Keynote lecture

Tuesday 1st September | Room A | 9:00–10:00

KL-1 Molecular mechanisms of nociception in the peripheral nerve endings

○Makoto Tominaga
Okazaki Institute for Integrative Bioscience, Japan

TRP (transient receptor potential) channels were first described in Drosophila in 1989, and in mammals, TRP channels comprise six related protein families (TRPC, TRPV, TRPM, TRPA, TRPML, TRPP). One subunit of the TRP channel is composed of six transmembrane domains and a putative pore region between the 5th and 6th transmembrane domains with both amino and carboxyl termini in the cytosolic side. The subunits form functional channels as homo- or hetero-tetramers, and most of the channels work as nonselective cation channels with high calcium permeability. The atomic-level structures of TRPV1 and TRPA1 have recently been clarified using a single particle analysis with cryoEM. TRP channels are best recognized for their contributions to sensory transduction, responding to temperature, nociceptive stimuli, touch, osmolarity, pheromones and other stimuli from both within and outside the cell. Among the huge TRP super family of ion channels, some have been proven to be involved in thermosensation detecting ambient temperatures from cold to hot. There are now ten thermosensitive TRP channels (TRPV1, TRPV2, TRPV3, TRPV4, TRPM2, TRPM3, TRPM4, TRPM5, TRPM8 and TRPA1) with distinct temperature thresholds for their activation. Because temperature ranges above 43℃ or below 15℃ are considered to cause pain sensation in our body, thermosensitive TRP channels whose temperature thresholds are in the range (TRPV1, TRPV2 and TRPA1) can be viewed as nocicpetive receptors as well. Thermosensitive TRP channels work as 'multimodal receptors' which respond to various chemical and physical stimuli. Some of the thermosensitive TRP channels are expressed in the tissues not exposed to the dynamic changes in the ambient temperature and activated by warm temperature around our body temperature, suggesting that they have some specific physiological functions. In addition, it is still not unclear how temperature activates thermosensitive TRP channels.

TRPV1, the first identified thermosensitive TRP channel, was found as a receptor for capsaicin, and later was found to have thermosensitivity with a temperature threshold for activation of about 43℃. TRPV1 was also found to show high Ca^{2+} permeability (P_{Ca}/P_{Na}= 9.6), and application of capsaicin to membrane patches excised from HEK293 cells expressing TRPV1 was shown to evoke clear single-channel openings (conductance of ～77 pS for Na^{+}), strongly suggesting that no cytosolic second messengers are necessary for TRPV1 activation. Behavioral responses to capsaicin were absent and responses to acute thermal stimuli were diminished in the TRPV1-deficient mice. The most prominent feature of the knockout mouse thermosensory phenotype was a virtual absence of thermal hypersensitivity in the setting of inflammation. These findings indicate that TRPV1 is essential for selective modalities of pain sensation and for tissue injury-induced thermal hyperalgesia.

TRPA1 was reported as a distantly related TRP channel which is activated by cold in mice with a lower activation threshold as compared to TRPM8. In heterologous expression systems, mouse TRPA1 was reported to be activated by cold stimuli with an activation temperature of about 17℃, which is close to the reported noxious cold threshold, suggesting that TRPA1 is involved in cold nociception. However, whether mouse TRPA1 is gated directly by cold remains to be elucidated even after the analyses of TRPA1-deficient mice while human TRPA1 is believed not to be temperature sensitive. Nevertheless, TRPA1 is activated by various chemical compounds causing pain sensation, indicating that TRPA1 is involved in nociception. Thus, both TRPV1 and TRPA1 can be good targets for development of anti-nociceptuve agents while no reliable compounds are currently available in the market.

Wednesday 2nd September | Room A | 8:30−9:30

KL-2 How to Use Pharmacokinetics and Pharmacodynamics in Clinical Practice

○Kenichi Masui
National Defense Medical College, Japan

Kenichi Masui, Senior Assistant Professor, Department of Anesthesiology, National Defense Medical College

Pharmacokinetics refers the drug movement in the body, and applies pharmacokinetic models to describe the drug concentration in the body. Pharmacodynamics refers the drug effect in the body, and applies the relationship between the drug concentration and its effect. Here, I will show the basics of pharmacokinetics and pharmacodynamics, and how to use the pharmacokinetics and pharmacodynamics to improve daily anesthesia practice.

Intravenous drugs such as propofol and opioids are generally infused by bolus and/or continuous infusion. Could you answer whether the plasma concentration of a drug increases, decreased or is stable during a constant rate intravenous infusion? The answer is you don't know unless the detail of the infusion after the start of the drug infusion. If a drug is infused at a constant rate without any prior infusion of the drug, the plasma concentration would gradually increase during a constant rate infusion. If a drug is infused at a constant rate after one bolus of the drug, the plasma concentration may decrease during the early phase of the constant rate infusion and may increase afterward.

Drug concentration is one of the principal factors to determine the drug effect. When using inhalation anesthetics, one can measure the inhaled and exhaled concentration of inhalation anesthetics, such as isoflurane, continuously. Meanwhile a good equipment is not available to measure the concentration of intravenous drug continuously for clinical practice.

