1. Recognition of the benefits
- Reducing fear/stress/pain
  - Blunts the maladaptive neuroendocrine responses
- Balanced Anesthesia and Analgesia
- Reduces Costs of Providing Care
- Improves Patient Recovery
  - Reducing immunosuppression
  - Return to feeding and nutritional balance
- Improved wound healing
  - Speeds discharge from veterinary care
- Reduces Client Fear, Anxiety, Apprehension, Stress
- Improves Client Approval, Cooperation, Satisfaction

2. Better tools for evaluation of pain – behavioral indices refined and validated
- Poor or lack of grooming, Inappetance (chronic)
- Hissing or aggression if the painful part is manipulated
- Unlike dogs, a tendency to hide the painful part and look normal
- Dissociation / Detachment
- Vocalization – rare sign in cats
- Validated feline behavioral pain scale for assessing surgical pain.

3. Better tools for evaluation of pain – facial grimace pain scale validated
Combine the power of the Feline Facial Grimace with an Interactive Behavioral Evaluation

4. Gentle handling refined
- AAFP and ISFM Feline-Friendly Handling Guidelines
  - With respect, admiration, and thanks to Dr. Sophia Yin
- Fear - Stress - Aggression
- Separated Areas for Cats or Feline Only Facilities
- Pheromone spray
- Towel wraps
- Remove the top and work in the cat carrier
- Avoid / Minimize “scruffing” or excessive stretching
- Gentle techniques, Less is More…
- Avoid chamber induction of anesthesia

5. Non-steroidal anti-inflammatory drug therapy in cats
- Perioperative NSAID for inflammatory pain
- Multi-Modal or Balanced Analgesia
- Patient Selection
- Changing paradigm for NSAIDs and Improving Options
- Chronic Non-Steroidal Anti-inflammatory Drug Therapy in Cats
- Feline ignored for too long
- Incidence of DJD is high in older cats
- Behavioral and Post Mortem evidence is clear
- Extra-Label Use in United States
- Chronic Use with informed consent in DJD/OA
- Dose to Lean Body Weight
- Regular laboratory testing for chronic therapy
- Regular Consultation / Adjust Therapy Plan
6. Long-term pain in cats

- Species-specific responses of cats to Chronic Pain:
- Cats - isolation from others in the household, decreased grooming, and cessation of eating
- Inappropriate behaviors
- Inappropriate elimination
- Pain - Stress – Fear – Aggression – Euthanasia
- Pain management becomes “life saving”
- DJD / OA
- Chronic infections
- FLUTD
- Oral Resorptive Lesions and Gingivitis/Stomatitis
- Diabetes
- Cancer - Value of Multi-Modal Balanced Management

7. Opportunities with opioids

- Butorphanol -
  - Short-acting (<90 min)
  - Highly valuable for sedation
  - Mild transient analgesia only
- Buprenorphine…(Stay tuned…)
- Hydromorphone - potential for hyperthermia
- Methadone - Dual mechanism actions: Opioid agonist & NMDA receptor antagonist
- Morphine - Low doses avoid hyperactivity / dysphoria Less effective analgesic metabolites in cats than in dogs
- Oxymorphone - Effective analgesic Potentially less hyperthermia / dysphoria
- Fentanyl – infusions… yes, patches… no
- Tramadol - May act as an opioid analgesic in cats
- Mu opioid receptor agonist activity - limited
- Serotonin / Norepinephrine Re-Uptake Inhibition
  - Not palatable – resolution....
  - Euphoria / dysphoria and mydriasis potential
  - Some human formulations contain acetaminophen
- (highly toxic to cats)

8. Buprenorphine – optimized as simbadol

- Simbadol – FDA Approved for 24 hour analgesia in cats
  - Repeat for 72hr total
  - Effective and safe analgesic for cats
  - Our first 24 hour duration opioid analgesic for cats
- Unique Profile in Cats
- Unique Physiology, Pharmacology of Higher Dose
- Excess Substrate Delays Elimination of Active Drug
- Once Daily Surgical Pain Control
- SIMBADOL™ (buprenorphine injection) Black Box Warning: A Human Safety Issue
- Trans-Mucosal Administration of Buprenorphine
- Buprenorphine-SR aqueous polymer vehicle - A compounded product, lack of evidence, concerns limit use.

9. Transform the “grumpy cat”

- The grouchy, fearful, angry, antisocial cat has “issues…”
  - Very often an unnecessary situation
- Turn it around with analgesic strategies
  - Pharmacologic
  - Behavioral
  - Management
- Strengthen the bonds
Practice - Client - Patient
Facilitated exam / management / procedures

- Caudal Epidural for blocked tomcats
- Chronic disease states:
  - Interstitial Cystitis
  - DJD / OA - greatly under-diagnosed in older cats
  - Chronic oral disease stomatitis / gingivitis
  - Cancer pain management
- Extension of health-span and life-span
- Prolongation of the Human-Animal Bond

10. Updated and expanded 2015 AAHA AAFP pain management guidelines

- Pharmacologic and non-pharmacologic modalities
- Evidence-based or consensus of expert opinion
- Behavioral changes – Validated pain scales
- Post-surgical pain is predictable
  - Strategies mitigate adaptive & maladaptive pain
- Chronic pain – DJD predominates
  - Prevalent, Under-diagnosed, Ubiquitous, Progressive Evidence-based strategies emerging in cats

Ten best things about feline pain management

1. Recognition of the Benefits
2. Behavioral Indices Refined and Validated
3. Facial Grimace Pain Scale Validated
4. Gentle Handling Refined
5. Non-Steroidal Anti-inflammatory Drug Therapy
6. Long-Term Pain in Cats
7. Better Use of Opioids
8. Buprenorphine – Optimized as Simbadol
9. Transform the “Grumpy Cat”
10. 2015 AAHA AAFP Pain Management Guidelines

Selected references

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2015 AAHA/AAFP Pain Management Guidelines for Dogs and Cats
Clinical Pain:
How to Prevent or Manage Pain and Suffering
Ralph Harvey, DVM, MS, DACVAA
University of Tennessee
Knoxville, TN

Clinical uses of opioids
- Antitussive: cough suppressant action of opioids
- Pre-anesthetic medication, analgesia and sedation
- Induction of anesthesia: sole drug for some species (humans), valuable adjuvant for veterinary patients
- Intraoperative analgesia: reduced anesthetic requirement, decrease complications and improve outcome
- Postoperative pain relief: improved outcome and quicker recovery, reasonable post-op comfort for all
- Critical care adjuvant: basic analgesia, facilitates mechanical ventilation, tolerance of tracheal tube, and other supportive measures. Providing good analgesia improves clinical outcome for critically injured patients.

Opioid analgesics and recommended doses

**Morphine**
- Dog: 0.25 - 0.5 mg/lb (0.5 - 1.0 mg/kg) IM, SC
- Cat: 0.025 - 0.05 mg/lb (0.05 - 0.1 mg/kg) IM, SC (Very useful at 1/10th the dog dose)
- Duration: 4-6 hours
- Sedation accompanying analgesia
- Vomiting, diarrhea, and bradycardia may occur
- Hypotension and bronchoconstriction (histamine release, especially with IV use) may occur

**Meperidine (Demerol)**
- Dog: 1-5 mg/lb (2-10 mg/kg) IM, SC
- Cat: (usually effective, avoid high doses)
- Duration: 0.5-1 hour
- Mild sedation
- Rarely histamine release and hypotension
- Cardiac and gastrointestinal effects are relatively minimal

**Hydromorphone**
- Dog: 0.025-0.05 mg/lb (0.05-0.1 mg/kg) IM, SC, IV
- Cat: 0.01-0.025 mg/lb (0.025-0.05 mg/kg) IM, SC, IV
- Duration: 4 hours
- Panting, vomiting, diarrhea, bradycardia may occur
- Dose-dependent sedation or excitement

**Fentanyl**
- Dog and Cats: 2-10 micrograms/kg/hr as a constant rate infusion after IV loading dose of 2-10 micrograms/kg
- Rapid onset and short duration
- Procedural uses and as a CRI for sustained and titratable analgesia in critical care
- May be combined with lidocaine CRI
- Recuvrya TransDermal fentanyl for dogs, sustained fentanyl analgesia

**Mixed-acting agonist-antagonist opioid analgesics**

**Pentazocine (Talwin)**
- Dog: 1-2 mg/lb (2-3 mg/kg) IM
- Cat: same as dog dose
- Duration: 4-6 hours
- Only mild analgesia
- Minimal systemic effects
- Narcotic reversal, ceiling effect

