# HOW SAFE IS ANESTHESIA FOR DOGS AND CATS?

## Introduction

"What are the risks of anesthesia in dogs and cats today?" – This was a question that until recently we did not have an accurate answer to. The data generated by the Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF), a prospective cohort study conducted in the United Kingdom is the most comprehensive information we have available. This study recorded patient outcome (alive, dead, euthanized) after pre-medication and within 48 hours of the end of the procedure and calculated species specific (cat, dog, rabbit and "other small animals") risks of anesthetic related death. Anesthetic or sedation related death was defined as "death where surgical or pre-existing medical causes did not solely cause death". This study has generated risk factors for the different species and paves the way for improving anesthetic related mortality in small animal practice. [1-4]

## Mortality risks

The study included 98,036 dogs and 79,178 cats. The *overall* risk in dogs was 0.17% and 0.24% in cats. In *healthy* dogs and cats the risks were 0.5% and 0.11% respectively. In *sick* dogs and cats the risks were 1.33% and 1.40% respectively (Table 1). "Healthy" [ASA I and 2] and "sick" [ASA 3-5] classifications were based in the American Society of Anesthesiologist's [ASA] classification; (http://www.asahq.org/clinical/physicalstatus.htm).

In both cats and dogs performing a major versus a minor procedure and prolonging the procedure led to an increase in mortality.

The risks for general anesthesia and sedation alone were compared. Although there were fewer sedation only cases in the study and no form conclusions can be made, it appears that there is less risk of death with sedation alone compared to anesthesia.

The risk of anesthetic related death have decreased since the last comparable survey in the mid-1980s but these numbers compare poorly to data for humans where the anesthetic related death rate is reported to be between 0.02 and 0.005%. Differences in the standards of anesthesia including training of those administering anesthesia, and having a person dedicated to anesthesia alone are likely the reason between the human and animal data, more than species differences alone.

## When do most deaths occur?

Analysis of the results reveals that most deaths occur post-operatively; 47% of deaths in dogs occur during this time and in cats the figure is 61% and in rabbits 64%. The most critical time appears to be in the *first three hours* after the end of anesthesia (Figure 1 and 2)

**What are the causes of death?**

An independent review panel reviewed details of each anesthetic death and tried to ascertain a cause. Cardiovascular or respiratory causes accounted for 74% and 72% of deaths in dogs and cats respectively. As in human anesthetic related deaths, human error plays a role. For example two dogs died after the pressure relief valve was left closed.

**Dogs**

Risk factors in dogs have been identified [2]. Dogs with lower body weights (< 5kg) are at increased risk of anesthetic related deaths (8 times more likely to die than dogs that weigh between 5 and 15kg) and this may a result of hypothermia as is suggested for the cat (see below).

Senior dogs (> 12 years) are at a significantly higher risk (7 times more likely to die than dogs in the 6 month to 8 year old range) and special attention must be paid to this population, including careful pre-anesthetic work-up.

Mask induction of anesthesia was found to significantly increase mortality (a 5.9 fold increase in risk compared to induction with an injectable agent followed by isoflurane) and must be discouraged; use of premedication followed by induction of anesthesia with injectable drugs is encouraged. Inhalant agents are the most cardiovascular and respiratory depressant anesthetic agents we use and “MAC” sparing techniques are encouraged – including premedication and intra-operative infusions of opioids, lidocaine and ketamine. There was insufficient data to compare Sevoflurane and isoflurane, but it was clear that the use of halothane increased the risks of dying compared to isoflurane.

**Cats**

The risk for cats is significantly higher than for dogs [1]. In cats respiratory obstruction as a cause of death was reported more frequently in cats indicating that close attention to the airway in this species is important; the propensity of cats to have laryngospasm may play a role.

The smaller size of cats may predispose them to hypothermia and the associated complications of this including shivering and increased oxygen consumption in the recovery period, slower metabolism of drugs and catecholamine release leading to cardiac complications. The small size of cats may also lead to more problems with intravenous catheter placement, intubation and monitoring. If cats are not accurately weighed, it is likely that relative drug overdoses occur.
Cats that weigh less than 2 kg are high risk cases (odds ratio of 15.7 – i.e. over 15 times more likely to die than cats weighing between 2-6 kg).

Obese cats were also at risk, perhaps this is related to a greater risk for respiratory compromise (reduced diaphragmatic excursions due to abdominal and thoracic fat, especially when placed in

dorsal recumbency) and reduced cardiovascular reserves (an increase in cardiac output is required as body fat increases).
As with dogs, older patients carry a higher anesthetic risk – cats older than 12 years are twice as likely to die compared to cats aged 6 months to 5years.

Unlike dogs, no specific anesthetic drug was implicated to contribute to mortality on cats.
The use of a pulse oximeter is strongly recommended in cats – use of this monitor reduced mortality significantly – likely because it alerted staff to a cardiovascular or oxygenation problem.

**Take home lessons**

Animals with a higher ASA status are more at risk therefore careful attention to choice of anesthetic techniques, monitoring and post-anesthetic care are especially important in the patient population. An increase in duration of the procedure contributes to mortality therefore every effort should be made to ensure procedures are done as quickly as possible and no "wasted" anesthesia time occurs because of poor scheduling or planning. When possible diagnostic (e.g. imaging, endoscopy) and surgical procedures should be performed separately. Because most deaths occur in the first three hours after the end of a procedure, the recovery area should be well staffed and animals should be continued to be monitored. More attention should be given to patient monitoring and support during this time, including providing warmth, fluids, maintaining a patent airway and providing pain relief. Having a person dedicated to the anesthetic needs of the animal and specialized training of this person reduces anesthetic mortality. When possible techniques that involve sedation with local anesthesia should be explored since the risks of sedation may be lower than general anesthesia.

Although anesthetic related mortality has decreased over the past 2 decades, there is still room for improvement and some key factors to focus on have been identified by the CEPSAF study.

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Table 1.

| | DOG Mortality rate | % | CAT Mortality rate | % |
|---|---|---|---|---|
| **OVERALL** | **1/601** | **0.17** | **1/419** | **0.24** |
| **HEALTHY ASA 1-2** | **1/1849** | **0.054** | **1/895** | **0.112** |
| **SICK ASA 3-5** | **1/75** | **1.33** | **1/71** | **1.4** |

Figure 1.