Well, how do you know the drug concentration of the administered intravenous drug? In human clinical practice, "PREDICTED CONCENTRATION" is used and well accepted all over the world. The predicted concentration is calculated using a pharmacokinetic model.

"Predicted concentration" is not "measured concentration." Therefore, one may question why the predicted concentration can be used in clinical practice. The relation between end-tidal carbon dioxide concentration ($ETCO_2$) and arterial carbon dioxide tension ($PaCO_2$) would be a nice example. $ETCO_2$ is measured noninvasively instead of $PaCO_2$ because $ETCO_2$ is useful to know the time course of $PaCO_2$ approximately. Although $ETCO_2$ may be different from $PaCO_2$, one can consider the reason of its difference, e.g. low cardiac output. Similarly, one can use the predicted concentration of an intravenous drug to know the time course of the measured concentration approximately when using a validated pharmacokinetic model. Also similarly, one can consider the reason of the difference between the predicted and measured concentration. For example, low cardiac output may increase the measured drug concentration during a constant rate infusion because low cardiac output results in the higher first-pass concentration than higher cardiac output. After the enormous experience of the usage of predicted concentration for more than 20 years, predicted concentration is now well accepted in both clinical practice and the research field.

Simulating the concentration of the intravenous drug, simulation software is available including AnestAssist PK/PD and TIVA trainer for mobile devices. These software can allow you to calculate drug concentration easily. In clinical practice in human, various commercial devices showing the predicted concentration are available including drug information displays such as Smart Pilot View, targeted-controlled infusion pumps, and simulation software on an anesthesia information management system.

Before using a pharmacokinetic model in clinical practice, one has to understand the prediction performance of the model. For example, when you can use the following two models for the prediction, which is better?

Model A: This model has a bias for the prediction. Predicted concentration is always 30% higher than measured concentration regardless the time after the start of the drug infusion.

Model B: This model over-predicts the drug concentration just after the start of the drug infusion (e.g. the predicted concentration is 50% higher than the measured concentration), predicts the concentration accurately (e.g. within 10% difference versus the measured concentration) 1 hour after the infusion, and under-predicts the concentration 2 hour after the infusion (e.g. the predicted concentration is 50% lower than the measured concentration).

Model C: This model under-predicts the drug concentration just after the start of the drug infusion, predicts the concentration accurately 1 hour after the infusion, and over-predicts the concentration 2 hour after the infusion.

Although all three models has a problem for the prediction of the drug concentration, the Model A has

less problem. On the other hand, the Model C is critical because the measured (real) concentration will gradually decreases when the predicted concentration is maintained constant.

A pharmacokinetic model such as a compartment model allows us to calculate "PLASMA CONCENTRATION" of a drug. However, when considering the concentration-effect relationship of an intravenous drug, one may realize the problem of using plasma concentration.

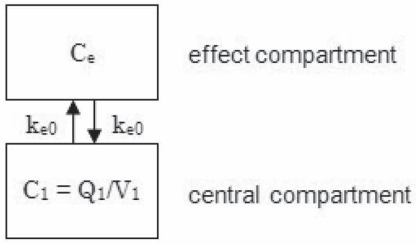
However, for anesthetics and opioids, the site of action is not plasma. After a drug was given to a body by bolus intravenously, time to peak plasma concentration would be very short, whereas time to peak effect of the drug would be longer. To predict this delay of the drug effect as a drug concentration, a hypothetical compartment connected to the central compartment of a conventional compartment model makes sense. The differential equations for typical effect compartment model with three compartment model are the followings:

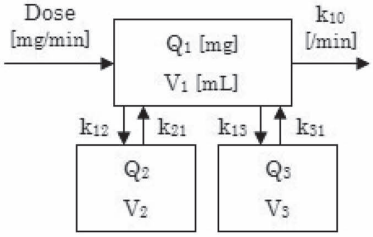
$$\frac{dQ_1}{dt} = \text{Dose} - (k_{10} + k_{12} + k_{13})Q_1 + k_{21}Q_2 + k_{31}Q_3$$

$$\frac{dQ_2}{dt} = k_{12}Q_1 - k_{21}Q_2$$

$$\frac{dQ_3}{dt} = k_{13}Q_1 - k_{31}Q_3$$

$$\frac{dC_e}{dt} = k_{e0}(C_1 - C_e)$$





, where Q is the amount of the drug in the compartment, Dose is the infusion rate of the drug, k10 is the elimination rate constant, the other k is the equilibration rate constant between the compartment, C is the drug concentration is the compartment, and V is the distribution volume of the compartment.

Using this pharmacodynamic model (effect compartment model) describing the time delay of the drug effect with a pharmacokinetic model such as three compartment model, one can calculate the effect-site concentration of the drug. This is a hypothetical concentration but it is suitable to describe the concentration-effect relationship of the drug. Note that the use of a pharmacokinetic model from a study with a ke0 value from another study is generally inappropriate. The ke0 values are different between two other pharmacokinetic models.

Predicted plasma concentration and effect-site concentration of a drug allow you to control drug effect in clinical practice. For the control, an anesthesiologist assesses the effect of the drug with predicted plasma or effect-site concentration. So that the one will decide the appropriate concentration for an individual animal. Examined pharmacokinetic and pharmacodynamic data may help you to control the drug effect. I will show you some data including the published and unpublished data for animals from our group in the lecture. To control the drug concentration of intravenous drug is similar to controlling the concentration of inhalation anesthetics using a vaporizer.

