**Introduction**

Anesthesia is an aspect of veterinary medicine that is used every day in every facet of care. Anesthetic drugs are administered to relieve pain and to facilitate routine to advanced procedures. Understanding anesthetic pharmacology helps provide the best patient care and can prevent emergencies.

Appreciating the difference between opioids and their receptors is the first step in knowing when and how to treat a patient. Furthermore, there is no drug protocol that is perfect for every patient which makes a comprehensive knowledge of anesthetic drugs paramount.

**Opioids**

**Opioids and Receptors**

Opioids are the most commonly used analgesic and pre-anesthetic. They are relied on to provide pain relief, sedation, and to help reduce the amount of anesthetic inhalant required. They are also the foundation to any anesthetic protocol. Opioids work by binding with one or more receptors. These receptors are located centrally and peripherally in the nervous system and GI tract.

**Side Effects of Opioids**

Administration of pure mu opioids are not without side effects. Intravenous, subcutaneous or intramuscular routes can cause nausea, vomiting, and diarrhea. Post-operative ileus is also common. Any of the listed side effects should not dissuade any practitioner from their use. Side effects can be managed by adjusted doses and route of administration.

**Pure Mu**

The opioid to which all others are compared is morphine. Pure mu opioids provide profound analgesia and sedation. Gastrointestinal side effects are also common with a pure mu administration.

**Partial Mu**

Buprenorphine (buprenex) is the partial mu agonist that is frequently used in veterinary medicine. This opioid is roughly 25 times stronger than morphine. Buprenorphine differs from a pure mu opioid in the method in which it binds to the mu receptor. Unlike pure mu opioids, buprenorphine has a long onset of action. Peak effects can be seen after 60-90 minutes but some effects can be
seen after 20 minutes.Timing of administration becomes vital when using buprenorphine, especially in post-operative situations. Buprenorphine also has a ceiling effect. This means increased dosing does not produce increased analgesia.

Buprenorphine transdermal patches are also available.

**Mu Antagonist/Kappa Agonist**
Butorphanol and nalbuphine agonize the kappa receptor and antagonize the mu receptor. These drugs produce mild analgesia and moderate sedation. Nalbuphine is not as common as butorphanol and is a non-controlled version of butorphanol with a 20mg/ml concentration. The use of mu antagonist/kappa agonist can be instrumental in partially antagonizing untoward effects caused by pure mu opioids.

**Mu Antagonist**
Mu antagonists completely reverse the effects generated from pure mu agonists. Mu antagonists are used in an emergency situation or to partially antagonize the unwanted effects of a pure mu opioid. Once used, the mu antagonist can make additional use of a mu agonist difficult.

**Dysphoria**
Dysphoria is a condition specific to opioids. One of the main goals when treating pain is to keep patients pain free and euphoric. The author uses the word “inconsolable” to describe dysphoric patients. How is pain differentiated from dysphoria? A systemic approach will yield the appropriate treatment method. Observing the patient prior to treatment may help determine what path is needed. A dysphoric patient may exhibit the following:

- Vocalization
- Bradycardia
- Reluctance/inability to move
- Visible third eyelids
- Restlessness

<table>
<thead>
<tr>
<th>Treating Dysphoria</th>
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<tbody>
<tr>
<td>Naloxone 0.01-0.02mg/kg IV</td>
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<tr>
<td>Butorphanol 0.05-0.2ml/kg IV</td>
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Treatment of dysphoria is specific to opioids. Resolution of dysphoria will not respond to sedatives or tranquilizers.

**GABA Agonists**
The GABA receptor is the main neurotransmitter in the central nervous system. Benzodiazepines agonize the GABA receptor which results in sedation, anxiolysis, muscle relaxation and anticonvulsant effects.