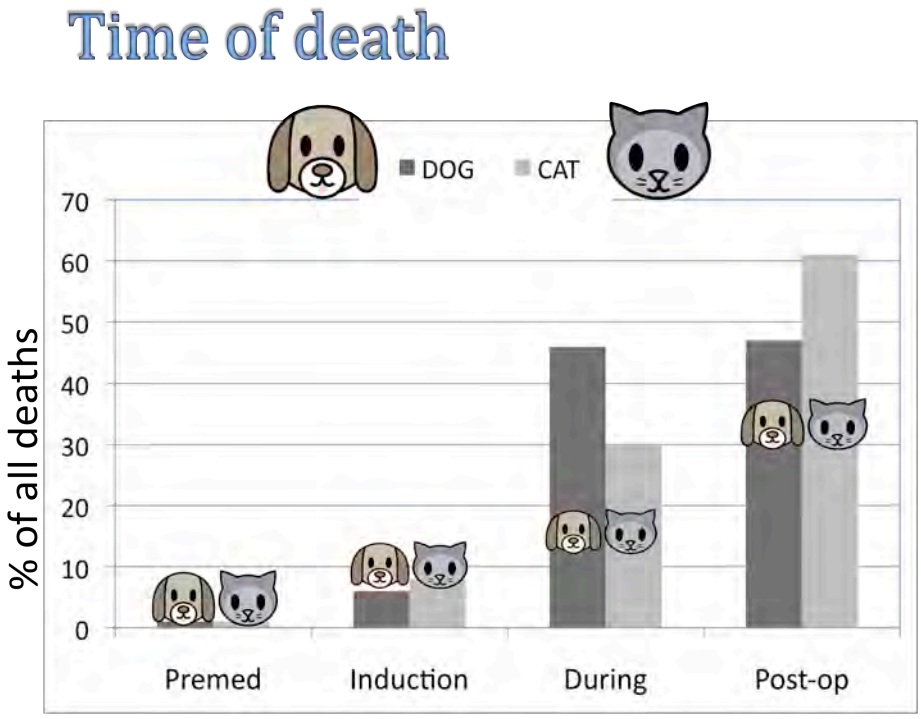
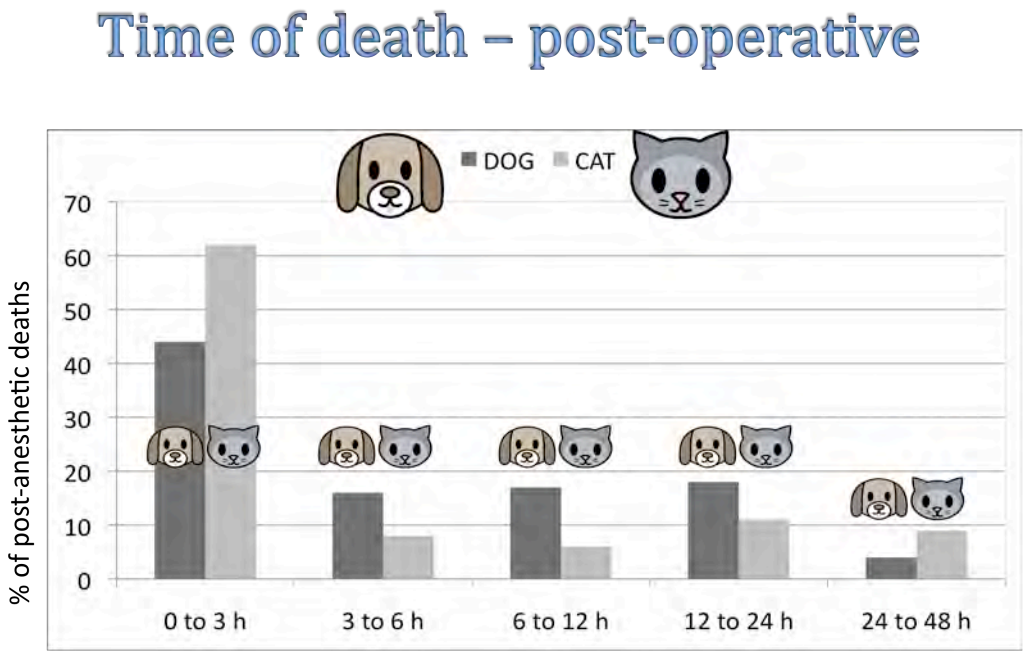


Figure 2.


Time of death – post-operative
DOG
CAT
% of post-anesthetic deaths
70
60
50
40
30
20
10
0
0 to 3 h
3 to 6 h
6 to 12 h
12 to 24 h
24 to 48 h

# THE 'BIG CHILL': WHY IS HYPOTHERMIA BAD AND WHAT TO DO ABOUT IT

## Introduction

Dogs and cats commonly lose heat when anesthetized. Maintaining body temperature within a narrow range is important for cardiac function, metabolism, normal enzyme activity, nerve conduction, and hemostasis. Several recent publications have reported that small patients for example cats that weigh less than 2 kg were 15 times more likely to die than cats weighing between 2-6 kg) and that old patients and those undergoing long procedures are also at a greatly increased risk of dying [1-3]. The negative impact of hypothermia is greatly underestimated and may be a contributing factor in anesthetic related deaths. These studies also reveal that intra-operative temperatures are rarely monitored.

## Thermal balance

Homeothermy, a balance between heat loss and heat gain involves complex sensing mechanisms that drive the mechanisms controlling heat loss or gain in the correct direction. Heat gains can be obligatory or facultative. Obligatory gains occur independently of thermoregulation and include heat from basal metabolism, eating and exercise. Facultative gains act to restore thermal balance and the most important source is from shivering. Three-quarters of heat loss occurs from the body surface and the remainder is lost from the respiratory tract. Losses occur through convection (transfer of heat from the animal to the air), conduction (transfer of heat from the animal to a surface that is cooler), evaporation (heat dissipated by evaporation of moisture from wet skin or the respiratory tract) and radiation (exchange of heat between the body and objects in the environment). Temperature sensors exist centrally (hypothalamus, spinal cord, brain stem, abdominal organs and skeletal muscles) and peripherally (warm and cold receptors in the skin). The hypothalamus acts by integrating thermal input and controlling effector organs; in many ways acting as a thermostat.

## Anaesthesia and thermoregulation

When an animal is anesthetized many factors interrupt normal thermoregulation. Anesthesia abolishes behavioral responses (the animal cannot seek out a warm environment), reduces metabolic rate, alters hypothalamic function, reduces muscle tone and effector responses (shivering). In addition operating room environments and surgical procedures impose large thermal stresses on patients.

In the conscious mammal body temperature rarely fluctuates more than ± 0.2 Celsius because the animal responds to minor changes. Under general anesthesia there is wider range of core temperature where the animal does not respond to maintain normothermia – often no response is mounted until body temperature has dropped by 2.5 Celsius. Vasoconstriction can occur in anesthetized patients and although it may slow down the rate of heat loss it has a negative effect

on tissue perfusion and is usually a late response. This reflex will be also be counteracted if vasodilating agents such as acetylpromazine or isoflurane and sevoflurane are used.
The greatest rate of heat loss is immediately after induction and during the first 20 minutes of anesthesia due to redistribution of heat from the core to periphery (figure 1). However it is important to note that heat loss begins immediately after premedication because sedatives and tranquillizers will depress the hypothalamus. This is a time that we can initiate intervention by keeping the animals that are waiting for anesthesia warm – so called “pre-induction warming”. Heat continues to be lost after the initial steep drop but at a lower rate. There is also an increase in the difference between core (esophageal) and peripheral (rectal) temperature over time. The smaller the animal the greater its body surface area: weight ratio and the more prone it is to hypothermia. When no attempt was made to preserve body heat, dogs and cats weighing < 10 kg dropped below their normal temperature by 3.4$^{o}$C after one hour of anesthesia [4]. The severity of hypothermia is also influenced by the environmental temperature, duration of anesthesia, and exposure of body cavities.

**Measuring temperature**

Ideally core temperature should be monitored with a probe placed in the esophagus or on the tympanic membrane. Rectal temperature reflects the peripheral temperature and this lags behind core temperature changes, giving a falsely high estimate of the animal’s true body temperature.

**Negative impact of hypothermia**

A drop in core temperature to 34$^{o}$C is cause for concern. As core temperature falls, the myocardium becomes more irritable and the sino-atrial node beats more slowly. This is in part associated with increases in circulating catecholamines. There is a drop in cardiac output and blood pressure and at subnormal temperatures, atropine and glycopyrrolate are unlikely to correct bradycardia. Changes in cardiac rhythm may be noted and at temperatures approaching 32.2$^{o}$C asystole or fibrillation may occur.

Fluid shifts result in hemoconcentration, increased blood viscosity and red blood cell sludging. Increased bleeding occurs secondary to prolonged coagulation times and altered platelet function. Tissue perfusion is impaired by hypothermia and shifting of the oxyhemoglobin curve to the left decreases oxygen unloading. This may partially be counteracted for by the developing metabolic acidosis. Lactate levels rise secondary to poor perfusion and decreased hepatic metabolism. Blood glucose levels may rise and complicate interpretation of laboratory results.