I will also introduce some tips for not only for clinical practice but also for research works including the target controlled infusion, drug interaction models describing isobologram and response surface.

Thursday 3rd September | Room A | 8:30−9:30

KL-3 Comparative Physiology: Discovery in Support of Clinical Advancement

○Eugene P. Steffey
University of California, Davis, U.S.A.

This talk is about discovery in comparative physiology and its importance to the evolution and continued progress of veterinary anesthesiology and in particular the clinical practice of veterinary anesthesia. It is also about veterinary anesthesiologists as recipients of discovery and, equally important, as contributors to advances in knowledge of comparative physiology.

The basic science roots of the clinical discipline of veterinary anesthesiology have many branches including anatomy, biochemistry, pharmacology, and physiology. Knowledge from these basic science roots is of undeniable importance to clinical practice and delivery of health care. **Physiology** is a branch of biology that deals with the function and activities of life or living matter and of the physical and chemical phenomena involved. It involves both a description of normal function and activities of life, and respective mechanisms of action. The term '**comparative**' conveys understanding that an examination of two or more conditions or circumstances has occurred and the purpose of comparison is to establish similarities and dissimilarities, and not to be forgotten, that such investigation of one vs the another or others, is performed on equal footing. The term **Comparative Physiology** then denotes the exploration of physiological principles and highlights the functional diversity among animal species. In our clinical specialty we regularly apply knowledge of comparative physiology to foster improved species-related health-care strategies. With this as introduction, I shall proceed to voice and expand on 2 convictions.

First, we *successfully, legitimately arrived at this point in the history of our clinical practice of veterinary anesthesiology in strong part by building upon a firm foundation of basic knowledge from comparative physiology*. That is, we got here based on knowledge derive from previous scientific discovery. Our specialty is based on broad concepts of physiology and knowledge of species-specific variations within our general understanding. Such fundamental knowledge permits us to meaningfully modify our clinical techniques according to individualized circumstances. It is important for us to know, for example, that the mechanics and pattern of breathing in terrestrial mammals such as humans and commonly managed non-human primates, as well as that of cats and dogs is similar, i.e., inspiration is active and begins from functional residual capacity (FRC), and expiration is passive and returns end-expired lung volume back to FRC. It is equally important that we know that breathing strategies of, for example, domestic horses and cattle differ markedly from that of the aforementioned group, as well as from each other (i.e., equine vs bovine). Additional differences are evident if we extend discussion to marine mammals or if we cross over into for example, avian species, or even beyond to reptiles or amphibians. Such knowledge is important, for example, to our continued evolution of techniques of mechanical ventilation and species-specific, if not individualized, respiratory care of animals because direct transposition of physician-based knowledge from human patients to our own often unique species-related circumstances frequently leaves our well-intended efforts lacking.

It is important to acknowledge a great deal of the earlier gathered information forming the basis of our general physiological approach to clinical practice came from work outside veterinary medicine, i.e., it was derived from general and specific biomedical investigative work supporting human health care advancements by physiologists, physicians, and other scientists using especially dogs and cats as models for discovery. Regardless the overriding motive of these investigators, since individual laboratory investigations were commonly conducted on species of clinical interest to veterinary medicine those data also could be, and was, used to directly advance the fledgling specialty of veterinary anesthesiology. We especially owe much to investigators of the past 50 years from within our clinical specialty ranks. Diplomate colleagues of both the American and European Colleges of Veterinary Anesthesia and Analgesia with special physiological investigative focus that come quickly to mind include (listing is alphabetic by family name): Jerry Gillespie, Robin Gleed, Leslie Hall, Steve Haskins, Jim Heavener, John Ludders, Wayne McDonell, Yves Moens, Bill Muir, Gorel Nyman, and Barbara Weaver (perhaps there is legitimacy in including myself in such a listing). Noteworthy contributions by these individuals and others were the result of sustained laboratory (basic and applied) investigation of target species to answer contemporary (often introductory to veterinary medicine) questions, and/or by researching and distilling pertinent published basic and applied physiological and human health care-related clinical literature. Important to later discussion is that 7 of the 11 individuals just highlighted are now retired, 2 are deceased, and the remaining 2 are very senior in the tenure of their academic careers.

The second conviction that I wish to highlight is, *although veterinary anesthesiology has come a long way in the past 50 years, areas of ignorance remain about how tissues and organs of the body function in general and especially how they may vary among species of special clinical importance to veterinary medicine.* Therefore, continued investigative activity by individuals of our discipline and others with appropriate knowledge and skills in scientific inquiry is undeniable. We must be active contributors to the ongoing discovery process.