**Butorphanol (torbutrol, torbugesic, stadol)**
- Dog: 0.1-0.2 mg/lb (0.2-0.5 mg/kg) IV, IM, SC
- Duration: 1-2 hours
- Antitussive effect (often desirable)
Minimal systemic effects
Narcotic reversal (partial reversal)
"Ceiling effect" – very limited analgesia, useful for mild sedation
Cat: (same as for dog, except for a longer duration of action 2-4 hours)

**Nalbuphine (nubain)**
- Dog: 0.2-1.0 mg/lb (0.5-2.0 mg/kg) IM, IV
- Limited effectiveness - “ceiling effect”
- Minimal sedation
- Minimal systemic effects
- Narcotic reversal, ceiling effect

**Partial agonist opioid analgesics**

**Buprenorphine (buprenex, temgesic, simbadol, buprenorphine-SR)**
- Dog: 0.005-0.01 mg/lb (0.01-0.02 mg/kg) IM, SC
- Cat: 0.005-0.01 mg/lb (0.01-0.02 mg/kg) IM, SC, and oral transmucosal with excellent uptake
- Duration:
  - Buprenorphine: 6-8 hours (slow onset, even with IV injection, 30-40 minutes)
  - Buprenorphine-SR: (claimed 72 hours, not FDA approved)
  - Simbadol: FDA approved, 24 hours duration in cats, euphoric behavior and mydriasis
- Complications: Minimal systemic effects, some “ceiling effect”, but rather potent analgesia.

**Non-opioid analgesics**

**Tramadol (ultram, ultracet, etc.)**
Mild opioid, non-NSAID analgesic with mu-opioid binding activity and interference with both serotonin storage and norepinephrine re-uptake. Analgesic action exceeds mu receptor binding characteristics. First metabolite has greater mu-binding than parent compound. Not a DEA controlled substance. Tramadol may be effective where a weak opioid such as codeine would be chosen.
Tramadol dose in Dogs: 1-4 mg/kg PO q 8-12 h for 5-7 days. 50mg tablets available in the US. Call Besse medical 1-800-477-7119.

**Ketamine (ketaset, ketaset, ketalar)**
- Very low doses (actually sub-anesthetic, “sub-psychogenic” doses) potentiate opioid analgesics.
- The use of these very low doses, in balanced analgesic combinations, is a relatively new strategy. Dog or Cat doses: 0.01-0.5 mg/lb (0.02-1 mg/kg) IM, SC, PO, combined with opioids, etc.
- "Cataleptic" effects are minimal or absent at these low doses. Duration of 4-6 hours.
- CRI: loading dose 0.5-2.0 mg/kg, CRI at 2-10 micrograms/kg/min

**Dex-medetomidine (dexdomitor, dexdomitor 0.1, precedex in humans)**
- Procedural analgesia, marked sedation. Standard dose is scaled to BSA in dogs (see box label).
- We use “lower dose” DexDomitor method: DexDomitor (5-10 microgram/lb, 2.5 to 5 microgram/kg) IM or IV, combined with Torbugesic (0.1-0.2 mg/lb, 0.2-0.4 mg/kg), or other opioids, IM or IV.
- Reversal with Antisedan (by IM injection only) leaves the mild Torbugesic effect intact.
- Recent evidence and extensive clinical experience in humans and veterinary patients supports expanded extra-label use, including post-operative management of delirium.
- Shorter duration and less need for reversal of DexDomitor relative to Domitor may be due to actions of Levo-Domitor in the previous formulation.

**Xylazine (rompun, anased)**
Lacks specificity. A poor substitute in dogs and cats for dexmedetomidine.

**Lidocaine CRI**
- Pro kinetic, reduced dose of other analgesics, possible anti-inflammatory action
- Loading dose 1-2 mg/kg, CRI at 25-100 micrograms/kg/min
- Easy set-up method: 68 cc of 2% lidocaine added to liter bag of IV fluid (or 34 cc lidocaine added to a 500 cc bag) administered at 1cc/pound/hour will provide 50 micrograms/kg/min
- Adjust rate between 0.5 and 2.0 cc/lb/hr to give lidocaine cri at 25 to 100 mcg/kg/min
- Reduce or discontinue if clinical signs of intolerance or overdose toxicity occur: nausea, CNS stimulation (twitching or seizures)
Non-steroidal anti-inflammatory drugs (NSAID’s) and related analgesics

Perioperative risks of renal damage may be reduced by the appropriate administration of IV fluids before and during anesthesia to maintain blood pressure and renal blood flow. GI irritation may be subject to great individual variation. Patients should be monitored for development of intolerance and side effects as well as for changes in efficacy. At this time, any chronic use of NSAIDs in cats in the US is an “extra-label” use. See 2015 AAHA Pain Management Guidelines. Some of these NSAID's are listed for historical reference only!

Meclofenamic acid (arquel) (meclomen)
- Dog: 0.5 mg/lb (1.1 mg/kg) PO q 24 h Short-term use only
- Recommended for medical management of orthopedic conditions, e.g. hip dysplasia
- Complications reported with chronic administration: vomiting, tarry stools, mucosal erosions, leukocytosis, and decreased hemoglobin

Ketoprofen tablets and injectable
- Dog or Cat: 0.5-1 mg/lb (1-2 mg/kg) q 24 hours, IV (dogs only), IM, SC, PO initially, then reduce this dose by 1/2 for subsequent doses
- Mild to moderate pain
- Recommended for not more than five days in dogs. Use may be limited to one day in cats.
- Complications may include GI irritation, ulcers, and renal damage.

Carprofen (rimadyl)
- Dog: 1mg/lb q12h (or 2 mg/lb q24h) per OS. Cat: 1 mg/lb q12-24h, 1-2 doses only
- Most popular NSAID in dogs
- Relatively specific for COX-2 (anti-inflammatory) effects.
- Oral formulation available in 25, 75, and 100mg caplets or chewable tablets.
- Injectable carprofen 2mg/lb (4 mg/kg)

Etodolac (etogesic)
- Dog: 4.5-6.8mg/lb (10-15 mg/kg) q24h per os.
- Newer NSAID with reduced GI toxicity.
- Relatively specific for COX-2 (anti-inflammatory) effects.
- Available in 150 and 300mg scored tablets.

Deracoxib (deramaxx)
- Dog: 1-2 mg/kg/day as single daily dose for OA; or at 3-4 mg/kg/day as a single daily dose not to exceed 7 days, for post operative inflammation and pain
- “Cox-2 specific” action
- Flavored tablets.

Tepoxalin (zubrin)
- Dog: 10-20 mg/kg on first day, then 10 mg/kg daily for OA or postoperative pain
- Rapidly disintegrating tablets (Redi-tabs)
- “Dual-pathway” inhibition of Cox/Lox. A different approach to the Cox-1/Cox-2 dogma on side effects of NSAID’s

Meloxicam (metacam)
- Dog: oral (flavored) liquid, 0.2 mg/kg on day one, then 0.1 mg/kg daily on food
- “Out-sells Rimadyl in Canada at 5:1” Work down to lowest effective dose.
- Extensive clinical experience in Canada and EU, including the injectable formulation
- Cats: 0.3 mg/kg (0.14 mg/lb), injectable by subcutaneous route, single dose
- Oral meloxicam for cats (extra-label): Recommended often for cats at one drop q24-48 hrs after loading dose of two drops. Chronic use is controversial but recommended by some experts. (Little research data as yet. Risk of renal toxicity: 0.1mg/kg as single dose Day 1; 0.05mg/kg as single dose Days 2,3,4; 0.025mg/kg as single dose on Days 5,6,7 and thereafter q48h

Firocoxib (previcox)
- Dog: Chewable tablets, 5 mg/kg (2.27 mg per pound) every 24 hours orally, with or without food. Available as 57 mg and 227 mg tablets. Selective inhibition of cyclooxygenase-2 (COX-2).

Robenacoxib (onsior)
- Very high margin of safety. Chemically modified diclofenac. Highly palatable in cats.
- Oral tablets (6mg) and injectable liquid (20 mg/ml, 2 mg/kg by subcutaneous injection)
Other NSAIDs
Many available. Toxic side effects can be prominent. Many reports warn of G.I. toxicity. Considerable patient-to-patient variation in susceptibility to toxic effects. Anti-inflammatory and analgesic effects are also quite individual (as in human patients). G.I. protective agents (e.g. misoprostol) can be beneficial.

