st premolars
- FDA approved for adults and children >40kg
- Tetracaine HCl 6mg & Oxymetazoline HCl .1mg (each .2ml spray)
Kovanaze Nasal Spray

### TABLE 1: DOSAGE

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (≥ 18 years)</td>
<td>2 sprays (0.2 mL per spray), 4 to 5 minutes apart</td>
</tr>
<tr>
<td>Children who weigh 40 kg or more</td>
<td>2 sprays (0.3 mL per spray), 4 to 5 minutes apart</td>
</tr>
</tbody>
</table>

Local Anesthesia - Ropivacaine

- Long-acting Aminoamide Anesthetic
- Clinically similar to Bupivacaine
- Fewer Cardiac and CNS Adverse Effects (Knudsen 1997)
- More Rapid Onset of Anesthesia Than Bupivacaine
- Ropivacaine Concentrations Cause Vasoconstriction
- 0.50%-0.75% Produce Adequate Dental Anesthesia (El-Sharrawy 2006)
Exparel (1.3% liposomal bupivacaine)

- Multiple phospholipid bilayers with an aqueous core that increases stability of liposome and extends drug release
- FDA approved for single dose intraoral infiltration the surgical site not for nerve blocks
- Clinical trials adult maximum dose: 20ml (260mg)
- Not FDA approved for patients <18 or pregnant

Exparel (1.3% liposomal bupivacaine)

- Injected as small alloquats, infiltrating the surgical area
- Avoid administration of non-bupivacaine local anesthetics less than 20 minutes prior to injecting Exparel to avoid disruption of liposomes
- Avoid administration of immediate release bupivicaine and other local anesthetics for 96 hours after Exparel infiltration to avoid unintentional overdose (wristband)

HTX-011
Extended Release Bupivacaine/Meloxicam

- 72 hours of analgesia
- Reduces need for opioids
- ‘Biochronomer’ technology
- Meloxicam reduces local inflammation
- Reverses the acidic environ in the surgical site
- Potentiates bupivacaine
HTX-011
Extended Release Bupivacaine/Meloxicam

Studied in:
❖ Hernia Repair
❖ Abdominoplasty
❖ Bunionectomy
❖ Total Knee Arthroplasty
❖ Breast Augmentation

FDA Fast Track Designation 4th Qtr 2017
Breakthrough Therapy Designation 2nd Qtr 2018
Submitted an NDA to FDA December 2018

Questions???