Change is inevitable and much is different today compared to the rapid expansion of knowledge in comparative physiology, basic and then applied, of the 1950's 60's, and early 70's. For example, during this period in the U.S. academic physiology departments were well funded for systemic physiology research and related graduate training programs were plentiful. Anesthesiology programs in medical schools of major research universities like for example, Harvard University, and the Universities of California, Pennsylvania, and Wisconsin, both partnered with physiologists and developed strong research programs of their own in applied systemic physiology. But then in mid-1970's there rapidly evolved a major investigative focus shift within physiology that was prompted by a number of factors that I'll not review here. However, what is important is that investigative focus rapidly moved from systemic physiology and the laboratory study of intact, whole organisms, to cellular and molecular physiology. This transition occurred in parallel to social discord regarding the use of especially cats and dogs as models for study of physiologic concepts. A direct consequence of these and other accompanying events was the loss of new information important to veterinary anesthesia from well controlled laboratory studies of some of our 'target' clinical species. Ironically, much of the systemic physiology and pathophysiology discovery during the recent past 3 decades has increasingly evolved from study of humans and in direct support of human health care delivery, i.e., less focus on comparative physiology. While veterinary anesthesiology continued to benefited in various ways from this shift in science focus, the clinically applied benefits to us have been mostly *qualitatively indirect, and compared to earlier times, modest or quantitatively* smaller .

Considering its importance, how do we at least sustain, but hopefully increase our discovery of new knowledge in support of advances in veterinary anesthesiology. Not surprisingly, we do so by focusing on people, time and funding. We have an ongoing obligation to our discipline and to society to ensure there is a sufficient core of individuals (i.e., the quantitative component) with training in science (i.e., the qualitative component) to provide necessary human resources for investigative activity. Such individuals must have time specifically identified for investigative activity. It made no sense in the past and less so in the future to invest costly energy and resources in appropriate training of the future creators of new knowledge if they are then not afforded protected time to carry out the important investigative work. But who will pay for the research to explore within the realm of physiology especially in relation to animal related health care? Herein is our greatest challenge, but a solution plan must be aggressively and creatively developed and implemented.

In summary, discovery in comparative physiology must continue because of the need to supply better patient care and to provide for evidenced-based medicine. Application of new knowledge will support the discarding of ineffective remedies and application of improved therapies, and both of these outcomes will improve patient well-being. Veterinary anesthesiologists should be continued contributors of new knowledge in this important basic science root of our clinical specialty. Indeed, our role can importantly increase should we so choose! Finally, we must endeavor to articulate our contributions in this regard to others outside of our specialty and to be sure these contributions are understood not just by our contemporaries but by other medical science colleagues and, yes, the public in general.

Friday 4th September | Room A | 8:30–9:30

KL-4 Perioperative Analgesia – too much or too little?

○Peter J Pascoe
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Over the last 15 years there has been increasing recognition in human medicine that the perioperative management of patients has an impact on chronic postoperative postsurgical pain (CPSP). This is a significant problem in terms of patient welfare and the costs of management. An example of the estimates of the incidence in human medicine is given in this table:

Table 1 Approximate numbers of operations carried out in England and the USA and incidence of CPSP modified from (Macrae 2008)

Type of operation	Incidence of chronic pain	No. of ops in UK in 2005–6	No. of ops in USA in 2003	No. of ops in Japan in 2010
Total operations		7,125,000	51,000,000	4,100,000
Mastectomy	20–50%	18,000	97,000	
Caesarean section	6%	139,000	1,171,000	
Amputation	50–85%	15,000	132,000	
Cardiac surgery	30–55%	29,000	630,000	
Hernia repair	5–35%	75,000	258,000	
Cholecystectomy	5–50%	51,000	467,000	
Hip replacement	12%	61,000	343,000	
Thoracotomy	5–65%		660,000	

From these data it is clear that there are many people are suffering as a result of their procedure and that the prevalence of postoperative pain is somewhat dependent on the type of procedure. However, even with relatively minor surgeries such as vasectomy the incidence is around 15% (Leslie et al. 2007).

The etiologies of CPSP have been investigated and a number of factors have been described:

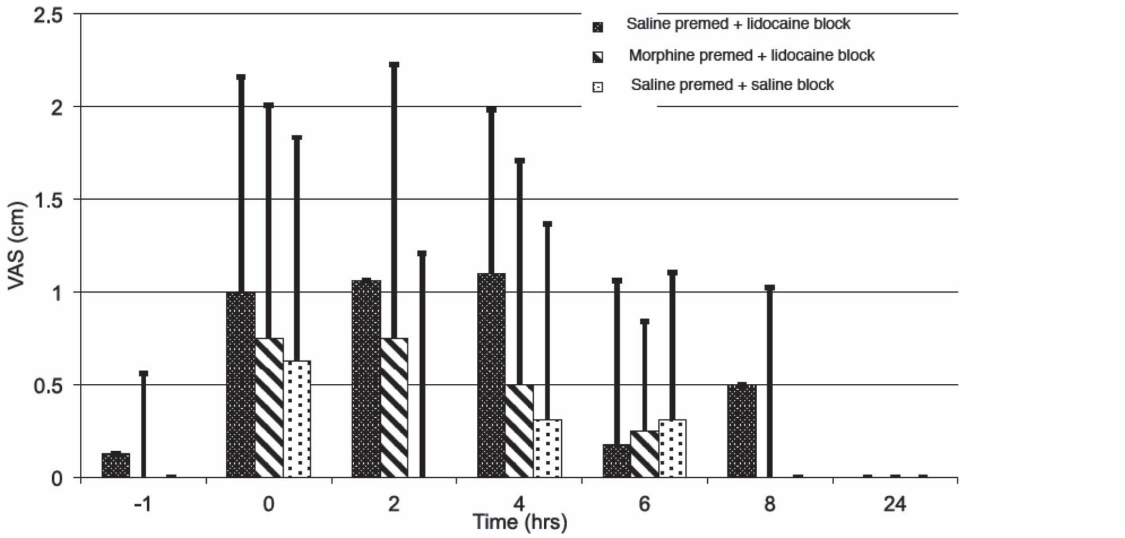
- Perioperative pain management has been shown to play a significant role with those patients that experience poor pain control in the perioperative period having higher likelihood for CPSP. In one study on post-thoracotomy pain (Katz et al. 1996) the patients who had chronic pain had higher scores for pain at rest and pain on movement than those patients who reported no chronic pain at 18 months after the surgery. This was despite using patient controlled analgesia with morphine. In another study more than 50% of the patients reported pain that affected them on a daily basis at 6 months after surgery (Perttunen et al. 1999). Similar results have been found for other surgical procedures.
- Nerve injury may play a part in this. In carrying out most surgical procedures there will be some degree of nerve injury. This might be damage to the peripheral nerve terminals in the site of the incision, it could be related to pressure or retraction of the surgical site that involves nerves or it could be due to section of a nerve trunk as required for the procedure. Nerve dysfunction following thoracic surgery has been documented in people using muscle-evoked potentials and established that both direct and indirect pressure from the retractor (the intercostal nerve in the next space away from the retractor) could cause neuropraxia (Rogers et al. 2002). Phantom limb pain is thought to be due, in some instances, to section and subsequent inflammation of the nerves during amputation.
- Central sensitization is definitely part of this and may be related to the management of perioperative pain in that the more the input is blocked during and immediately after the procedure the less likely that central changes will occur.
- Genetic factors are being examined for their role in CPSP. In rodents it has been shown that there are genetic factors that determine the responses to different types of pain (Devor & Raber 1990; Mogil et al. 1999; Devor et al. 2005) and there is some evidence in humans that there are genetic predispositions to pain sensitivity (Nielsen et al. 2009). There are also genetic factors that play a part in drug metabolism e.g. the proportion of Caucasians that do not metabolize codeine to morphine and for whom codeine is not a very good analgesic. We are also beginning to understand the genetic changes associated with some receptors and in humans it has been shown that the A118G mu opioid receptor gene affects the requirements for postoperative opioids, especially in Asian patients (Hwang et al. 2014).
- Type of surgery has been shown to be important as indicated above. Amputation in humans carries a greater risk of CPSP whereas minimally invasive procedures such as laparoscopy may carry lower risks (Cocozza et al. 2014). The skill of the surgeon

has also been implicated in human breast surgery for cancer and found higher rates of CPSP from centers with low volume and less experience (Tasmuth et al. 1999)

- Psychosocial factors are important in people but are hopefully less important for our patients.

There are very few studies that have evaluated CPSP in animals. In one study examining the outcome of surgical techniques for cranial cruciate repair in dogs about 48% of the dogs showed some pain 1 year after the surgery (Christopher et al. 2013). In cats following onychectomy there was no difference in peak vertical force exerted during walking compared with normal cats, 6 months after surgery (Romans et al. 2004) but other studies report some pain 4-6 months after the procedure (Patronek 2001). There are no studies of chronic pain after ovariohysterectomy in dogs or cats and very few reports of such cases. In a study of over 1800 animals presented to a veterinary teaching hospital pain was reported as a sign in 323 animals but none of these were reported to be due to previous surgical procedures. Are these relatively low values for CPSP because the animals we treat overcome pain better than people or do they hide it more effectively? Without the psychosocial issues that humans have do animals recover faster because they don't get depressed or catastrophize about their situation? Or perhaps veterinarians do a much better job of controlling perioperative pain so that CPSP is less likely to occur.

The treatment of pain in veterinary practice has increased over the last two decades and several studies examining the attitudes and management practices in a variety of countries have confirmed this (Dohoo & Dohoo 1996; Dohoo & Dohoo 1998; Weber et al. 2012; Lorena et al. 2014; Hunt et al. 2015). Most recently the WSAVA has produced a document that describes standard management for a variety of procedures. The therapies for routine procedures such as ovariohysterectomy and castration in dogs and cats include opioids, NSAID, tramadol, local anesthetics and epidural injections (Mathews et al. 2014). Studies that have examined pain following these procedures often examine the first 6 hours following the procedure and many have also looked at the first 24 hours. In these latter studies it is usually shown that pain scores decrease to levels similar to the control values by the end of the first day especially if the surgery has been done by a practiced surgeon. In the figure below the dogs were spayed by experienced surgeons with a surgical time of about 20 minutes. The visual analog pain scores (VAS) show that the scores by 24 hours were similar to those before the procedure even in animals that received no analgesics (saline premed and saline block) (McKune et al. 2014).



Even in studies that examine pain scores following more invasive surgeries the results show a major decrease over this first day (Romano et al. 2015).