Misoprostol for G.I protection
Misoprostol (Cytotec) can be given to dogs or cats at 2-5 mcg/kg orally (once a day in cats, twice daily in dogs). It is used to increase tolerance to NSAID’s by reducing G.I. ulceration. Toxicity/side effects are anorexia and hepatopathy. Liver function testing (or liver enzyme analysis) should be performed monthly with misoprostol use (especially if misoprostol and NSAID’s are administered concurrently).

Acetaminophen (Tylenol, etc.)
- Analgesic and antipyretic for dogs, but not anti-inflammatory.
- Dog: 4.5-6.8mg/lb (10-15 mg/kg) q8h per os.
- Lacks G.I toxicity. Can be most useful for dogs in opioid combinations, particularly for cancer pain, but also popular for postoperative use as Tylenol # 3 or #4.
- VERY TOXIC FOR CATS!

Acetaminophen toxicosis in Cats
- Clinical Signs: cyanosis, dyspnea, facial edema, depression, and emesis
- Etiology: glucuronyl transferase deficiency (relative to other species)
- Therapy: Avoid stress!! If recent ingestion - induce vomiting Activated charcoal (2gms/kg) along with a saline cathartic, e.g. sodium sulfate (0.5 mg/kg) as a 20% slurry. Oxygen ASAP if cyanotic, but without adding further stress. Acetylcysteine (Mucomyst, Mucosol) 140 mg/kg PO or IV, and repeat at 70 mg/kg q6h for 36 hrs (seven treatments). Ascorbic acid 30mg/kg orally or parenterally with the acetylcysteine. Fluid therapy - lactated Ringer's solution. Continued intensive care and physiological support.
- (See: Cullison, R.F., Comp. Cont. Ed. 6(4): 315-320, April 1984.)

Epidural analgesia and anesthesia
Spinal or epidural opioid analgesia has been well described and proven effective in veterinary medicine. Epidural morphine analgesia is widely used in referral and academic centers and is increasingly popular as a method for providing long-lasting profound analgesia. The technique is rather simple, easily accomplished with basic clinical skill, and can be very cost-effective for providing substantial analgesia.

A relatively very small dose of morphine (0.1 mg/kg) is administered by epidural injection after induction of general anesthesia but prior to the surgical procedure. Effective pain relief persists into the following day (12 - 24 hrs) and is accompanied by a blunting of deleterious post-operative increases in stress hormones and the metabolic response to surgery. Combinations of morphine and bupivacaine provide the greatest analgesic effect.

Anatomical landmarks for lumbosacral epidural injection:
- Iliac crests, dorsal midline, and lumbar vertebral spinous processes
- For epidural injection, patients are under anesthesia and positioned in either sternal or lateral recumbency based on personal preference and best recognition of anatomic landmarks.

Dose recommendations:
- Morphine* 0.1 mg/kg
- Diluted to total volume of 0.2 ml/kg
- (Maximum of 6 ml for dogs and 1.5 ml for cats) using:
  - Saline
  - (or) Lidocaine (2.0%)
  - (or) Bupivacaine (0.5 %)

Duration of analgesia: 12-24 hrs.
- Contraindications:
  - Local infection
  - Neurological dysfunction
  - Marked obesity (increased difficulty)
  - Hypovolemia / Hypotension (avoid the local anesthetics)

*Preservative-free morphine (e.g. Duramorph), designed for epidural use, is the best-recommended product. With the preservative-free morphine preparation, cost is increased. We currently do use the preservative-free morphine, usually in combination with either saline or 0.5% bupivacaine. The Duramorph preparation is at a concentration of 1.0 mg/ml. We administer 1 cc Duramorph per 10 kg body weight (0.1 cc/kg) mixed with either saline or bupivacaine, also at 1 cc per 10 kg, for a total volume of 2 cc per 10 kg, with a
maximum total volume of 6 cc. The 30-pound dog in this illustration would receive 1.4 cc of Duramorph mixed with 1.4 cc of either saline or bupivacaine.

Combinations of opioids, alpha-2 agonists, and local anesthetics are becoming popular (once again) for epidural regional analgesia/anesthesia in various large animals including horses, cattle, and llamas.

**Fentanyl patches for sustained analgesia**

Trans-dermal uptake of sustained-release fentanyl from a patch applied to the skin can provide long-term analgesia. This relatively new technology has now moved from the management of cancer pain in human patients to veterinary care where it is useful for sustained analgesia in animals with significant trauma, e.g. multiple fractures after vehicular trauma, as a portion of the management of post-operative pain, and in some cancer patients. Fentanyl patches can be very useful in cats as well as dogs.

The fentanyl patches sold as Duragesic from Janssen. They are available in different rates of drug delivery: 25, 50, 75, and 100 microgram/hour. Fifty mcg patches have been reported effective for small and medium size dogs. The 25mcg patches have been used extensively in cats. The behavioral effect of dysphoria and dementia may be unacceptable in some animals and may require tranquilization or removal of the patch. Uncovering only half of the barrier layer before application has been used in an attempt to reduce the dose, and minimize this problem, particularly in smaller dogs and in smaller cats, but is unreliable.

Patches are applied to clipped skin in an area that the animal cannot reach, such as the dorsal neck or the interscapular area of the dorsal midline. Uptake is somewhat variable among patients and clinical efficacy may be related, in part, to differences in uptake of fentanyl. Onset of analgesia is probably several hours after application of the patch. Hence, for operative or traumatic pain, some other drug should be used initially to provide analgesia. It is very important that the patient is prevented from damaging or ingesting these patches or the contents. Be aware that application of a heating pad, as during surgery, can greatly increase uptake of the drug with significant overdose possible. Duration of effectiveness is roughly four days.

Fentanyl can be a highly abused opioid and there have been reports of clients diverting fentanyl patches from their animals for drug abuse/diversion purposes. Some clinicians find the fentanyl patches a very useful part of managing cancer pain in outpatients, including the terminally ill. It is important to emphasize the potential dangers and the importance of protecting other pets and children from ingestion or other possible exposures. Expended (used) patches still contain fentanyl, and should be handled with care. Duragesic Patches are approved for use in human patients only. All veterinary use is strictly off-label.

**Analgesic CRI (constant rate infusion)**

**CRI options for analgesia**

- Lidocaine
- Low-dose ketamine
- Fentanyl
- Morphine
- Combinations of analgesics (e.g. lidocaine plus fentanyl cri)

**Adjunctive analgesics**

- Tramadol 4-6 mg/kg q 8 hours. Interesting mechanisms of action. Challenging validation for the management of suffering aspects of pain.
- Gabapentin: 3-10 mg/kg q 6-12 hours. Endorsed in 2015 Updated AAHA Pain Management Guidelines.
- Amantadine 3-5 mg/kg q 24 hours.
- Other adjunctive medications.
Obvious (but important) principles

- Appropriate physical exam and other evaluation as indicated
- Customize protocol for each patient's unique situation
- Pharmaceuticals do not take the place of clinical finesse
- Monitor for physiological effects and respond as needed
- Determine adequacy of recovery / fitness for return to ward/owners
- Counsel owners that recovering outpatient animals should be allowed to recover quietly and can not be trusted to respond typically for +/-24 hrs.
- Consult me or another anesthesiologist at any time for specific suggestions.
- Nobody likes an adventurous anesthetist!

There are many other useful options and an infinite variety of clinical situations may occur.