Metabolism is slowed and liver function is impaired, delaying breakdown of anesthetic drugs which delays recovery. The requirements for inhalant agents drop and if anesthetic depth is not closely monitored, animals will receive a relative overdose. As a patient cools, the amount of anesthetic required to produce apnea decreases and responses to hypercapnia and hypoxia are blunted.
In human studies, intra-operative hypothermia has been linked to increased post-operative wound infection. This is a result of poor perfusion to the periphery, vasoconstriction and low oxygen tension at the surgical site. Hypothermia also impairs immune function, including the killing ability

of neutrophils. One veterinary study linked wound infection to duration of surgery [5] when animals tend to become colder and there is no doubt that maintaining normothermia is in the best interests of the patient.

Cold animals take longer to recover, shiver and look miserable. Shivering increases their metabolic rate and heat production, but also increases oxygen demand. This, combined with a decreased ventilatory drive can lead to hypoxemia. Pain from the surgical incision is likely to be worse when an animal shivers.

**Techniques for maintaining body temperature**

Thermal losses should be minimized. Although re-warming is possible in the post-operative period, rapid re-warming can cause vasodilation, which is not well tolerated by some surgical patients. Suggestions for preventing hypothermia:

- Pre-warm patients by using forced warm air units and blankets after premedication.
- Surgical preparation – avoid cold solutions especially alcohol. Warm sterile saline is a good choice.
- Anesthesia time should be kept to a minimum
- Ambient temperature – Normal operating room temperatures are often 24-26$^{o}$C. Warmer temperatures would benefit the patients but may increase discomfort for personnel. The induction and recovery areas should be kept warm.
- Warm inspired gases – this requires specialized anesthetic equipment. If a circle system is used, low flow anesthesia minimizes heat loss from the respiratory tract.
- Circulating warm water blankets are effective in small patients [6] and are more effective when placed on the limbs than on or under the trunk [7]. Electric blankets must be avoided as severe skin burns can occur in hypothermic animals.
- Forced warm air devices are effective [8].
- Blankets – fleece blankets and thermal insulating blankets can minimize radiation and convective losses. New technology using blankets made of thermal conductive materials show promise.
- Infra-red lamps – great care should be used when using these as skin burns can occur.
- Warm intravenous fluids – when large volumes of fluid are given to patients they should be warmed to minimize thermal stress.

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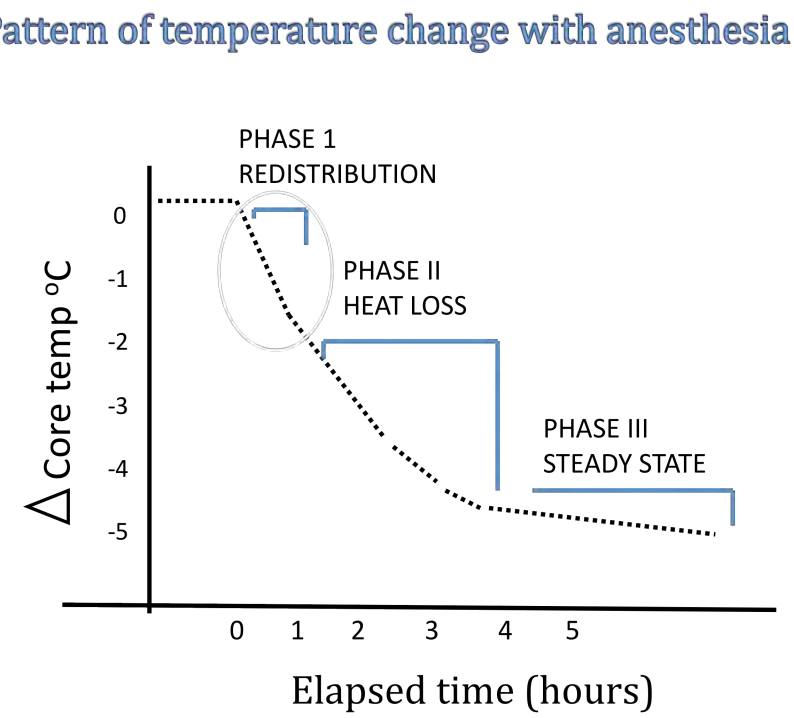
Figure 1.



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# THE USE OF NSAIDS IN CATS

## Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used both on a short term and long term basis for the alleviation of pain in many species including humans. However, the use of this category of drug in the cat remains controversial and widely debated. There is information on the pharmacology, disposition, efficacy and adverse effects of both approved and non-approved NSAIDS (Table 1) in cats [1]. NSAIDs have also been used as anti-neoplastic agents because cyclooxygenase-2 (COX-2) is over expressed in many tumors, but perhaps less so in the cat [1]. Piroxicam has been used for this purpose in the cat and although the side-effects of this drug have been well described its anti-cancer efficacy has not [2].

## NSAID use in cats

There is a considerable body of data on the short term use of NSAIDs in cats and several are approved (approval varies between countries) and used with excellent success in the perioperative period [1, 3]. NSAIDs have the advantage of being non-scheduled drugs and have a relatively long duration of action; usually 18-24 hours. Many are either available in an injectable formulation or as a palatable oral liquid or tablet formulation which simplifies administration in cats. Until recently, meloxicam (injection) was the only approved NSAID for use in cats in the USA and this is as a single dose for the control of post-operative pain and inflammation associated with orthopedic surgery, ovariohysterectomy and castration. In March 2011 robenacoxib was approved by the FDA for use in cats. It is approved for the control of post-operative pain associated with inflammation related to orthopedic surgery, ovariohysterectomy and castration, and can be given for a maximum of three days. This is the first coxib class of drug approved for cats. At clinical doses COX-1 inhibition is minimal and short lasting. Robenacoxib has a unique pharmacokinetic profile, with a short half-life but long residence time in target (inflamed) tissues [4, 5].

Clinical conditions likely to result in long-term pain and discomfort in cats include interstitial cystitis, neoplasia, dermatologic diseases, dental and oral diseases and degenerative joint disease (DJD). There is a growing awareness of DJD in cats [6, 7] and it is likely that this affects a large percentage of the feline population and is an important welfare issue. Decreased mobility (especially the ability and willingness to jump up and/or down), activity, grooming and changes in temperament are the most commonly reported clinical signs [8, 9]. Since degenerative joint disease is not curable, the focus of the treatment plan is relief of pain. This disease is likely the most common disease in cats in which NSAIDs are used long-term. This class of drug is the first line of treatment of arthritis in most species including humans and are very effective. The use of NSAIDs, especially for extended periods of time, has not always been widely or enthusiastically embraced in cats because of fears of toxicity. However, it is becoming clear that this group of drugs will play an important role in the relief of chronic (maladaptive) pain in this species. In some parts of the world, meloxicam is now approved for indefinite use in cats for the alleviation of inflammation and pain associated with chronic musculoskeletal disorders (0.1 mg/kg on day one followed by 0.05 mg/kg orally once daily†). NOTE: this is currently an off label use of the drug in the United States. Although not

currently approved for long-term use, the freedom of information summary for robenacoxib (available at http://www.fda.gov) contains encouraging safety information when it was administered to cats for 6 months.

It should be noted that we have considerably less experience with chronic use of NSAIDs in cats than we do in other species. For this reason and because of diverse opinions and conflicting information, the International Society of Feline Medicine (ISFM) and the American Association of Feline Practitioners (AAFP) published a set of guidelines for the Long-Term use of NSAIDs in cats [10]. These guidelines aim to promote the effective and safe use of NSAIDs in this species. The guidelines cover common causes of chronic pain in cats, why NSAIDs can have many positive and potentially negative actions, patient selection, techniques for promoting owner and cat compliance, dosing recommendations, concurrent conditions which may make a patient a "higher risk" candidate for NSAID therapy, and they also discuss pre-treatment screening and monitoring for adverse effects during therapy. The guidelines can be downloaded at the ISFM and AAFP websites.