It is often routine, in general practice, to prescribe analgesics for the first 4-7 days after surgery and in the USA this is commonly an NSAID and tramadol. Given that the pain scores on most patients are very low by 24 hours this seems to be an over-prescription of drugs. Unfortunately there are no studies in veterinary medicine that have examined the risk:benefit ratio of such treatments.

One class of drugs that is very effective in the management of pain are the local anesthetics and, while there is increasing use of local anesthetic blocks in institutional practice, this is not commonly done in general practice (Hunt et al. 2015). In most countries these are relatively inexpensive drugs that can be applied to provide better analgesia than almost any other compound. The use of intratesticular blocks for castration and intraperitoneal instillation of bupivacaine for ovariohysterectomy have both been shown to be useful adjuncts to these common surgeries (Campagnol et al. 2012; Kim et al. 2012; Perez et al. 2013). The use of regional blocks is proving to be a very effective technique compared with systemic analgesics (Romano et al. 2015). This concept is not new (Lundy 1926) but deserves emphasis in our clinics and teaching to veterinary students and practitioners.

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Lecture

L-1 Peripheral nerve blocks, the basics: anatomy and indications

○Manuel Martin-Flores
Cornell University, U.S.A.

Basics of peripheral nerve blocks: Indications, anatomy and electrolocation.

Anesthesia of peripheral nerves has gained substantial popularity in veterinary anesthesia in recent years. Several advantages make this technique an appealing one, and an important number of scientific manuscripts are now available.

Risks and complications:

- Local anesthetic toxicity.
- Neurological injury can also arise from direct trauma to the nerve with the needle, or from an increase in pressure due to accidental intraneural injection. As a general rule, if resistance is encountered during injection, the likelihood if intraneural injection is higher, and the needle should be withdrawn before further volume is injected. Also as a general rule, if a nerve block is being guided by electrolocation, positive motor responses elicited at a current of 0.2mA can indicate that the needle is in direct contact with the nerve. Lastly, if using ultrasound, injection of local anesthetic produce a 'doughnut sign', where the local anesthetic can be observed around the nerve.
- Direct trauma to nerves can result in long lasting injuries producing chronic pain and/or motor deficits. Such injuries are difficult to treat and can be of devastating outcome to the pet, owner, and the clinician who performed the block. It is important to keep in mind that nerve blocks are not devoid of risks.

Principles of electrolocation

Nerve stimulators are used in conjunction with insulated stimulating needles. When a stimulating needle approaches a nerve carrying motor fibers, depolarization of the nerve occurs resulting in synchronous contractions in the effector muscles that are innervated by that nerve. There are several factors that determine the stimulus threshold of a nerve:

The distance between electrode (needle) and nerve plays a major role during nerve stimulation, and it's dictated by Coulomb's Law [$E = k (Q / r^2)$ where E = current required, K = a constant, Q = minimal current, and r = distance]. The electrical current required to trigger a muscle contraction correlates with the distance of the tip of the needle to the nerve.

Prior to injection, negative blood aspiration should first be observed. Injection of the first 1 mL of local anesthetic will cause the motor response to cease since the solution will dissipate the current. Intraneural injections are associated with high injection pressures (>20psi, 138kPa). If resistance to injection is experienced, the needle should be repositioned before further local anesthetic is injected.

Nerve blocks of the thoracic limb.

In the majority of dogs, the brachial plexus is formed by the ventral branches of the C6, C7, C8 and T1 spinal nerves, which exit the spinal column through their respective intervertebral foramina. The most relevant nerves, from cranial to caudal, are the suprascapular, subscapular, axillary, musculocutaneous, radial, median, and ulnar nerves. The axillary artery and vein are also located in the axillary space, immediately caudal to the median and ulnar nerves and cranial to the first rib.

Anesthesia or analgesia of the entire thoracic limb can be provided. A cervical paravertebral or axillary brachial plexus will be necessary for shoulder or humeral procedures. Procedures involving the elbow and or radius and ulna can be blocked with a brachial plexus (traditional axillary approach) whereas procedures involving the carpus can be successfully blocked just proximal to the elbow using a RUMM block.

Cervical paravertebral block

This block may be useful for providing anesthesia to the scapula, shoulder and brachium including their associated soft tissues. When performing a cervical paravertebral block, the goal is to deposit local anesthetic solution near the C6 and C7 nerves as they cross the cranial and caudal margins of the large ventral wing of the transverse process of sixth cervical vertebra, and near the C8 and T1 nerves as they cross the cranial and caudal margins of the head of the first rib before they coalesce at the brachial plexus. The phrenic nerve also originates in this general area.

Technique

The scapula is shifted caudally to expose the transverse process of C6 and the first rib. The tip of the needle is then gently walked off of the cranial and caudal margins of the transverse process until the ventral branches of the nerves are encountered. After identifying the head of the first rib, the needle is slowly advanced in a caudomedial direction until the rib is encountered at this dorsal location. The needle is then gently walked off of the first rib medially at its cranial and caudal margins until the C8 and T1 nerves are encountered.

Response to stimulation is as follows:

Musculocutaneous nerve (C6-7); Contraction of biceps

Radial nerve (C7,8 T1); Contraction of triceps

Median and ulnar nerve (C8 T1); Contraction of flexor carpi radialis

Risks and complications

Phrenic nerve blockade (hemidiaphragmatic paralysis); vascular puncture (vertebral arteries); epidural migration of local anesthetic.