A Few of our favorite methods

1) Acepromazine - reliable tranquilization, not recommended for vicious or potentially dangerous animals, side effects are primarily hypotension but rarely some seizure-prone patients may develop seizures, contraindicated in shock or other hypovolemic conditions and in patients with liver disease, duration of effect 2 - 4 hrs, which is too long for most purposes. Very rarely do we use the higher doses.
   - Ace at 0.01 to 0.05 mg/kg (0.02 to 0.1 mg/lb), max.3 mg total dose, SC, IM, IV

2) Acepromazine & Torbugesic (or other opioid) - substantial and reliable effect; not as often recommended for older/compromised patients; fairly prolonged effect, particularly if hepatic function is impaired; may not be the best choice for outpatients since return to "street fitness" often requires 4-6 hrs.
   - Ace at 0.01 to 0.05 mg/kg, max.1.0 mg, SC, IM, or IV
   - Torbugesic at 0.2 to 0.4 mg/kg, SC, IM, or IV
   - Optional anticholinergics, to avoid or treat bradycardia:
     - Glycopyrrolate at 0.005 to 0.015 mg/kg, SC, or IM
     - Atropine at 0.02 to 0.05 mg/kg, SC, or IM

3) Valium (diazepam) & Torbugesic - less "heavy handed" than Ace & Torbugesic, but also a less substantial and less reliable effect; one of our favorite pre-anesthetic choices for the debilitated generic or geriatric/high risk patient; expect peak effects to last for about 30 min with return to "street fitness" within 1-2 hrs. Midazolam (Versed) is currently taking the place of diazepam. One-half the listed dose of Valium or Versed is often adequate. Excitement and disorientation may occur and patient should not be stimulated nor trusted to remain sedate.
   - Torbugesic at 0.2 to 0.4 mg/kg SC, IM, or IV. Followed by:
     - Valium at 0.25 to 0.4 mg/kg IV (IV route strongly preferred)
     - or Versed at 0.1 to 0.5 mg/kg SC, IM, or IV
   - Optional anticholinergic (infrequently needed):
     - Glycopyrrolate at 0.005 to 0.015 mg/kg, SC, or IM
     - Atropine at 0.02 to 0.05 mg/kg, SC, or IM

4) Telazol - remarkable physiologic stability, but beware of respiratory depression and potential to initiate seizures; avoid in patients with respiratory compromise and in those with hypertrophic cardiomyopathy or seizure history or certain intracranial or intraocular disorders (increases IOP and ICP). Expect fairly full recovery within 2 hours, but some residual effects are unfortunately too common.
   - Telazol at 1-3 mg/lb (2-6 mg/kg) SC or IM
     - Begin with lower doses for restraint
   - Torbugesic at 0.1-0.2 mg/lb (0.2-0.4 mg/kg) mixed with Telazol
     - May be given carefully by IV route - increases side-effects
   - Optional anticholinergic to reduce salivation:
     - Glycopyrrolate at 0.005 mg/lb (0.01 mg/kg) SC or IM
5) Dex-Medetomidine (DexDomitor, DexDomitor 0.1)) – powerful sedative/hypnotic, similar to medetomidine (Domitor). Recommended for young, healthy, exercise-tolerant dogs. Current evidence and clinical experience both support expanded extra-label use in broader categories of patients, both human and veterinary. Very low doses quite useful to prevent or manage post-operative delirium. Patient monitoring is important. Availability of specific antagonist (Antisedan) contributes to safety and utility. Useful for examinations and brief procedures. Profound bradycardia and hypertension may occur. Tissue perfusion is decreased. Pulse oximeters may fail to detect signal. Use of atropine or other anticholinergics is controversial. We avoid the anticholinergics. Standard dosing in dogs is scaled to body surface area (see insert or dosing guides).

We use a low dose Dexdomitor method (typically 0.0005 to 0.0025 mg/kg), combined with Torbugesic (0.2-0.4 mg/kg) or other opioids. These low doses of Dexdomitor, when combined with an opioid, are very effective. Reversal with Antisedan (by IM injection only) leaves the mild Torbugesic effect intact. Reversal is less often needed with Dexdomitor than with Domitor. Differences in duration of effect and in sedation is interestingly related to the presence of "levo-domitor" in the earlier (Domitor) formulation.
When to Treat Pain - Newly available analgesics and novel methods for the use of standard medications have greatly expanded options for safe and effective relief of pain in veterinary patients. Analgesic therapy should be considered an integral part of our care when there is a reasonable possibility that pain might result from a medical procedure or condition. The best results are obtained when the analgesics are given before surgery. The key concept is “pre-emptive analgesia”. Recognizing pain in animals requires consideration of overt signs and subtle behavioral changes. As in people, individual analgesic requirements and responses vary with the animal and the peculiarities of each situation through recovery from surgery or critical illness. Therefore, always “dose to effect.”

Pre-emptive analgesia
The best results are obtained when the analgesics are given before surgery. New routes and methods of drug administration are being developed and validated. These include patient-controlled analgesia (PCA) for humans, trans-dermal opioids (patches), controlled release gels, and neuroaxial (epidural and spinal) analgesics.

Multi-modal analgesia
Combination of pain-management methods works much in the same way that we can use anesthetic agents in various combinations for the best patient care. For “balanced analgesia” this may be represented in using some opioid as a pre-anesthetic and post-operative analgesic, along with use of a local anesthetic block. Or perhaps a pre-operative opioid, a local anesthetic infusion both during and after surgery, and an NSAID post operatively. Multi-modal or balanced analgesia has been shown to greatly improve analgesia with fewer side effects than might result from a more massive dose of any single analgesic medication.

Local anesthetic regional analgesia techniques
Techniques for use of local and regional anesthetics in small animal patients are easily learned and applied to substantially reduce the doses of other anesthetics and analgesics needed. These techniques are very cost-effective and greatly improve patient care. In combinations with other strategies (e.g. opioids, NSAID's, dissociative anesthetics) for preventing and relieving clinical pain, these anesthetic/analgesic procedures contribute to “balanced” analgesia or “multi-modal” analgesia.

To avoid toxic effects, the total volume of bupivacaine (0.5%) or lidocaine (2%) should always be less than 0.4 ml/kg or 0.2 ml/lb. Signs of an overdose include nausea, twitching or possibly seizures. At higher doses, cardiac depression can occur, particularly with overdoses or accidental IV injections of bupivacaine. To minimize the risk of accidental IV injections, always aspirate before injection.

Epidural injection
Landmarks are the Iliac crests, dorsal midline, and dorsal lumbar vertebral spinous processes.
Drugs used are typically preservative-free morphine (e.g. Duramorph), designed for epidural use, as the best-recommended product. With the preservative-free morphine preparation, cost is substantially greater than with parenteral morphine. We currently do use the parenteral morphine, usually in combination with either saline or 0.25% bupivacaine. The 0.1 mg/ kg body weight mixed with either saline or bupivacaine, at 0.5 mg/kg.

Brachial plexus nerve block
Produces anesthesia / analgesia distal to the and including the elbow, using bupivacaine at 0.2 ml/kg (0.1 ml/lb) with a 22 ga. 1.5-3.5 inch needle inserted between the shoulder joint and ribs, parallel to vertebrae. Aspirate, inject 0.2cc, withdraw slightly, repeatedly to distribute the bupivacaine. Keys to success include efforts to distribute drug, aspirate to avoid IV injection and toxicity, and minimize volume at each injection site to avoid nerve damage.

Maxillary nerve block
The field blocked includes the maxilla, upper teeth, lip, and nose of the injected side.
Insert needle toward the pterygopalatine fossa from the transition of the hard palate and soft palate or from caudal to the last maxillary tooth, or from below the ventral margin of zygomatic arch, 0.5 cm lateral to the lateral canthus of the eye. Aspirate, to rule out vascular injection, and deposit drug. Dose: 0.1-1.0 ml bupivacaine or Septocaine (preferred).

Mandibular nerve block
The mandibular nerve block is very easy to perform and very inexpensive. The mandibular foramen is located on the medial aspect of the mandible, at the transition from the vertical portion to the horizontal portion of the mandible. We slide the needle, usually a 22ga., 1.5 inch needle, along the interior aspect (medial or oral surface) of the mandible to a site about 1/2 way across that surface (easy to
see the foramen on a skull or in a textbook figure). The block can be performed either from inside or outside the oral cavity. Obviously, this nerve block should be performed AFTER induction of anesthesia, but should be done BEFORE surgery is begun.

**Mandibular nerve block**

Blocking the Inferior Alveolar Branch blocks the mandible, lower teeth, and lip. Insert the needle at the lower angle of the jaw, rostral to the angular process, and advance dorsally to the mid-portion on the medial aspect of the mandible. Aspirate, and then deposit the drug at the surface of the bone. The usual dose range is 0.1-1.0 ml bupivacaine or the dental anesthetic Septocaine (preferred) at lower volume. Doses have not yet been adequately defined.

**Declaw analgesia fore limb blocks**

Distal Fore Limb Blocks (declaw analgesia blocks) are performed at a level just proximal to the carpus to block the Superficial Radial Nerve (dorsomedial carpus), Ulnar Nerve (branches), lateral carpus, Median Nerve, Ulnar Nerve (branch) on the palmar carpus adjacent to the accessory carpal pad. Deposit 0.1-0.3 ml Bupivacaine 0.5% at each site. Note: Never use locals containing epinephrine (e.g. Septocaine or lidocaine with epinephrine) for any extremities or tissues with terminal arterial supply (nothing involving the feet, ears or tail)!