Many of the concerns about the use of NSAIDs relate to the cat's unique metabolism; the relative deficiency of glucuronyl transferase enzymes in this species may lead to a prolonged half-life for some drugs, however some NSAIDs including meloxicam, piroxicam and robenacoxib are cleared by oxidative enzymes and do not appear to have prolonged half-lives in cats [1, 4]. (Table 2)

Several clinical studies report marked improvement in cats diagnosed with DJD after therapeutic intervention with an NSAID [8, 11, 12]. In a prospective study, [11] most cats improved within one month of NSAID intervention; 61% showed a marked improvement, 14% a moderate improvement and 25% a slight improvement. In a study of 40 cats over a 5.8 month period 85% of owners scored the efficacy of NSAID treatment as good or excellent; in this study the dose of meloxicam was 0.01-0.03mg/kg once daily [12]. There are anecdotal reports of long term use of other NSAIDs such as ketoprofen and aspirin in cats, however there are no published reports and as this is an "off label" or unapproved use, there is no pharmacovigilance data and therefore the incidence of adverse drug effects is unknown.

For long term use, a drug should be highly palatable and voluntarily taken by the cat – for example in food or as a treat. Meloxicam liquid is considered highly palatable in cats [12, 13] as is robenacoxib which is available as a flavored tablet. If other NSAIDs are chosen by the practitioner they may require compounding to improve acceptability by cats; in this case it is important to be informed of all regulations and implications related to this [14]. The owner must be consistent and remember to administer the drug and based on the long duration of action of many NSAIDs in cats, this should be at a set time on the chosen treatment days. Creative reminder systems may be needed to ensure that cats do receive medication on the correct day(s), time(s) and at the correct dose. Timing of medication, a concept termed chronotherapy [15] is often overlooked in veterinary medicine. Theoretically long-term dosing may result in a "steady-state", however "peaks and troughs" may still occur. Timing of medication may depend on a cat's lifestyle; for example if the peak effect on joint pain occurs 5 hours after dosing, treatment may be tailored so that the cat has the maximum clinical effect when it is most active. Alternatively an owner may find that at "peak

effect" the cat is more comfortable, it rests for longer periods of time and may choose to administer the drug to promote sleeping at the most suitable time. It is suggested that NSAIDs only be administered with food or after the cat has eaten because inappetence may be an early sign of an adverse drug side effect.

Due to individual variation in metabolism and responses to drugs, it is unlikely that a set dose and dosing interval of an NSAID will work equally well for all cats. The level of pain related to chronic diseases is likely to fluctuate so that a cat's needs may increase or decrease over time. To avoid potential side-effects, owners should be encouraged to find the lowest effective dose [LED] that works for their cat, with the understanding that this may change over time. This dose will often be less than the currently published, recommended or labeled dose [12].

There is no validated assessment tool for chronic feline pain. However in addition to monitoring safety of long-term NSAID use we must also monitor efficacy. In studies that have looked at the efficacy of NSAIDs in cats with musculoskeletal pain, an improvement in mobility, and in particular the willingness to jump and the height of the jump have been the most obvious signs of a positive response [11, 12]. When treating animals with long-term diseases, an overall assessment of Quality of Life is needed; this includes but is not limited to pain. An assessment tool may need to be individually designed since what is important to each cat and their owner will be different (can the cat jump up to its favorite spot in the window, play with other pets or people in the household, etc). The owner is the best person to judge and track the cat's behavior and attitude. Since the long-term use of NSAIDs in cats in the United States is currently "off label" it is important to discuss the "pros and cons" of treatment with the owner and obtain their consent. Veterinarians must also be familiar with the Animal Medical Drug use Clarification Act and the extralabel drug use algorithm including record and label requirements. (http://www.avma.org/reference/amduca/amduca1.asp).

Adverse Drug Effects (ADEs) related to NSAID use most commonly affect the gastrointestinal system, liver, kidneys and platelet function. Lessons learned from the long-term use of NSAIDs in dogs suggest that this class of drug is often used inappropriately and without screening and monitoring [16].

Absolute contraindications to NSAID use are 1) in combination with another NSAID or corticosteroid, 2) in a dehydrated or hypovolemic cat, and 3) in a cat with preexisting gastrointestinal ulceration. Under conditions of hypovolemia or hypotension (e.g. vomiting, diarrhea, anesthesia) renal perfusion drops and the kidney compensates for this by releasing vasodilatory prostaglandins which maintain renal blood flow and glomerular filtration rate. If an NSAID has been given, this autoregulation is inhibited and resultant renal damage is a concern. The true incidence of ADEs related to long-term dosing of NSAIDs in cats is unknown but the most commonly reported side-effect of oral meloxicam is gastrointestinal upset. In a month long study18% of cats showed intermittent signs of gastrointestinal upset (vomiting and or diarrhea), but signs were not severe enough to terminate treatment in any cat [11]. In the largest clinical study to date [12] 4 out of 46 cats vomited during meloxicam treatment and 2 of these cats were withdrawn from the study. The most common adverse effect associated with piroxicam in cats with neoplasia was vomiting [2].

There is no accepted “best protocol” for screening and monitoring cats on long-term NSAID therapy. Before embarking on treatment, laboratory testing focusing on the renal and hepatic system, total plasma protein, albumin and a hematocrit is recommended to identify potential problems and establish a baseline for later comparison [10]. Abnormalities in laboratory tests do not necessarily preclude the use of NSAIDs, but the risks and benefits of embarking on therapy must be discussed with the owner. In dogs, most ADEs related to NSAID use occurs between 14 and 30 (range 3-90) days after the start of treatment [17] therefore screening before use, and then at 2 to 4 weeks is logical. The question of how often to screen after this will depend on factors such as the overall health of the cat, cost and convenience.

Chronic drug therapy can induce liver enzymes. A three- to four fold increase in hepatic enzyme values from baseline may indicate hepatotoxicity. Two courses of action could be taken;

1. The drug could be discontinued and if values return to baseline a link between treatment and hepatic impairment is likely.
2. More specific liver function tests such as bile acid assays can be performed.

A decrease in hematocrit and an increase in BUN suggest gastrointestinal bleeding, but any change in BUN warrants measurement of creatinine and urine specific gravity to assess renal function.

Educating owners about the signs of early problems is vital to preventing problems. Clients should be advised to stop administering the NSAID and to call their veterinarian if they notice any changes in their cat, such as inappetence, vomiting, diarrhea, lethargy, or bloody feces. The decision to stop or continue NSAID treatment would depend on further consultation and diagnostic tests. The key is to catch problems early and err on the side of caution. All adverse drug events should be reported to the relevant pharmaceutical company or regulatory board so that we can learn more.

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**Footnote**

† Metacam European package insert, Metacam (Meloxicam) 0.5 mg/ml oral suspension for cats.

**Table 1.** NSAIDs used for the control of acute and chronic pain in cats

| **No market authorization** | **Market authorization*** |
|---|---|
| Aspirin | Carprofen |
| Flunixin | Ketoprofen |
| Phenylbutazone | Meloxicam |
| Piroxicam | Robenacoxib |
| Vedaprofen | Tolfenamic acid |

*Indications and duration of use varies between drugs and countries.

