Choosing the correct analgesic therapy requires an understanding of both the pharmacokinetics of a wide range of drugs as well as the levels or type of pain associated with various conditions. Also, it has been recognized in human patients that there is great individual variation in responsiveness to drugs. In other words, the same drug can produce vastly different results in different individuals. These differences are partly a result of individual genetic differences. They are also due to the non-physiologic modulating factors that come to bear on any pain state; anxiety, fear, sense of control, ethno cultural background, and meaning of the pain state to the individual. This phenomenon appears to hold true for animals as well. Individual personality, breed traits, and the psychological states of fear and anxiety all seem to play a role in the animal patient’s perception of pain and response to treatment. This is one reason that protocols for treating pain in veterinary patients have been difficult to develop. Ultimately, pain relief, as assessed by the criteria previously described, is the only true measure of successful treatment.

**ANALGESIC DRUGS**

**Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**

NSAIDs are among the most widely used analgesics in the treatment of chronic pain. They are also effective in reducing acute pain in the peri-operative period. Research shows that pretreatment with NSAIDS greatly reduces intraoperative and postoperative pain. Also, NSAIDS have been shown to have synergistic effect when combined with other classes of drugs such as opioids. Patients with severe acute pain can be weaned to NSAIDS alone as their pain diminishes. NSAIDS are ideal for managing mild-moderate postoperative pain as a take home medication. They have the advantages of being convenient to administer (SID, chewable), relatively inexpensive and providing long lasting pain relief compared to other analgesics.

**Local and Regional Anesthetics**

Applying analgesia directly to the affected nerve endings can provide excellent pain control while reducing the need for systemic drugs. Local anesthetics work by totally disrupting neural transmission of information by axons at the treatment site and provide true analgesia. This is extremely effective in managing pain associated with feline declaw and dental extractions in all species. Many techniques using local anesthetics can safely and effectively pre-empt and manage pain. These compounds are unique in their ability to completely block sensory nerves. Local anesthetics block nerve impulse conduction by inactivating sodium channels. These lipid-soluble molecules are rapidly absorbed by mucosal, pleural, and peritoneal surfaces. Onset of action is also quick in epidural administrations.

Lidocaine, the most widely used local anesthetic, takes effect in 3 to 5 minutes and is effective for 60-90 minutes. All local anesthetics cause vasodilation that decrease their duration of action. The duration of lidocaine can be extended by combination with a 1:200,000 dilution of epinephrine. Epinephrine should NEVER be used in circumferential limb block such as feline declaw. Bupivacaine takes longer to take effect (15 to 20 minutes), but its anesthetic and analgesic effects last 3 to 6 hours. Bupivacaine is not effective as a topical analgesic, but is an excellent choice for local infiltration.

**Local Infiltration**

Injection of lidocaine or bupivacaine into local tissue can reduce pain associated with various painful procedures. This technique is useful for small mass removal, digit amputation, arterial catheter placement, thoracocentesis, abdominoctensis, bone marrow sampling, etc. The entry area is infiltrated with small amounts of anesthetic prior to tissue penetration. An appropriate waiting time must be observed to insure adequate desensitization of the area as described above.
**Dental (oral) nerve block**

The entire muzzle can be anesthetized by blocking the infraorbital and mandibular foramen. Mandibular and maxillary nerve blocks provide excellent analgesia for pain anywhere in the muzzle. Tooth extraction is the obvious indication for these blocks but they are also quite effective for gingival surgery, mandibulectomy, maxillectomy, jaw fracture repairs, nasal surgery or biopsy. Small amounts of bupivacaine (not to exceed 1cc of 0.5% bupivacaine per 10lbs of body weight) are injected near or into the infraorbital and mandibular foramina anesthetizing the main nerve branches. This technique is relatively easy to perform by a skilled veterinary nurse and has minimal associated risks.

The addition of epinephrine to dental blocks causes local vasoconstriction. The benefits are twofold. First, the anesthetic is held in place longer increasing its duration of action and second, local bleeding is controlled. Epinephrine can be added to the syringe by simply “washing” with epi prior to drawing up local anesthetic.

**Intra-ARTICULAR (joint space)**

Effective analgesia in pre and post-operative orthopedic cases has been achieved by injection of local anesthetics directly into the joint space such as in cruciate ligament repair. Intra-articular morphine has also been shown to effectively reduce joint pain. The effectiveness of this technique when used pre-operatively is evident in the smooth plane of anesthesia maintained when the joint capsule is incised. This is in sharp contrast the spike in heart rate and “lightness” that is observed when the capsule is entered without anesthetic. No doubt, these responses are due to pain.