**Intra-articular stifle block**

For the Intra-articular Stifle Block, a 1” 22g needle is used. With the patient in lateral recumbency, with the affected limb uppermost, flex the stifle and apply digital pressure to the medial side of the straight patellar ligament. Insert the needle on the opposite side of the straight patellar ligament midway between the patella and the tibial tuberosity and direct it obliquely and distally toward the intercondylar space of the tibia. Note: possible chondrotoxicity of bupivacaine suggests that this use be reserved for special circumstances and is not routine in our hospital.

Distention of the joint is noted during injection with the long-lasting local anesthetic Bupivacaine 0.5%. This provides 3-6+ hours of duration with a dose 0.2 ml/kg (0.1 ml/lb). Injection is made both pre-op and post-op for best effect.

**Wound diffusion or soaker catheters**

This is a powerful, effective, easy and cheap way to deliver local anesthetics right to the site of nociceptive transduction and primary afferent transmission. Catheters are commercially available or can be easily fabricated. Elastomeric pumps, syringes and a variety of other devices can be applied to control delivery of local anesthetic to the wound.

**Lidocaine intravenous CRI (constant rate infusion) for dogs**

Provides an analgesic contribution and reduction in anesthetic requirements. The reduced inhalant anesthetic requirement improves blood pressures and is prokinetic. There is also possible anti-inflammatory contribution. This is a very cost-effective analgesic contribution to opioid analgesics.

Lidocaine loading dose of 1-2 mg/kg may be administered by slow IV injection over three minutes, but is usually not necessary as onset is rapid. Constant Rate Infusion is provided at 20-100 micrograms/kg/minute (0.05-0.1 mg/kg/min) by syringe pump or by controlled drip.

Easy set-up method is as follows: 68 cc of 2% lidocaine is added to a liter bag of IV fluid, administered at 1cc/pound/hour will provide 50 micrograms/kg/min. Adjust between 0.5 and 2.0 cc/pound/hr. Reduce or discontinue if clinical signs of intolerance or overdose occur: nausea, CNS stimulation (twitching or seizures).

Other CRI options for analgesia include: low-dose ketamine, fentanyl, or morphine. A combination of analgesics, one of our favorites, is lidocaine and fentanyl (1:1 mixture) adjusting the rate as needed. Begin at 50 mcg/kg/min for lidocaine and 7.5 mcg/kg/min fentanyl which is achieved at an infusion rate of 0.3 ml/kg/hr of the 1:1 mixture of lidocaine and fentanyl. Adjust the infusion rate as needed to achieve and balance the desired analgesia and sedation.
High Risk Cases:
Anesthesia for Patients too Sick for Anesthesia
Ralph Harvey, DVM, MS, DACVAA
University of Tennessee
Knoxville, TN

- Supportive care is based on recognition of patients needs.
- Focused monitoring and patient evaluation leads to individualized care.
  - Appropriate patient evaluation provides for the recognition of anesthetic risks and anesthetic concerns for that specific patient and procedure. “Problem-based” anesthetic management is the framework for individualized patient care.
- What “anesthetic concerns” have you identified for this patient? “100 things are missed due to not looking for every 1 thing missed due to not knowing”.
- Preanesthetic physical examination and laboratory analyses - individualized
- “minimum data base” based on risk
diagnostic imaging
  - radiographs, contrast studies, CT, MRI,
  - ultrasonography, scintigraphy, etc.
- other directed testing

ASA physical status categories
- American Society of Anesthesiologists (ASA)
- ASA I - excellent anesthetic risk
- ASA II - good anesthetic risk
- ASA III - fair anesthetic risk
- ASA IV - poor anesthetic risk
- ASA V - guarded anesthetic risk
  - additional “Emergency” designation (x)-E

Ventilatory complications
- Airway obstruction
- Inadequate Delivery of Oxygen
- Hypoventilation
- Inadequate Ventilation, Apnea
- Hyperventilation: Tachypnea or panting
- Irregular patterns of ventilation
- All anesthetics are respiratory depressants!
- Anesthetic overdose: Relative or Absolute
- Direct depression of central respiratory centers
- Secondary to circulatory depression
- Specific drug actions

Hypoventilation requires patient support.
Endotracheal intubation, ventilatory support by IPPV manual or mechanical ventilation based on patient monitoring, evaluate and address the underlying problem.

Hyperventilation and/or panting are less common, but may reflect hyperthermia, pain, or occur as a side-effect of specific drugs. Control of body temperature, management of pain, and control of ventilation may be necessary.

Support for Circulatory compromise
Hypotension is a common problem due to hemorrhage and/or vasodilatation. Circulatory support is largely based on fluid therapy, including crystalloids, and colloids. A variety of fluids are now available, with blood substitutes serving and important need. Vaso-active agents help support blood pressure, cardiac function, and tissue perfusion.
Temperature support
Hypothermia is an almost universal problem in small animal anesthesia and many areas of critical care. Risks of thermal support have been great with older heating strategies. The forced warm air systems offer a new method and much better means of providing thermal support.

- Metabolic and endocrine support is needed by some at-risk patients due to immaturity or disease.
- Inadequate glycogen storage or availability
- Adrenal insufficiency
- Excessive physiological demands

Delayed recovery from anesthesia
- Anesthetic overdose
- Inadequate elimination or metabolism
- MDR-1 Mutations, Heterozygous or homozygous, Genetic testing is available
- Hypothermia
- Debilitation
- Neurological deterioration

Management of delayed recovery
- Physiological support
- “SOP” - monitor, evaluate, diagnose, treat
- Facilitate elimination or metabolism
- Reversal of anesthetic drugs only when appropriate
Improving the standards of anesthesia and pain management across our entire profession was a goal in developing the AAHA Guidelines for anesthesia and pain management. There are many areas to consider with considerable potential for practical value-added improvement. Anesthetic care of veterinary patients has not gotten easier over the years. Really, has any part of medical care become “easier”? It is clear that anesthesia has become better and safer in that we are now able to provide successful anesthetic management for patients who would not have had a reasonable chance a few years ago. In many cases, these are even managed as outpatients, quickly returned to their owners in full recovery. Our choice of anesthetic drugs has greatly expanded, and safer anesthetic agents are indeed responsible for much of the improvement noted. The use of more sophisticated monitoring and better physiologic support has become widespread, with continued rapid growth apparent in this area. In spite of increased owner expectations and the fact that veterinarians now have sicker patients presenting with concurrent diseases, injuries, or debilitation, we can increasingly manage our patients successfully with the improvements in anesthesia and related peri-operative care.

Better training and ongoing training
This collection of proceedings on veterinary anesthesia helps to provide an update on current and developing methods. Continuing education seminars and numerous other contemporary publications attempt to further these same goals. The education of veterinarians and veterinary technicians now includes rather extensive attention to anesthesia and related topics. Veterinarians with advanced training in anesthesia and board certification by the American College of Veterinary Anesthesia and Analgesia are now involved in the training of new veterinary students at almost all North American colleges of veterinary medicine. Through the North American Veterinary Technician Association, licensed veterinary technicians with advanced knowledge, training, and skills in veterinary anesthesia may now pursue Veterinary Technician Specialist certification.

Monitoring and attention to detail
In addition to veterinarians, well-trained technicians continuously evaluate the patient throughout anesthesia. Awareness of the ever-changing condition of the anesthetized patient is a shared responsibility that can only be shared effectively and safely when the medical team works together. We intend to remain aware of even subtle changes in patient status under anesthesia. We must always recognize that challenges to the welfare of our patients come not only from their underlying illness or injury, but also as undesired effects that even the best anesthetic care may present.

Modern monitoring equipment is increasingly available at reasonable cost for veterinary use. We no longer need to rely upon out of date, poorly serviced, unsafe, and inappropriate equipment that has been discarded from human patient use. Fortunately, however, there is good quality equipment still available from the human patient market. Increasingly, that equipment now can be found with good warranty protection, recent service records, and, importantly, with design and function capabilities well suited to veterinary patient needs. There is also good quality equipment available specifically for the veterinary patient. Medical equipment sold exclusively for veterinary use does not receive the degree of oversight and approval required for human-use equipment. In spite of this, there is very good veterinary-specific medical equipment. The demands of veterinarians, and of the animal owners, for improved anesthetic delivery, monitoring, and support has fueled the growth of this industry.

No longer is the application of relatively advanced monitoring equipment and anesthesia machines limited to academic institutions or referral practices with heavy surgical caseloads. Monitoring of electrocardiogram, temperature, blood pressure, and pulse oximetry are rapidly becoming more routine, even in general veterinary practices. Airway monitoring of carbon dioxide and anesthetic gases in the breathing circuit is also becoming more popular. Proper use of these technologies requires a good working knowledge of the normal values, the significance of deviations, and an understanding of appropriate management options.