**Table 2.** Half-life and clearance mechanisms of selected NSAIDs in cats.

G = Glucuronidation, T = Thioesterification O = Oxidation

| **NSAID** | **½ Life (hours)** | **Clearance mechanism** |
|---|---|---|
| Carprofen | 20 | G, O |
| Ketoprofen | 1.5 | G, T |
| Meloxicam | 15 | O |
| Piroxicam | 12 | O |
| Robenacoxib | 1.1-1.7 | O |

Sheilah A Robertson - Delaware Valley Academy of Veterinary Medicine Meeting, April 2012

**HOW DO WE KNOW THEY HURT? ASSESSING PAIN IN DOGS AND CATS**

One of the main reasons for under treating pain in dogs and cats is the *difficulty in recognizing and "measuring" their pain.*

To treat pain we must first recognize it and quantify it in some way so we can assess the efficacy of our interventions. Pain is a complex multidimensional experience with both sensory and emotional components.

The sensory component includes:
1. What type of pain is it?
2. Where is it?
3. How intense is it?

The emotional component is "how does it make the animal *feel?"* Because animals, and some sub-populations of humans are non-verbal and cannot self-report (for example, neonates and cognitively impaired adults), the International Association for the Study of Pain (IASP) [a] added the following important caveat to its definition of pain: "The inability to communicate (verbally) in no way negates the possibility that an individual is experiencing pain and is in need of appropriate pain relieving treatment". Because animals lack language they also fall into this category and assessing their pain is challenging but can be achieved by observing behavior, postures and facial expressions.[1]

Pain is subjective and no one can "feel" another person's pain. Even after the same surgical procedure, humans who can self-report do not experience the same quality and intensity of pain so how can we determine with any degree of certainty what an animal feels? Put simply, in most humans, pain is what the patient says it is and in animals it is what we say it is. This puts an extra burden on us, and others that are advocates for non-verbal populations to "get it right". There is a consensus that animal pain does have an important emotional component but this is difficult to measure. [b]

There is no gold standard for assessing pain in animals at this time. Many different scoring methods that include physiologic and behavioural variables have been published, but few are validated. Systems must take into account different types and sources of pain, for example abdominal versus musculoskeletal or oral pain. As more studies focus on species-specific pain behaviours our ability to recognize and treat pain in animals will improve but at present the assessment of pain in animals, including dogs and cats is subjective and likely inaccurate.

The correlations between pain and easily measured physiologic (objective) variables such as heart rate, respiratory rate, and blood pressure, have been disappointing.[2-4] In cats, no study found a consistently reliable objective measure, which is not surprising since these parameters can be affected by many factors other than pain. Cats and dogs suffer from "white coat" syndrome just as humans do; for example fear and the stress of a journey to a veterinary hospital will alter heart rate

in most animals. Plasma cortisol and β-endorphins are components of the “stress response” to anaesthesia and surgery and much effort has gone into trying to correlate these hormones with pain in laboratory and clinical trials. In cats, plasma cortisol is unreliable as a direct indicator of pain.[4,5] Mechanical nociceptive threshold testing with devices such as palpometers has proved a useful technique for evaluating both primary (wound) and secondary (remote areas) hyperalgesia in dogs and cats. Changes in wound sensitivity do correlate with visual analogue scoring [6] suggesting that an assessment of wound tenderness should be incorporated into an overall assessment of post-operative pain.

All scoring systems that depend on human observers must by definition be subjective to some degree and leave room for error, which could be either under, or over assessment of the animal’s pain. Any system that is used must be valid, reliable and sensitive. Without strictly defined criteria and use of well-trained and experienced observers, many scoring systems are highly variable; one scoring system may show an analgesic agent to be effective yet another will show that same analgesic to be ineffective. These differences are inevitable if a system is insensitive and results in large inter-observer variability.

The most basic pain scales are simple descriptive scales (SDS). These usually have four or five descriptors to choose from; for example “no pain”, “mild”, “moderate”, “severe / very severe” pain. Although simple to use these scales are extremely subjective and do not detect small changes in pain. Numerical rating scales (NRS) are similar to simple descriptive scales but with numbers assigned for ease of tabulation and analyses; for example no pain could be assigned the number 0, and very severe pain the number 5. This system implies equal difference or weighting between each category, which is unlikely to be the case. A further development of these systems is a categorized numerical rating system where certain behaviours thought to be related to pain are chosen and assigned a value.[4]

In an attempt to improve on these discontinuous scales, the visual analogue scale (VAS) has been widely used in veterinary medicine. This tool consists of a continuous line, anchored at either end with a description of the limits of the scale, for example **no pain** at one end and **severe pain** at the other end. The observer places a mark vertically through the horizontal line that they think correlates to the animal they are observing and this is later translated into a number by measuring the distance of that mark from zero. These scales can be improved by adding a descriptor that says “worst possible pain for *this* procedure”, because the worst pain associated with an elective castration is likely to be different from the worst pain after a limb amputation. Holton and others [7] compared the use of a simple descriptive, numerical rating and visual analogue scales for assessing pain in dogs following surgery. They showed significant observer variability, which could be as high as 36%, with all three scales.

An extension of the classic VAS system is the dynamic and interactive visual analogue scale (DIVAS). With this system, the animals are first observed undisturbed and from a distance. The reason for this is that some animals do not display overt pain behaviours in the presence of a caregiver, but will when they think they are unobserved – this has been documented by the use of video cameras and is likely a protective mechanism against potential “predators”. After observing

form a distance the assessor approaches handles and encourages the patient to move around. Finally the surgical incision (or injured area) and surrounding area is gently palpated and a final overall assessment of pain is made. This approach overcomes some of the deficiencies of purely observational systems; for example a painful animal may remain very still and quiet *because* they are painful and this would go undetected without interaction with the animal. The DIVAS system has been used to assess postoperative pain in cats and dogs [8-10] and when performed by observers who were unaware of treatments they were able to detected differences between analgesics and between treated and untreated patients [8]. However there are situations where interaction is not possible, for example when working with feral animals.

It is now accepted that quantitative measurements of behaviour are the most reliable methods for assessing pain in animals and that if the methodology used to develop and validate these systems is rigorous they can be objective with minimal observer bias [11]. Multidimensional systems are particularly important when self-reporting is not possible. However they must incorporate components that have been proven as sensitive and specific indicators of pain in the species being studied. Knowledge of the normal behaviour for the individual being evaluated is important and deviations from normal behaviour may suggest pain, anxiety, fear or some combination of stressors. Normal behaviours should be maintained post-operatively if an animal is comfortable. Grooming is a normal behaviour but licking excessively at a wound or incision can be an indicator of pain, so the two should be differentiated. The occurrence of new behaviours such as a previously friendly animal becoming aggressive, or a playful and friendly animal becoming reclusive should raise our suspicion that pain may not have been adequately addressed.

Developing these systems is a daunting task; Fox et al [12] identified 166 possible pain behaviours associated with ovariohysterectomy in bitches. The importance of non-interactive (videotaped in absence of caregivers) and interactive behaviours has also been demonstrated [12,13]. In these studies dogs that had undergone surgery without analgesics spent more time sleeping than control animals, but also showed increased cage circling activity, lip licking and flank gazing. However, these activities would be easy to miss in a busy clinical setting. Although reduced after surgery (with and without analgesics), tail wagging and positive interactions still occurred in the presence of a caregiver and with a cursory examination the dog could easily be scored as “not painful.”

In dogs, the most vigorously tested composite acute pain scoring system is the Glasgow Composite Pain Assessment Scale [11] (see attached) which can be used with permission and downloaded at:
http://www.gla.ac.uk/schools/vet/smallanimalhospital/ourservices/painmanagement/
The categories for assessment included in this system are:

1. Posture
2. Comfort
3. Vocalization
4. Attention to the wound
5. Demeanour and response to people
6. Mobility

7. Response to touch

Each descriptor is well defined to avoid misinterpretation. Assessment involves both observation from a distance followed by interaction with the patient.