**Pleural space**

Interpleural bupivacaine infusion following thoracotomy surgery may have some analgesic benefit. Bupivacaine (1.5-2 mg/kg) is injected via an indwelling chest tube into the pleural space. Analgesia is thought to occur by direct blocking of the intercostal nerves. For maximum coverage, patients are held in sternal recumbency for 5-10 minutes post injection and gently rolled from side to side. Drug absorption through the pleural tissue should be considered. The addition of 0.1 cc/10cc of NaBicarbonate may reduce the stinging sensation in awake patients.

**Epidural Nerve Blocks**

Injection of opioids (morphine, fentanyl) and or local anesthetics (lidocaine, bupivacaine) directly into the epidural space have been used to provide analgesia to the caudal half of the body while minimizing sedative effects. This is a fairly simple and safe technique. Injection is generally made at the lumbosacral space. Epidural catheters can be inserted to allow long-term analgesic administration.

**OPIOIDS**

Opioids are the most commonly used analgesics in hospitalized critical patients due to their efficacy, rapid onset of action and safety. The efficacy of various opioids is determined by the specific receptors in the brain and spinal cord they affect. The receptors are classified as mu, kappa or sigma. Mu and kappa receptors are responsible for sedation, analgesia, and respiratory depression. Kappa receptors are responsible for analgesia and sedation. Sigma receptors are less clinically relevant are thought to be responsible for the adverse effects of opioid administration such as dysphoria, excitement, restlessness and anxiety. Opioid drugs are classified as agonists (meaning they stimulate the opioid receptors) or antagonists (meaning they block particular opioid receptors). There are also mixed agonist/antagonist opioids that stimulate some receptors while blocking others as well as partial agonists with overall decreased effects at all receptor sites. In general, pure agonists are the most potent of the opioids but also have the most severe adverse side effects. Side effects may include vomiting, constipation, excitement, respiratory depression, bradycardia and panting. Pure antagonists have the effect of reversing the narcotic properties of agonists. The availability of opioid antagonists makes opioid use extremely safe because the drug effects can be rapidly removed. Mixed agonist/antagonist and partial agonist opioids can provide reasonably good analgesia without many of the deleterious side effects of pure agonists. Opioids are metabolized by the liver and excreted via the kidneys and should be used with caution in patients with renal or hepatic disease.
Pure Agonists
Pure agonists are the most potent of the opioid drugs. They provide excellent analgesia but can have adverse effects including respiratory and central nervous system (CNS) depression, gastric stimulation, bradycardia and hypotension. A disadvantage of pure opioids is habituation necessitating ever increasing dosage to achieve therapeutic effects. Regimented treatment that is, dosing at regular intervals is helpful in maintaining an analgesic plane. Otherwise a roller coaster effect occurs leaving the patient in varying degrees of pain between treatments. Keeping a patient out of pain is always more efficacious than continually taking the patient out of pain. The type of opioid is chosen based on the degree of analgesia required and the specific needs or limitations of the individual patient. The most commonly used pure agonists in the United States are morphine, hydromorphone, oxymorphone and fentanyl.

Morphine Sulfate is the gold standard for pure opioid agonists. All other drugs in this class are compared to morphine in terms of efficacy, duration of action, cost etc. Morphine is commonly used to provide maximal analgesia and sedation. Its relatively low cost and similar efficacy makes it preferential over other opioids in some cases. However, it’s additional side effects; particularly systemic hypotension and vomiting that make it less desirable in many instances. Cats are particularly sensitive to morphine therefore lower doses are used in the cat. Typical dosage for dogs is 1.0-1.5 mg/kg IV q 4-6 hrs.

Fentanyl Citrate is an extremely potent synthetic opioid with rapid onset but short duration of action when administered IV or IM. It is most efficaciously used as a transdermal patch for long-term (3 days) analgesia. Fentanyl is contained in an adhesive patch of varying concentration to deliver 25, 75 or 100 μg/hr. Once applied to shaved cleaned skin the drug is continually absorbed. Onset of action is from 12 to 24 hours, therefore, supplemental analgesia is recommended during the initial treatment period. Use of mixed agonist/antagonist opioids will reverse the effects of the fentanyl patch and should be avoided.