New options in anesthetics
Through the use of a good variety of injectable and inhalant anesthetics, great anesthetic safety and convenience is possible for our patients. Remarkable improvements for rapid and smooth recovery have developed in “out-patient” anesthesia. The recent popularity of several injectable anesthetics, most popularly propofol, and our new injectable anesthetic, alfaxalone have greatly improved our options. Propofol shortages resulted from the removal of defective generic products, but we all managed that temporary supply and demand issue. Isoflurane has been the strongly predominant inhalant anesthetic for several years. The more newly available inhalant, sevoflurane, can be used to provide for a remarkably rapid yet smooth induction and recovery from anesthesia, and can provide for a rapid change in the level of anesthesia as needed. Appropriate use of these new agents requires skill and knowledge and will be addressed more fully. All anesthetics have a limited therapeutic index, or margin of safety. All can depress vital functions, and
inappropriate use can result in loss of life. It is useful to remember the old guideline: “There are no safe anesthetics, just safe anesthetists.”

While we enjoy a wealth of new options and opportunities in veterinary anesthesia, we must make changes in our anesthetic strategies carefully, recognizing that experience is necessary to identify any abnormal responses from those that should be expected. Careful and conservative use of any new anesthetic or technique is crucial. “Nobody likes an adventurous anesthetist!”

**Individualized anesthetic care**

Much more important than the choice of which specific anesthetic drugs or equipment we use, however, is the manner in which we select them and the skill and care with which they are used in our patients. Best use of various options requires an individualized approach to anesthetic management. In treating infectious diseases, veterinarians wouldn’t choose the same antibiotic for every patient or condition encountered. Similarly, the best choice among options in anesthetic care of individual needs and individual risks vary widely among veterinary patients. We recognize breed sensitivities and relative contraindications in choice of anesthetics. For many years, breed associations have provided warnings based on anecdotal reports. With continued research, some of these have been or will be substantiated. Others perhaps will be refuted. In the absence of clarifying data, caution dictates selection and use of the best anesthetics from among the many choices available. Patient differences that are important in anesthetic care are obviously not only those that relate to species, breed and age differences. As a simple example, patients undergoing elective surgery or those traumatically injured both need analgesic therapy. Opioid analgesics, for instance, have varying efficacy and duration of action. The range of choices allows for brief, mild analgesia such as for an outpatient neuter, all the way to profound analgesia for the care of a substantially traumatized animal.

**Preanesthetic evaluation and screening**

Better anesthetic care also includes more thorough preanesthetic evaluation, which can fit nicely into a comprehensive approach of well-patient care and the work-up of the non-elective patient. Preanesthetic evaluations should be tailored to the needs of the patient. For example, the preanesthetic evaluation of a diabetic patient would include blood glucose determination(s) to help guide physiologic support as a part of the anesthetic care. Basic physical findings may lead to more extensive evaluations. For example, if a heart murmur is detected in a young cat, an echocardiogram may be performed to rule out cardiomyopathy before subjecting the animal to the stresses of anesthesia. Not all patients need the same level or intensity of preanesthetic evaluation or screening. Matching the process to the patient becomes cost-effective for the pet owner as well as for the practice owner.

**Geriatric patient care**

It is fortunate that the improved role of pets in our society has in various ways kept animals as a part of the family for more years. With an aging pet population, and with keen interest in keeping pets as very functional members of the family group, we have the opportunity to care for many more geriatric patients. These much-loved older pets often receive more extensive preanesthetic evaluation, which helps us identify marginal reserve function and any subclinical organ disease or dysfunction. Geriatric patients have dramatically reduced requirement for many anesthetics, and could be overdosed at standard recommended drug doses. Armed with this information, the veterinarian can individualize anesthetic care to minimize the risks of complications. Typical of this patient type would be the older dog presented for routine dental care. Through our improved care, we can extend not only the lifespan, but also the “healthspan” of these animals.

**Outpatient anesthesia**

As human patients, we expect to have most minimally invasive medical procedures, and even many substantial surgeries, conducted on an outpatient or same-day basis. Reduced hospital costs are not the only concern driving this change in human patient care. Everyone is happier and can return to daily routines more quickly when we are able to shorten hospital stays. This all applies to veterinary medicine as well. Better anesthetic care is a major component of this change. Clients personally experience it in their own medical care from the perspective of patients, and now they expect it in the veterinary care we deliver for their pets. Reliable, fast, and smooth recovery from anesthesia is a wonderful feature of many of the more modern anesthetic methods. While every patient differs, we’ve come to expect more and more of our patients to bounce back quickly.

**Prior preparation prevents problems**

Readiness includes anticipation of contingencies and willingness to consider, and perhaps move along to, what we have in mind as the “Plan B” for that patient. This is recognition of whatever else might be likely to happen for this animal other than the expected course of events. Those who are ready for these contingencies can intercept developing problems before they reach the “crisis” stage. This requires attentiveness to warning signs. Good anesthetic monitoring and appropriate responses to changing patient status are much more successful strategies for patient care than would be any level of expertise in crisis management.
Pain management
Our clients expect optimal control of animal pain. Clients expect the best in anesthetic survival and in relief of pain. Their most basic expectations are that their pet will survive and that it will not hurt. We do have the tools available to effectively manage procedural, traumatic, and peri-operative pain. We also have increasingly fine methods for very effectively managing the more chronic pains of degenerative joint disease and cancer. The three principles of effective pain management are: (1) pre-emptive analgesia, (2) balanced analgesia, and (3) willingness to dose-to-effect. Application of these principles can help us devise very effective pain management for every patient. Smart use of analgesic strategies offers tremendous benefit through relief of unnecessary pain and suffering. Improvements in the areas of the recognition and management of animal pain have been arguably greater than in any other aspect of veterinary anesthesia. Benefits include improved patient comfort, but also reduced anesthetic requirements, shortened hospital stays, improved immune function, and reduced morbidity and mortality. Good quality pain relief is also very cost-effective.

Supportive care
As an example of basic physiological support, the provision of fluid therapy and appropriate patient warming devices is increasingly commonplace in veterinary anesthetic care. Fluid therapy is an appropriate measure to compensate for the vasodilatation and hypotension that can commonly occur with the best of anesthetic techniques. We also recognize, through the increased use of blood pressure monitoring, that many of our patients can become hypotensive. Our older patients may be particularly susceptible to deleterious consequences of inadequate tissue perfusion. Patient warming devices that gently circulate warm air or warm water have replaced dangerous electric heating pads and bags or bottles of warm (or hot) water. All too often, electric heating pads and hot water bags have either burned animals or failed to properly prevent hypothermia. With individualized patient management, which includes physiologic support, those animals with particular needs or susceptibilities are better prepared for the rigors of anesthesia and surgery.

Summary
There seems to be little upper limit to the sophistication of medical care demanded by the pet owning public. Improvements in all areas of veterinary medicine are being rapidly embraced. The standard of care is indeed moving forward in all of our profession, and that was the larger goal in establishing the AAHA Guidelines for Anesthesia and for Pain Management. As tools to facilitate incremental improvements, they aid the profession and each of us. Full implementation of the AAHA Guidelines is very practical for many of our hospitals. Our best clients assume that the veterinary anesthetic care and pain management their animals receive are already at a very high level of sophistication, perhaps even comparable to that afforded human patients. Our obligation to do the best we can for our patients and for our clients requires that we move forward and maintain very high standards in providing anesthesia and analgesia.