The injectable benzodiazepines which are routinely added to anesthetic protocols are midazolam (versed) and diazepam (valium). Midazolam is water soluble and readily crosses the blood brain barrier. This water solubility also allows it to be given intramuscularly. Diazepam is not water soluble and is more acidic than midazolam. Diazepam is also persevered with propylene glycol and ethanol which makes it viscous and painful upon intramuscular injection. Alone, benzodiazepines can produce unpredictable sedation. The author has anecdotally noted that more predictable sedation occurs in patients that are pediatric, geriatric, and debilitated. Midazolam and valium are commonly used to Benzodiazepines cause minimal cardiovascular effects and have a wide dose range.

**GABA Antagonists**
Undesired effects from benzodiazepines can be reversed with flumazenil (romazicon). Flumazenil will completely remove all muscle relaxation and any sedation.

**NMDA Agonist**
Ketamine, a dissociative, agonizes the NMDA receptor. Its properties create a dissociative effect. It should be remembered that ketamine is not a sedative. Using ketamine in conjunction with an opioid can generate a synergistic effect which could lead to a decreased amount of inhalant of opioid needed. The NMDA agonist quality of ketamine is specifically ideal to treat and manage wind up pain. Wind up is the result a nerve that is over-stimulated from a pain response. This causes the pain level to increase with each stimulus. Subsequent stimuli results in wind up of the nerve. Wind up then causes the threshold for what causes pain to be decreased, even after the initial pain or injury may have healed.

**Phenothiazine Sedatives**
Unlike benzodiazepines, phenothiazine sedatives have predictable sedation when used alone. Acepromazine is a sedative/tranquilizer that does not contain any analgesic effects. Unlike other drugs discussed, acepromazine cannot be reversed. The deleterious effects could last several hours depending on dose and route of administration. Of the adverse effects, hypotension is the most expected. This is secondary to vasodilation. During anesthesia, care should be taken to recognize that acepromazine coupled with isoflurane (a very potent vasodilating drug) could lead to profound hypotension.
Alpha 2 Agonists
This class of drugs binds to the alpha 2 adrenoceptors which are located in the nervous system. With use, alpha 2's produce a significant amount of sedation that is accompanied with a small amount of analgesia. The newer alpha 2 agonists are more specific for the alpha 2 receptor.

NSAIDs
Non-Steroidal Anti-Inflammatory Drugs
Perioperative use of non-steroidal anti-inflammatory drugs (NSAIDs) varies from practice to practice and drug to drug. NSAIDs provide mild to moderate analgesia. When used with an opioid, non-steroidals have reduced the amount of opioid needed.

Regardless of non-steroidal used, management of a patient surrounding its administration is similar. The use of concurrent steroids or additional NSAID is contraindicated. The use of NSAIDs should also be avoided in patients suffering from any gastrointestinal distress. The use of any non-steroidal, regardless of type, should be limited to patients who are older than 6 weeks of age, who are well hydrated and who were normotensive throughout their anesthetic event. Protecting renal profusion and gastrointestinal integrity is the focus when using non-steroidal drugs.

Choosing an Appropriate Drug Protocol
Pain and patients are unique. Each patient’s needs should be treated individually. As previously mentioned, there is no one perfect drug protocol. Similar considerations can be made for but doses and drugs should be adjusted per individual needs. When determining an anesthetic protocol, concerns should be made for cost, expected level of nociceptive pain, blood work results, and post-operative plan. Remembering anticipated side effects can also assist the anesthetist in their drug choices. Finally, anesthetists should appreciate that opioids, sedatives, and tranquilizers create a balanced anesthetic protocol and are necessary in procedures that are not traditionally considered painful; for example, MRI and CT imaging.

<table>
<thead>
<tr>
<th>Commonly Used Pre and Post-Operative Opioids</th>
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<td><strong>Opioid</strong></td>
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<tr>
<td>Morphine</td>
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<td>Fentanyl</td>
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<td>Hydromorphone</td>
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<td>Butorphanol</td>
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<td>Buprenex</td>
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