Partial Agonist
Buprenorphine (Buprenex®) is a partial mu agonist that is longer duration than morphine due to slow dissociation from receptors, providing analgesia for approximately 6 hours. Partial agonists avidly bind and partially activate mu receptors. Buprenorphine is recommended for mild to moderate pain. If the dose is increased beyond the recommended level, analgesia may be reduced and is difficult to reestablish with a pure agonist because of avid binding of buprenorphine to mu receptors. Recent work has been done to demonstrate that buprenorphine is readily absorbed across mucous membranes in the feline due to the unique oral pH in this species. This allows for buccal mucosal administration in the cat, providing analgesia for up to 8 hours from a single dose.

Agonist-Antagonist
Butorphenol Tartrate (Torbugesic®) is a kappa agonist and a mu antagonist. The overall effectiveness of butorphenol as an analgesic is questionable. It is expensive compared to morphine but has a markedly lowered incidence of respiratory depression and dysphoria. Butorphenol is used in patients experiencing mild to moderate pain. Available in oral and injectable forms, the dosage is 0.1-0.8 mg/kg IV. While the sedative effects of Butorphenol may last for 2 or more hours, the effect of analgesia is only about 40 minutes, an important consideration when managing pain of any greater duration. Butorphenol can be used to partially reverse pure agonists by blocking their action at mu receptors.

Pure Antagonists
Naloxone Hydrochloride works by blocking opioid action at the mu receptors. Onset of reversal occurs within 1-2 minutes of IV administration and can last for 1-4 hours. Treatment may be repeated when reversing narcotics with a longer duration. Typical dosage is 2 μg/kg IV.
Synthetic Opioid
Tramadol has opioid like activity at the mu receptor and appears to be quite effective in controlling moderate to severe pain. It is available in oral form making it suitable for long term at home management of post operative, cancer, orthopedic and other chronic pain. Current dosing recommendation is for 4mg/kg PO BID to TID in the dog and cat.

ALPHA₂-AGONISTS
The provision of analgesia is a component of alpha-2 agonists that is often overlooked. Other commonly used sedatives (e.g., acepromazine and diazepam) do not provide pain relief. The analgesia achieved with alpha-2 agonists is of moderate intensity and moderate duration, much like the analgesia achieved with butorphanol. Obviously, this analgesia is not potent enough for major pain but is appropriate for control of mild pain. Even more importantly, alpha-2 agonists work synergistically with opioids (like butorphanol or morphine) and improve both the intensity and the duration of pain relief.

Dexmedetomidine is a dose-dependent sedative analgesic commonly used as a preanesthetic agent in healthy animals. Onset of effect takes 5 to 15 minutes depending on route of administration (IV or IM) and sedation can last up to 90 minutes. Dexedetomidine administration results in physiologically normal peripheral vasoconstriction, temporary decreased heart rate, and a transient increase in blood pressure. All cardiovascular parameters smoothly return to pre-sedation levels upon reversal with atipamezole.

Dexdomitor Doses
Dogs
Premed for routine surgeries
Combine ¼ label dose with opioid of choice at standard dose and administer IM 15-20 minutes prior to induction. Induction drug volume should be reduced to ½ the usual amount or less. Inhalant anesthesia should be reduced to 0.5-1%

Protocol for short nonpainful or mildly painful procedures
Combine ½ label dose Dexdomitor with 0.2mg/kg Torbugesic and administer IM or IV
Can reverse with equal volume Antisedan (to Dexdomitor) IM

Mini Micro Rescue dose for rough recovery
Administer 2-5ug/kg IV. (0.2ccs for a 25kg dog) Provides about 30 minutes of sedation to transition smoothly from anesthesia. Can repeat or deliver as a CRI.

CRI dose for continued dysphoria/anxiety/pain
Deliver at 2ug/kg/hr. The same dosage can be used in cats. Can be added to other infusions

Cats
“Kitty Magic” for surgical or painful procedures. In a 5kg cat combine and administer IM:
0.2cc Dexdomitor
0.2cc Ketamine
0.2cc Buprenorphine (or other opioid)
This combination provides 30 minutes of profound sedation and analgesia typically sufficient to perform castration or less painful procedures or intubation. Occasionally small amounts of inhalant anesthesia by mask are required.

For simple non painful procedures dose can be reduced to
0.1cc Dexdomitor
0.1cc Ketamine
0.1cc Torbugesic