We are beginning to learn "what pain looks like" in our feline patient and there are some useful, albeit non-validated scales such as the Colorado State University cat scale (see attached) that certainly alert observers to individuals that require intervention. Brondani and colleagues [2] have recently developed a multidimensional composite scale for use in cats following ovariohysterectomy. This study suggests that the following are important criteria for use in assessing acute post-operative pain in cats: *posture, activity, mental status* – for example the cat is alert and interested in its surroundings and interacts with an observer versus a cat that is not interested in its surroundings, is aggressive and tries to bite or scratch the observer, *reaction to palpation of the wound*, *miscellaneous behaviours* including *eye position*, *tail activity* and *chewing and licking at the wound, appetite and vocalization*. These investigators also emphasise that it is necessary to record data preoperatively (baseline) for comparison.

**Behaviours and postures suggestive of acute pain in cats**

**Figure 1** shows a normal comfortable cat, note the facial expression and body posture in comparison to the other images. Cats that adopt a hunched posture, with their head down are likely experiencing pain **(Figure 2).** In one study detailed behavioral ethograms were constructed for cats before and after abdominal surgery; a hunched or tucked up posture was rarely recorded in cats before surgery but occurred on a frequent basis afterwards.[14] It has been suggested that assessment of facial expression may measure the emotional component of pain and could be a useful tool in animals.[1] Certainly there is evidence that pain may be expressed by the face in human neonates [15] and in mice.[16] The presence of half closed eyes ("squinty eyes") in cats may correlate with pain [2] **(Figure 3).** A cat sitting quietly in the back of the cage after surgery may be painful; however, pain would not be recognized if the caregiver expects to see more active signs of pain such as pacing, agitation, or vocalizing. As previously stated, assessing the cat before and after a procedure is very helpful – a cat that is timid or fearful may sit at the back of the cage and try to hide before surgery therefore when this behavior also occurs after surgery it is not unexpected and is likely not an indicator of pain. However if a cat was previously inquisitive and always up at the front of the cage and interested in what is going on but then is disinterested in its surroundings and trying to hide after a procedure, this is a significant change in normal behavior that raises one's suspicion about this cat's comfort level.
In general most cats dislike any restrictive dressings or bandages and may roll around, pay excessive attention to, or try to remove these. These behaviours could indicate pain or dislike of the bandage so it is important to differentiate between these two by performing a careful assessment.

**Figure 1.** Normal facial expression and body posture – this posture has been referred to as the croissant or pretzel.

**Figure 2.** This image is of a cat following an ovariohysterectomy. The hunched and “head down” posture of this cat is frequently associated with abdominal pain and has been dubbed the “humpy” cat.

**Figure 3.** This image is of a cat following dental surgery.
The facial expression shown in this cat often correlates with pain – the cat's eyes are slanted and are held half shut – sometimes referred to as the "squinty" cat.

**Behaviors and postures suggestive of acute pain in dogs**

Facial expressions can be useful and a furrowed brow and closed eyes may indicate pain **(Figure 4).** An anxious expression and low hung head is also suggestive of pain **(Figure 5).** Untreated abdominal pain prevents a dog from lying down even when exhausted and may cause them to adopt a "praying" posture **(Figures 6 and 7).**

**Figure 4.** Despite this being a "wrinkly" breed of dog, it is still clear that the brow is furrowed and the eyes are held closed.

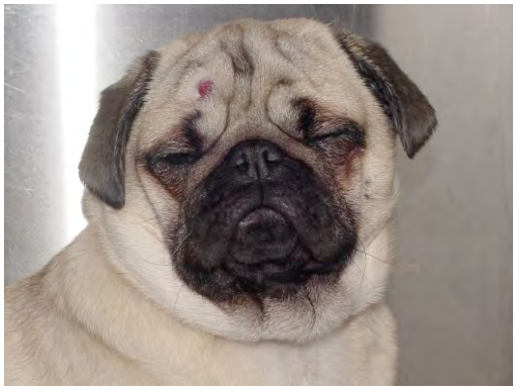

**Figure 5.** This dog has adopted a “head held low” posture and it is reluctant to lie down following abdominal surgery.

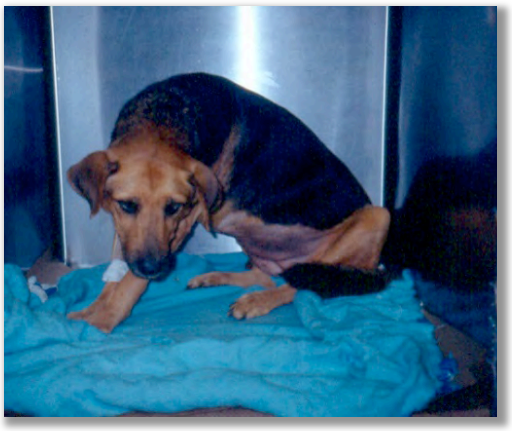

**Figure 6 and 7.** On the left is a dog the day following a splenectomy, on the right is a dog several hours after an ovariohysterectomy; both have adopted a “praying” posture which is indicative of abdominal pain.

**Using a scoring system in your clinic**

Each clinic should choose a scoring system that fits their specific needs, and this may require some trial and error. Whichever one is chosen should be user friendly, quick to complete and readily used by all caretakers and should be an integral part of the animal's evaluation. After temperature, pulse and respiration are checked, pain, which has been coined the "fourth vital sign," should also be assessed. A scale should include both non-interactive and interactive components and rely heavily on changes in behaviour.

The health status of the animal, extent of surgery/injuries, and anticipated duration of analgesic drugs determine the frequency and interval of evaluations. In general, evaluations should be made hourly for the first four to six hours after surgery provided the animal has recovered from anesthesia, has stable vital signs, and is resting comfortably. Patient response to analgesic therapy, and expected duration of analgesic drug(s) administered, will help to determine frequency of evaluations. For example, if an animal is resting comfortably following the postoperative administration of an opioid, it may not need to be re-assessed for two to four hours. Animals should be allowed to sleep following analgesic therapy. Vital signs can often be checked without unduly disturbing a sleeping animal. In general, animals are not woken up to check their pain status; however this does not mean they should not receive their scheduled analgesics. Continuous, undisturbed observations, coupled with periodic interactive observations (open the cage, palpate wound, etc) are likely to provide more information than occasionally observing the animal through the cage door. Unfortunately, continuous observations are not practical for most clinical situations. In general, the more frequent the observations, the more likely that subtle signs of pain will be detected.

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Glasgow Composite Pain Scale/ Permission and downloaded available at:
http://www.gla.ac.uk/schools/vet/smallanimalhospital/ourservices/painmanagement/

## SHORT FORM OF THE GLASGOW COMPOSITE PAIN SCALE

**Dog's name** _____

**Hospital Number** _____ **Date** / / **Time**

**Surgery** Yes/No (delete as appropriate)

**Procedure or Condition**_____

_____

*In the sections below please circle the appropriate score in each list and sum these to give the total score.*

### A. Look at dog in Kennel

*Is the dog?*

| (i) | | (ii) | |
|---|---|---|---|
| Quiet | 0 | Ignoring any wound or painful area | 0 |
| Crying or whimpering | 1 | Looking at wound or painful area | 1 |
| Groaning | 2 | Licking wound or painful area | 2 |
| Screaming | 3 | Rubbing wound or painful area | 3 |
| | | Chewing wound or painful area | 4 |

In the case of spinal, pelvic or multiple limb fractures, or where assistance is required to aid locomotion do not carry out section **B** and proceed to **C**
*Please tick if this is the case* ☐ then proceed to C.