Brachial plexus block

This block will typically result in anesthesia of the elbow and structures distal to it. The same nerves roots as mentioned above are anesthetized.

Technique

This block I approached with the dog in lateral position, with the side being blocked located uppermost. Draw an imaginary line between the acromion and the cranial border of the greater tubercle. A second line is drawn perpendicular to the first, from the cranial border of the acromion. This line provides the direction of needle advancement. To assess the maximum depth of the needle insertion, the first rib is palpated under the scapula. The axillary vessels are located in close proximity to this region. To avoid accidental vessel penetration, care must be taken not to advance the needle past this line. Insert the needle and carefully advance it medial to the scapula in a caudal direction. When the tip of the insulated needle stimulates the musculocutaneous nerve, contraction of the biceps will be evoked. Stimulation of the radial nerve may also be elicited (flexion of elbow). It is acceptable to use that response to guide injection, however, the most rostral component of the plexus might be missed.

Risks and complications

Inadvertent puncture of vessels, especially during deep needle insertions (caudal and ventral to the radial nerve) can occur. Penetration of the thorax is also possible and has been reported.

Nerve blocks of the pelvic limb.

The pelvic limb is innervated by the lumbar and sacral plexuses; both require desensitization to provide surgical anesthesia to the entire pelvic limb.

Our service uses these blocks routinely for fracture repairs and articular procedures (femoral head osteotomies, knee arthroscopy, anterior cruciate ligament repair, tibial plateau levelling osteotomy (TPLO), tibial tuberosity advancement (TTA), foot and ankle surgery, etc.). A sciatic nerve block alone is sufficient to perform surgery of the foot and the hock. If the surgical procedure involves the tibia or the stifle, a femoral nerve should also be performed.

Femoral nerve block

The femoral triangle is delimited by the iliopsoas muscle proximally, the pectineus muscle caudally, and the sartorius muscle cranially. Within the triangle, the femoral nerve is located cranial to the femoral artery and vein, running deep to the caudal belly of the sartorius muscle. The femoral nerve then continues distally, entering the quadriceps muscle, between the vastus medialis and rectus femoris. Desensitization of the femoral nerve provides anesthesia of the femur, femoro-tibial joint, femorotibial intra-articular structures, skin of dorsomedial tarsus and first digit.

Technique

The stimulating needle is inserted cranial to the femoral artery and advanced towards the iliopsoas muscle at 20-30 degrees. The nerve is located directly medial to the caudal belly of the Sartorius muscle. Femoral nerve stimulation evokes contractions of the quadriceps muscle (stifle extension).

Risks and complications

The lateral circumflex vessels originate from the femoral artery and vein, and cross the femoral triangle in a cranio-caudal direction. Puncture of these vessels can result in hematoma or lack of response to electrostimulation.

Sciatic nerve block

This block results in anesthesia of the stifle (partial) and the structures distal to it. The sciatic nerve is formed by the ventral branches of the L6, L7 and S1 nerves, and passes between the middle and deep gluteal muscles. It exits the pelvis through the greater sciatic notch. The sciatic nerve descends between the greater trochanter and the ischiatic tuberosity and gives rise to the muscular branches that supply the caudal thigh muscles. Immediately distal to the greater trochanter and ischiatic tuberosity, the sciatic nerve lies between the biceps femoris muscle laterally and the semimembranosus muscle caudal and medially. The sciatic nerve then divides into its two branches, the tibial nerve medially and the common peroneal nerve laterally. The location of this division is variable and can occur anywhere from the level of the hip joint to just proximal to the stifle joint.

Technique

The greater trochanter and the ischiatic tuberosity are identified. The site of puncture is located approximately at a point between the cranial and middle thirds of an imaginary line between those 2 landmarks. The needle is inserted at that point with a 45 degree angle to the skin. Upon needle advancement, contractions of the biceps femoris might be encountered, commonly from direct muscle stimulation. The correct response to sciatic nerve stimulation is the dorsiflexion or plantar extension of the foot. Contractions of the semimbranosus muscle may also be observed, without foot movement; in that case the sciatic nerve might not be blocked.

Risks and complications

The main risk with sciatic nerve block is – as with other blocks – the direct trauma to the nerve, which can result in temporary or permanent foot knuckling.

Tuesday 1st September | Room A | 11:20−12:20

L-2 Ultrasound-Guided Regional Anesthesia

○Fernando Garcia-Pereira
University of Florida, U.S.A.

Regional Anesthesia of the Thoracic Limb (Brachial Plexus)

The brachial plexus is responsible for the motor and sensory input of most of the thoracic limb. It is formed most commonly by the ventral nerve roots of C6, C7, C8 and T1, sometimes C5 and T2 fibers may also contribute to its formation in a small percentage of dogs. The most significant nerves are Suprascapular, Subscapular, Axillary, Musculocutaneous, Radial, Ulnar and Medial. Only the Musculocutaneous, Axillary, Radial, Median and Ulnar have cutaneous somatic afferents for the thoracic limb. The skin cranial to the scapularhumeral joint (often incised during shoulder surgery) is innervated by the ventral branch of the C5 root, therefore a paravertebral block on this root is necessary to cover this area. Several different techniques have been described in veterinary medicine. We will focus in few new approaches, besides the conventional brachial plexus at the level of the scapula-humeral joint.