References
Non-steroidal anti-inflammatory drug therapy in cats
- Perioperative NSAID for inflammatory pain
- Multi-Modal or Balanced Analgesia
- Patient Selection

Changing paradigm for NSAIDs
- Feline ignored for too long
- Incidence of DJD is high in older cats
- Behavioral and Post Mortem evidence is clear

Extra-label use in United States
- Use with Caution in DJD / Chronic use
- Dose to Lean Body Weight
- Regular laboratory testing for chronic therapy
- Regular Consultation / Adjust Therapy Plan

Robenacoxib (Onsior)
- Tablets approved (US) three day course of periop therapy
  - Rapid onset, short plasma T1/2, pKa 4.7, Freed from albumin at low pH - sites of injury or inflammation
  - Limited toxicity
  - Dose 1 mg/kg (1-2.4 mg/kg) up to 3 days approved in US
    - avoid combinations with other NSAIDS, avoid with renal disease
    - Injectable form approved in other markets – awaiting changes
  - Paradigm shift in pre-op use: Oral! and NSAID!
  - Highly palatable (Compliance improved)

Alfaxalone
  - Alfaxan from Jurox
    - Injectable Steroidal Anesthetic
    - Analogue of Progesterone
    - Approved for IM as well as IV administration
    - Solubility Issues Resolved via Cyclodextrin Cage

Comparative studies: Alfaxan / Propofol infusions
- Favorable Therapeutic Index
- Pharmacodynamics Similar to Propofol

Natural neuroactive steroids
- Synthesized by the brain and nervous system
- Regulation of myelinization
- Neuroprotection
- Growth of axons and dendrites
*Modulate expression of particular subunits of GABA$_A$

Alfaxalone
- Alfaxalone (3α-hydroxy-5α – pregnane -11, 20 – dione) is an ultra-short acting anaesthetic a neuroactive steroid producing anaesthetic effects through activity at the GABA-$A$ receptor
- Similar molecular structure to progesterone, however, at clinical concentrations alfaxalone does not bind to sex hormone, glucocorticoid or mineralocorticoid receptors
Saffan® (vet product) and Althesin® (human product)

- Alfaxalone (9 mg/mL) plus Alphadalone (3 mg/mL)
  - A different neurosteroid that improved solubility but has little anaesthetic potency
  - Cremophor®-EL
    - Castor oil derivative to allow solubility
    - Caused histamine release

Alfaxalone - many beneficial properties as an anaesthetic

- It is potent. It has a wide safety margin. It is rapidly metabolised.
- Work on cyclodextrins started to highlight a new way to solubilize lipophilic compounds in the mid 1990s
- In Alfaxan, the alfaxalone molecule is solubilised in cyclodextrin. Cyclodextrins are round complex sugars derived from starch.
- Lipophilic (fat soluble) drugs like alfaxalone can be hidden inside to allow the complex to be dissolved in water.

Pharmacokinetics

- Alfaxalone is rapidly and consistently cleared, as the metabolic pathways are the same as those used for metabolism of endogenous steroids.
- Cats and dogs do produce different metabolites, however accumulation of drug does not appear to occur with repeated dosing to maintain clinical anaesthesia in either species.

Pharmacodynamics

- Duration of anaesthesia after full induction dose
- Unpremedicated Dogs (~10 min)
- Unpremedicated Cats (~25 min)
- Cardiovascular and respiratory function is well maintained
- Rapid and smooth induction
- Appropriate muscle relaxation
- Short recovery times even when used as CRI
- Not cumulative in tissues after repeated doses
- Dose-dependent cardiopulmonary depression

Usage tips

- Best administered slowly IV over 60 seconds
  - Decreases the risk of apnea and allows the patient to choose the dose required for induction
- Not analgesic
  - Ensure to address pain
- Rapidly cleared
  - Can result in very rapid / uncontrolled recoveries if not well premedicated
- Minimize stimulation during recovery. Keep the recovery area quiet.

Alfaxalone – Propofol similarities

- Smooth and rapid induction and recovery
- Apnea as most prominent effect at higher doses
- Short duration of action
- Good muscle relaxation
- Wider margin of safety
- IM Injection Option

Buprenorphine – optimized options

- Simbadol – 24 hours FDA Approved for Cats
- Unique Profile in Cats
- Unique Physiology, Pharmacology of Higher Dose
- Excess Substrate Delays Elimination of Active Drug
- Once Daily Surgical Pain Control
Buprenorphine-SR
- aqueous polymer vehicle compounded product, lack of evidence, concerns limit use

Recuvyra – extended release transdermal fentanyl
Exposure concerns
- Precautions
  - Application
  - Supervision
  - Protection

Analgesia – long duration, for dogs only
- Mild sedation or euphoria
  - infrequent dysphoria
- Reduced food intake

Cerenia® (maropitant citrate)
An antiemetic therapy for the prevention and treatment of acute vomiting in dogs, and for the prevention of vomiting due to motion sickness in dogs. Oral, or by SC (stings), or IV injection.
- Greatly improves return to spontaneous feeding following opioids!
- Value added for many clients.
What to Worry About: Anesthetic Emergencies and Crisis Management
Ralph Harvey, DVM, MS, DACVAA
University of Tennessee
Knoxville, TN

Things can go wrong!
Anesthesia is intended to be a controlled, benign, and reversible process. Unfortunately, anesthetic drugs produce their effects primarily by limited depression of vital processes. The inherent dangers of anesthesia and the debilitation of injuries and illness that require anesthesia and surgery predispose the patient to risks of serious complications and emergencies. Most anesthetic complications and emergencies can be related to human errors, equipment problems, ventilatory problems, or circulatory problems. Most anesthetic emergencies and complications can be prevented or adequately managed.

Human error
Human error is ultimately responsible for the majority of problems encountered with anesthetic management. The importance of vigilance in anesthetic care cannot be overemphasized. It has been noted that hundreds of errors are made due to not looking for every one error made due to not knowing.

It should be recognized that there is a significant degree of safety with familiarity. Errors are more common when the anesthetist is not familiar with either the drugs or equipment being used. Miscalculation of anesthetic drug doses is a common error. The narrow therapeutic index of most anesthetic drugs makes correct dose determination or titration crucial. An absolute or relative overdose of anesthetic can cause every problem from minor excess physiologic depression to death.

An overdose with barbiturates should be managed with physiologic support of ventilation, continuous monitoring of cardiopulmonary function, and IV fluid therapy to speed recovery and improve cardiopulmonary function. In the context of cumulative overdoses from repeated injections of barbiturates to prolong anesthesia, the intravenous administration of bicarbonate at 0.5 to 1.0 mEq/kg can speed recovery from barbiturate overdose by favoring elimination. The non-specific stimulant-antagonist drug, doxapram, can be dangerous in treating depression due to barbiturate overdose. This stimulant can result in very deleterious stress and should not substitute for good care and proper dosing of anesthetics. Overdoses with other anesthetics are also managed with supportive care which is often adequate in mild to moderate overdose situations.

Fortunately there are specific antagonist drugs available to counteract the effects of some anesthetic drugs. For narcotics, the pure antagonist agent, naloxone, will reverse effects of an overdose. With a large overdose or a long lasting narcotic, renarcotization can occur with a return to the effects of the narcotic agent. For the tranquilizer/sedatives xylazine and dexmedetomidine, and other alpha-2 agonists, there are specific antagonists available. One of these, yohimbine, was approved for use in dogs years ago to reverse the effects of xylazine. Atipamezole is a better antagonist for dexmedetomidine and is often effective by titration of reduced doses (approved for SC administration) to secure prompt recovery with less excitement and stress than would result from the administration of a higher dose.

Non-specific partial reversal of anesthetic depression is possible by administration of the respiratory stimulant doxapram, but this is usually not an appropriate replacement for positive pressure ventilation and other supportive care. Although the net effect can be life saving, non-specific reversal has been associated with residual undesirable effects related to CNS stimulation and even deaths! Other stimulants have been advocated to correct excessive effects of various anesthetics but the benefits are usually very limited.

Anesthetics administered by an incorrect route can have very adverse effects. The extravascular injection of barbiturates can cause severe irritation and sloughing of surrounding tissue. Extravasation should be treated immediately with generous infiltration of the site with lidocaine and saline, followed by warm compresses. Errors in the administration of anesthetics also include the misidentification of drugs and accidental use of the wrong medication.

Equipment problems
Among the most serious anesthetic complications is the failure to deliver oxygen to the patient. This can be caused by respiratory obstruction or misused or defective anesthetic equipment. Empty tanks or misconnected gas lines and breathing circuits prevent the delivery of oxygen. Such problems must be recognized and corrected immediately. Empty anesthetic vaporizers, vaporizers filled with the wrong agent, or overfilled vaporizers are common problems. Delivery of nitrous oxide in combination with too little oxygen should be carefully avoided and is not always prevented by "fail-safe" systems incorporated in modern machines.

Kinked or plugged endotracheal tubes cause respiratory obstruction. Improper cuff inflation can result in obstruction, tracheal injury, or allow for aspiration pneumonitis. Improper placement of endotracheal tubes is very common, even in species that are easily intubated. Correct placement should always be verified.