### B. Put lead on dog and lead out of the kennel.

*When the dog rises/walks is it?*

| (iii) | |
|---|---|
| Normal | 0 |
| Lame | 1 |
| Slow or reluctant | 2 |
| Stiff | 3 |
| It refuses to move | 4 |

### C. If it has a wound or painful area including abdomen, apply gentle pressure 2 inches round the site.

*Does it?*

| (iv) | |
|---|---|
| Do nothing | 0 |
| Look round | 1 |
| Flinch | 2 |
| Growl or guard area | 3 |
| Snap | 4 |
| Cry | 5 |

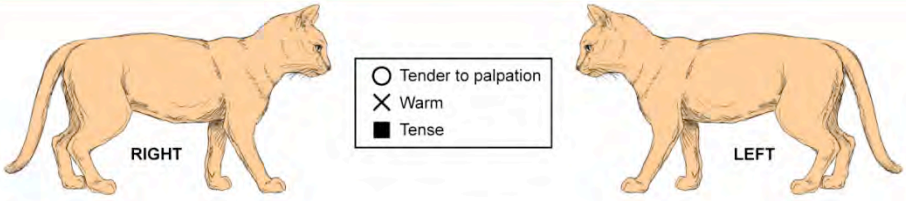
### D. Overall

| *Is the dog?* (v) | | *Is the dog?* (vi) | |
|---|---|---|---|
| Happy and content or happy and bouncy | 0 | Comfortable | 0 |
| Quiet | 1 | Unsettled | 1 |
| Indifferent or non-responsive to surroundings | 2 | Restless | 2 |
| Nervous or anxious or fearful | 3 | Hunched or tense | 3 |
| Depressed or non-responsive to stimulation | 4 | Rigid | 4 |



**Total Score (i+ii+iii+iv+v+vi) =** _____

| Pain Score | Example | Psychological & Behavioral | Response to Palpation | Body Tension |
|---|---|---|---|---|
| 0 |  | ☐ **Content and quiet** when unattended<br>☐ **Comfortable** when resting<br>☐ Interested in or **curious** about surroundings | ☐ **Not bothered** by palpation of wound or surgery site, or to palpation elsewhere | Minimal |
| 1 |  | ☐ **Signs are often subtle and not easily detected in the hospital setting**; more likely to be detected by the owner(s) at home<br>☐ Earliest signs at home may be **withdrawal from surroundings or change in normal routine**<br>☐ In the hospital, may be content or slightly unsettled<br>☐ **Less interested** in surroundings but will look around to see what is going on | ☐ May or may not react to palpation of wound or surgery site | Mild |
| 2 |  | ☐ Decreased responsiveness, **seeks solitude**<br>☐ **Quiet**, loss of brightness in eyes<br>☐ **Lays curled up or sits tucked up** (all four feet under body, shoulders hunched, head held slightly lower than shoulders, tail curled tightly around body) with eyes partially or mostly closed<br>☐ **Hair coat appears rough** or fluffed up<br>☐ May intensively groom an area that is painful or irritating<br>☐ Decreased appetite, **not interested in food** | ☐ **Responds aggressively or tries to escape** if painful area is palpated or approached<br>☐ Tolerates attention, may even perk up when petted as long as painful area is avoided | Mild to Moderate<br>**Reassess analgesic plan** |
| 3 |  | ☐ Constantly **yowling, growling, or hissing** when unattended<br>☐ May bite or chew at wound, but **unlikely to move** if left alone | ☐ **Growls or hisses at non-painful palpation** (may be experiencing allodynia, wind-up, or fearful that pain could be made worse)<br>☐ **Reacts aggressively** to palpation, **adamantly pulls away** to avoid any contact | Moderate<br>**Reassess analgesic plan** |
| 4 |  | ☐ Prostrate<br>☐ Potentially **unresponsive** to or unaware of surroundings, difficult to distract from pain<br>☐ Receptive to care (even mean or wild cats will be more tolerant of contact) | ☐ **May not respond** to palpation<br>☐ **May be rigid to avoid painful movement** | Moderate to Severe<br>**May be rigid to avoid painful movement**<br>**Reassess analgesic plan** |



**CASES FROM THE REAL WORLD**

**"Buddy"**
Buddy is a 5 year old male Golden Retriever. He weighs 38kg and is considered "overweight". He became acutely lame one month ago after playing Frisbee with his owner. He has been diagnosed with a torn cruciate ligament.

**Treatment plan:**

*Surgery*: Tibial Plateau Leveling Osteotomy [TPLO]
*Anesthesia and pain management plan*: Buddy has already been started on an NSAID to alleviate his pain while surgery was scheduled. He is on oral carprofen 4 mg/kg once daily. His CBC and chemistry values are all within normal limits.
He was premedicated with dexmedetomidine (5 µg/kg IM) and methadone 0.4 mg/kg IM. Anesthesia was induced with diazepam (0.25 mg/kg IV) and ketamine (5 mg/kg IV). Anesthesia was maintained with isoflurane. A locoregional (sciatic and femoral nerve) block was performed with bupivacaine. Part of his immediate post-operative care included the use of cold compression therapy. Post-operatively methadone was continued (IV then IM) for 24 hours, after this he was given oral tramadol for 1 week and his carprofen was continued for two weeks.

Discussion

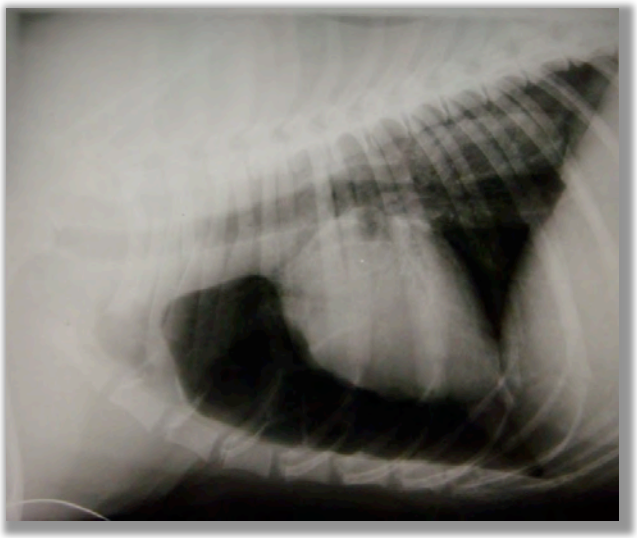
Final outcome

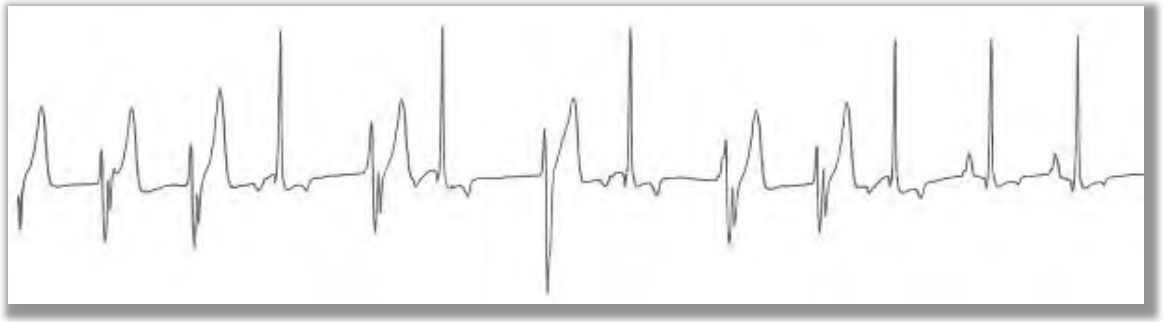
Lessons learned

Notes

**“Nixon”**

Nixon is a 7 year old male Golden Retriever. He was hit by a car earlier in the day and brought into the emergency service for evaluation. He has a fractured left femur, pneumothorax and an arrhythmia (ventricular premature contractions). He has a history of osteoarthritis and has been on carprofen and a “joint diet” for the past two years.





**Treatment plan:**

*Surgery*: repair of the femur fracture
*Anesthesia and pain management plan*:
*Immediate assessment*: His leg was very swollen and bruised – a hematocrit and total plasma protein were run and were normal. An indirect blood pressure measurement revealed a systolic blood pressure of 80 mmHg and a mean pressure of 54 mmHg. An IV catheter was placed and crystalloid fluids given and his blood pressure responded well. He was given IV methadone. After this initial treatment he was comfortable, he was not

dyspneic and a pulse oximeter reading was 98%. Carprofen was stopped. He was scheduled for surgery the next day.
On the day of surgery he was given IV methadone (0.4 mg/kg IV), diazepam (0.25 mg/kg), ketamine (5 mg/kg), intubated and maintained on isoflurane. A bolus of lidocaine was given (2mg/kg) followed by an infusion at 50 µg/kg/minute. Ketamine was also given as an infusion at 10µg/kg/minute. Methadone was given as an infusion at 0.1 mg/kg/hour. Post-operatively lidocaine was continued at 25 µg/kg/minute and ketamine reduced to 3 µg/kg/minute. Methadone was continued at 0.1mg/kg/hour. Lidocaine and ketamine were discontinued after 24 hours and methadone was switched to every 5-6 hours IV for the next 24 hours, then IM for another 48 hours. Carprofen was started on post-op day 2, after Nixon was eating and drinking normally.

Discussion

Final outcome

Lessons learned

Notes

**“Oreo”**

Oreo is an 8 week old female kitten who weighs 0.8kg. She was brought to the emergency room because she was having trouble breathing and was not eating. She had recently been weaned from her mother. Her body temperature was normal. Based on her respiratory pattern and muffling of the heart on chest auscultation, a ruptured diaphragm was suspected although there was no known history of trauma. The diagnosis was confirmed by radiographs.

**Treatment plan:**

*Surgery*: To repair the ruptured diaphragm
*Anesthesia and pain management plan*: Transmucosal buprenorphine 20 µg/kg was given. Topical local anesthetic was placed over the cephalic vein to facilitate IV catheter placement. She was given 100% oxygen to breath for 3 minutes before inducing anesthesia. Induction was accomplished with IV propofol and midazolam and she was intubated and maintained on isoflurane. Bupivacaine was “splashed” on the incision after the linea alba was closed. Post-operatively she received buprenorphine IV (2 doses) then one more dose given transmucosally when the catheter had been removed.

Discussion

Final outcome

Lessons learned

Notes

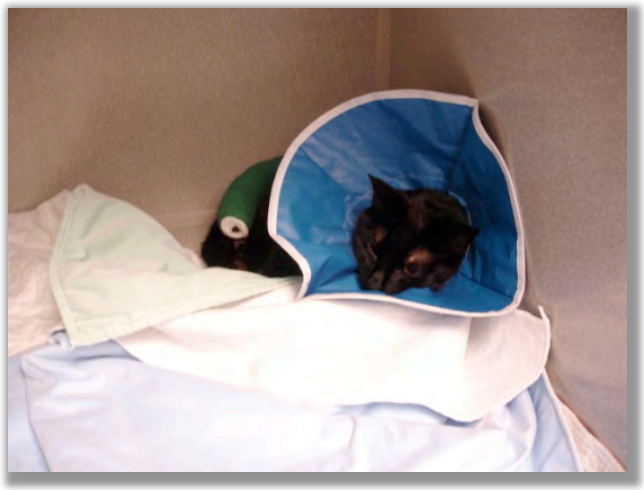
**“Tripper”**

Tripper is a male, neutered black domestic short hair cat. His age is estimated to be between 3 and 4 years and he was recently adopted. On presentation Tripper was non-weight bearing on his right hind leg. Pain was elicited on flexion and extension of the right hock and the range of motion in this joint was severely decreased. A detailed history prior to his adoption was not available, however there was a history that Tripper had been previously attacked by a dog and sustained a fracture of his right hind limb which had been repaired.

**Treatment plan:**

*Radiographs*: There was severe degenerative joint disease of the tarsus. There was partial ankylosis of the hock joint.
*Surgery*: Stabilization of the right tarsus by arthrodesis
*Anesthesia and pain management plan*: Tripper weighed 4kg and was premedicated with 0.03 mg/kg of acetylpromazine plus 0.2 mg/kg of morphine, both given subcutaneously. Anesthesia was induced with diazepam (0.25 mg/kg IV) and propofol (4 mg/kg IV). He was intubated and anesthesia maintained with sevoflurane. Preservative free morphine (0.4 mg total dose) was administered epidurally. The surgical procedure lasted 1 hour and 20 minutes.
This image is of Tripper before surgery.

This image is of Tripper in the immediate post-operative period



Videos of Tripper in the recovery unit in the immediate post-operative period will be shown.

- What is your assessment of Tripper?
- What would you do now?

Discussion

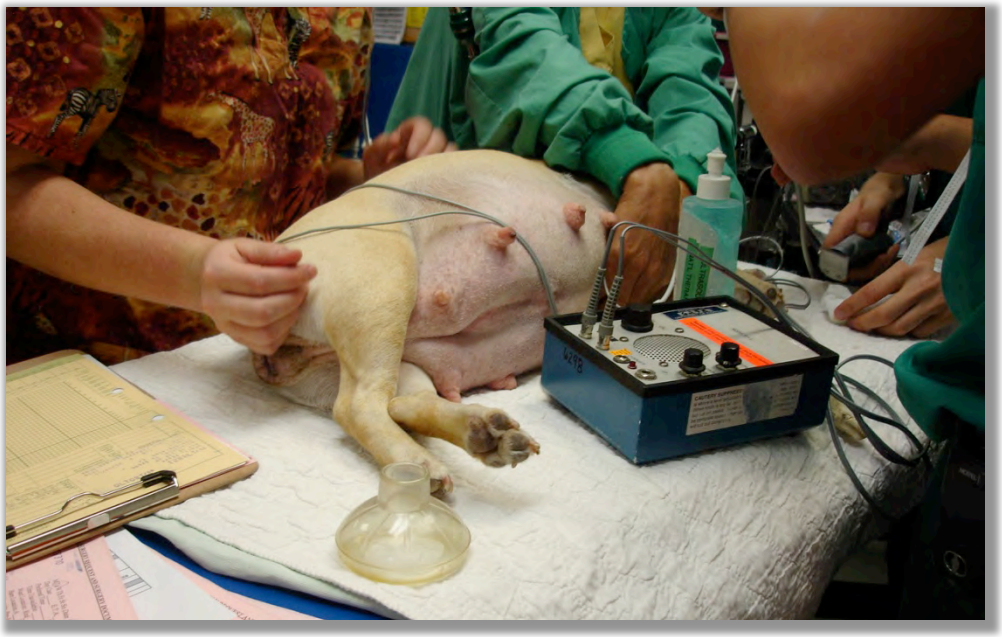
Final outcome

Lessons learned

Notes

**“Bella”**

Bella is a 6 year old English Bulldog. She has previously had a litter of puppies born by C-section and she is scheduled again for an elective C-section. She is in good health and has had several checkups during the pregnancy. Based on ultrasound she has 5 live puppies.



**Treatment plan**

*Surgery* – elective C-section
*Anesthesia* - ?
*Analgesia* - ?
*Resuscitation of the puppies*

Discussion

Final outcome

Lessons learned

Notes