An inability to adequately fill the rebreathing bag or to provide positive pressure ventilation by squeezing the bag often indicates major leaks or disconnections. These can result in a failure to deliver anesthetics and oxygen and substantially contribute to anesthetic
gas pollution of the veterinary hospital. Stuck valves in the anesthesia machine or circuit can cause difficulty in ventilation. Inappropriate rebreathing of exhaled gases or the accumulation of excessive pressure results. Patients that consistently seem to be too deep or too light may indicate that the vaporizer is out of calibration due to wear and tear, there is accumulation of deposits within the vaporizer, or other factors. These common problems emphasize the importance of regular inspection and maintenance of equipment.

Electrical problems with monitoring or supportive equipment risk injury to personnel as well as to patients. Inadequately grounded or protected equipment can cause electrical burns, electrocution, or fires. Unsafe or sub-standard equipment should be repaired or replaced.

Ventilatory complications
Hypoventilation due to anesthetic overdose is one of the most frequently encountered and serious complications in anesthesia. Inadequate breathing occurs with either relative or absolute overdoses of many anesthetics. Weakened, debilitated animals are more susceptible to the ventilatory depression which may occur secondary to circulatory depression and inadequate perfusion of CNS respiratory centers, electrolyte imbalances, muscle relaxant drugs, or thoracic injury. Support of ventilation requires endotracheal intubation and positive pressure breathing, preferably with oxygen. Identification and correction of the primary problem is then undertaken.

Hyperventilation is often due to inadequate anesthetic depth and represents an excessive response to surgical stimulation. It is important to rule out the possibility of carbon dioxide accumulation, due to exhausted absorber granules or improper connection of the breathing circuit, as the cause of hyperventilation. Panting can occur with narcotics and thereby decrease the effective ventilation. Most often this represents an inconvenience to the surgeon. A less common cause of panting is actual hyperthermia. Erratic or jerky breathing patterns also usually indicate improper anesthetic depth. As before, airway obstruction and various causes of carbon dioxide accumulation should be ruled out.

Palor and cyanosis
Palor of mucous membranes is a complex sign in that it may occur as a compensatory response to either excessively light or deep planes of anesthesia. Reduced cardiac output due to anesthetic depression or increased sympathetic tone due to pain can cause palor. It is important to identify the cause in order to appropriately treat the problem. Incorrect management may compound the problem and cause decompensation and immediate deterioration.

Cyanosis rarely occurs in anesthetized patients breathing oxygen. In order for cyanosis to develop, hemoglobin must be present in sufficient quantities and in the reduced (non-oxygenated) state. Hypoxemia that accompanies anemia therefore will not become evident through cyanosis. When cyanosis of either mucous membranes or blood in the operative field does occur, oxygen should be administered and adequate ventilation and pulse quality assured.

Bradycardia
Bradycardia is often favored as we more fully understand the benefits of extended diastole. This is particularly recognized with regard to alpha-2 agonist related relative bradycardia. Bradycardia in dogs is often associated with procedures or drugs that cause increases in vagal parasympathetic nervous system tone. Difficult endotracheal intubations, deep abdominal surgical procedures, intraocular surgeries, and some surgeries on the neck or in the thorax can all cause vagal-mediated bradycardia. Atropine or glycopyrrolate administration is effective in prevention of most vagal effects. Treatment after the vagal effects become evident is often less rewarding.

Non-vagal bradycardias may result from excessive anesthetic depth, hypoxia or hypothermia. Bradycardia can be a very serious sign of a significant anesthetic emergency. Administration of atropine and attention to possible causes is imperative.

Cardio-pulmonary arrest and cardio-pulmonary resuscitation
Every member of a veterinary hospital staff should be prepared to constructively contribute in an emergency resuscitation. Although not addressed here, CPR must be addressed in every hospital.

Hypotension
Hypotension is caused by either decreased cardiac output, increased capacitance of the vasculature, or inadequate blood volume. Intraoperative fluid therapy at 10 ml/kg/hr is often appropriate for replacement in many surgical patients but increased volumes can be necessary. Clinical evaluation to distinguish between hypovolemia and reduced cardiac output states as causes of hypotension can be based on patient history and evaluation, including central venous and arterial pressures.

Vasodilatation is a very common side effect of many anesthetic drugs. The tranquilizer acepromazine is a hypotensive drug, particularly at higher doses. The volatile anesthetics also cause significant vasodilatation. Most anesthetics also are potent cardiac depressants, again particularly at higher doses. Hypotension under anesthesia is therefore most appropriately managed by reduction of anesthetics and fluid administration as primary management.
Tachycardia
Heart rates above 180/min in dogs and 200/min in cats are associated with decreased efficiency and increased workload. Tachycardia can be due to fear, pain, inadequate anesthetic depth, pre-anesthetic excitement, or a rough induction of anesthesia. Hypotension causes a compensatory tachycardia. These causes of supra-ventricular tachycardia should be recognized and treated.

Compensatory tachycardia in response to hypovolemia and hypotension results in decreased coronary artery blood flow and increased myocardial workload. If other conditions contribute to hypoxia there is significant risk of development of more serious arrhythmias. Fluid therapy for hypovolemia, adjustment of anesthetic plane, and support measures to avoid cardiovascular deterioration are necessary.

Ventricular tachycardias are a much more serious emergency. An occasional ventricular ectopic beat is cause for concern but not necessarily indicative of patient distress. When ventricular arrhythmias become frequent or progress to ventricular tachycardia, immediate treatment is required. Ventricular arrhythmias indicate an irritated, hypoxic, or diseased myocardium.

Ventricular tachycardia should be treated with intravenous bolus injection of 2% lidocaine at a dose of 1, 2, or 3 cc in small, medium, or large size dogs respectively. This rule-of-thumb will allow for immediate therapy without an accurate dose calculation which could contribute to a life-threatening delay. It has been recommended that propranolol is the drug of choice for treating ventricular arrhythmias in cats. Lidocaine is also effective in cats. Total dose limitation is more important in cats due to their smaller body size and blood volume.

Success in emergency management of ventricular arrhythmias is evaluated by continuous ECG monitoring. Bolus injections of lidocaine can be repeated to a total accumulated dose of about 10 mg/kg without significant risk of overdose. When two or three injections are required over a period of 15-20 minutes it is necessary to convert to a continuous IV infusion of lidocaine at 30-80 micrograms/kg/min. Refractory arrhythmias may require conversion to therapy based on alternative antiarrhythmic medication.

Delayed recovery
Delayed recovery from anesthesia is managed by recognition of differential causes and a rule-out of individual possibilities. A systematic approach to potential causes will provide for balanced care with correction of often multiple factors such as hypothermia, inadequate fluid support, reduced metabolism or clearance of drugs, and debilitation associated with the stress of anesthesia and surgical trauma. Deterioration due to a hypoxic episode must be considered.

Hypothermia
Hypothermia is among the most common of anesthetic complications. Body heat is lost with preparation of the surgical site, contact with cool surfaces such as surgical tables, breathing of dry anesthetic gases, and evaporation from the airways and the surgical field. Moderate hypothermia is a frequent problem even with attention to each of these factors. Body temperatures down to approximately 92 F increase oxygen and energy requirements during recovery, but most patients can tolerate this level of hypothermia. More extreme hypothermia causes delayed recovery, reduces tissue perfusion, and increases morbidity and mortality.

The risks of thermal injury are so great with older styles of consumer style electric heating pads that their use in anesthetized, sedated, or depressed (many critically ill) patients is considered extremely hazardous. A very different dispersed field or amorphous resistance electrical heating blanket is now available from at least two sources. These new dispersed field resistance electric heating systems are very effective and can be much less costly to use. Warm water bottles or surgical gloves filled with warm water have been shown to be rather ineffective in raising the body temperature of hypothermic patients and at the same time constitute a significant risk of causing thermal burns at the site of contact. Circulating warm water blankets are a much better alternative to warm water bottles or gloves, but these are of limited efficacy in rewarming hypothermic patients. Forced warm air heating systems are more effective than circulating warm water blankets and can also be used to cool hyperthermic patients when set to deliver unheated ambient air. Proper use of forced air systems must include some type of dispersive blankets to envelop the patient in warmed air and avoid hot spots by distributing the warmed air. The disposable blankets and the high consumption of electricity both increase the cost of use of the forced warm air systems. All warming systems must be used carefully in order to avoid or minimize the risks of overheating or burning patients.

Other complications
Many other complications and emergencies can occur during or be associated with anesthesia. These include anaphylactic-like reactions, hyperthermia, biochemical imbalances, gastroesophageal reflux, regurgitation, vomiting, aspiration, and many surgical complications such as hemorrhage and pneumothorax. Avoidance of complications and effective management of emergencies requires continued vigilance and immediate appropriate action.