Most common disposition of brachial plexus nerves on the dog is display on the table below:

Root	Nerve	Supply	Relationship to Vasculature
C6-C7	Suprascapular	Supraspinatus and infraspinatus muscles.	Dorso-cranial
C6-C7	Subscapular	Subcapularis muscle.	Dorso-cranial
C6 to C8	Musculocutaneous	Skin over the medial arm and forearm, Brachialis, Biceps Brachii and Coracobrachialis muscles.	Dorsal
C7-C8	Axillary	Skin over the lateral portion of the shoulder. Teres major and minor, deltoideus and part of subscapularis muscles.	Dorsal
C7 to T1	Radial	Skin over the latero-dorsal aspect of the arm, forearm and paw. All extensor muscles to elbow, carpus and phalangeal joints.	Dorsal
C8 to T2	Median	Skin over the palmar side of the paw. Flexor carpi radialis, superficial and deep digital flexors, pronators muscles.	Dorso-caudal
C8 to T2	Ulnar	Skin over the caudal aspect of elbow and caudolateral aspect of forearm and paw.	Dorso-caudal

Axillary Approach (Luis Campoy's approach)

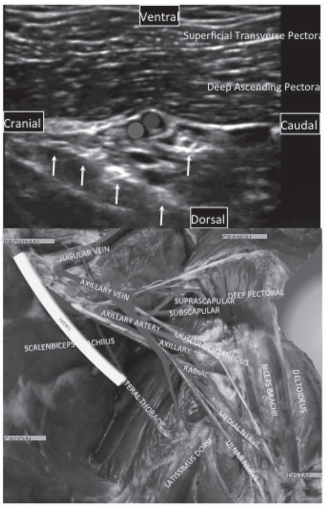
In this approach, a rectilinear transducer (generally 3 inches) is used in a parasagittal plane on the ventral axilla while the animal is in dorsal recumbency. On this ultrasonographic image the operator is able to see ventrally the pectorals muscles followed dorsally by the axillary artery and vein. Further dorsally to the vasculature the operator is then able to see roots or nerves serving the brachial plexus in a disposition cranial to caudal in relationship to the axillary artery and vein. The needle is advanced on a craniocaudal direction in plane with the transducer.

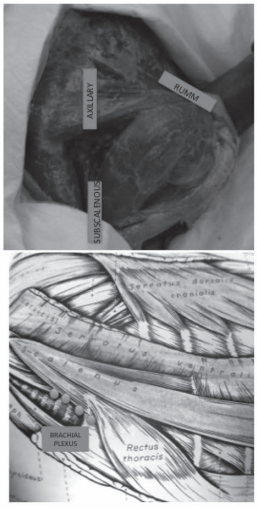
Sub-Scalenus Approach (Pablo Otero's approach)

On this approach the animal is in lateral recumbency with the side to be blocked uppermost. A rolled towel or pillow is used to raise the caudal neck and to displace the scapula caudally, improving visualization of brachial plexus during ultrasonography. With the linear transducer parallel to the vertebral column, just cranial to the first rib, the probe is slowly moved on a ventrodorsal direction until the ventral nerve roots of the brachial plexus are visualized. The needle is place on a craniocaudal direction in plane with the transducer.

RUMM

On this technique the innervation below the elbow will be anesthetized, therefore it is used only for procedures distal to the elbow joint. The linear transducer is placed transversely lateral and medially on the arm to be anesthetized. The musculocutaneous, median and ulnar nerve are visualized on the medial portion of the arm, cranial to the elbow joint, close to the mid point of the humerus. The radial nerve is visualized and anesthetized on the lateral side of the arm, where it appears caudal lateral to the Brachialis muscle an under the lateral head of the Triceps on the distal third of the humerus.





Regional Anesthesia of the Pelvic Limb (Lumbosacral Plexus) Femoral Nerve

Femoral Triangle Approach (Campoy's description)

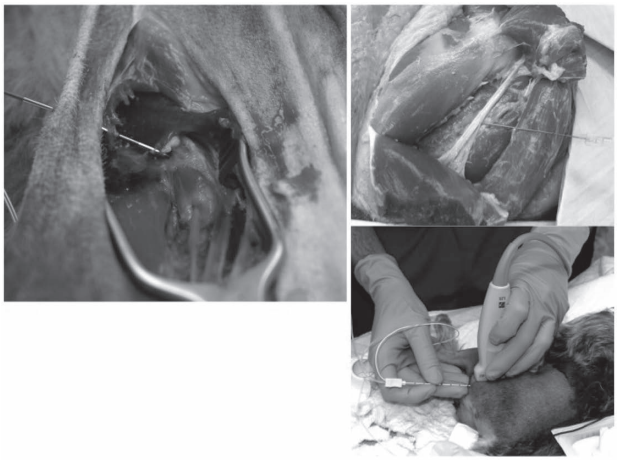
On this approach the animal is put on lateral recumbency and the pelvic limb is abducted and extended. The transducer is placed transversally on the medial portion of the thigh on the region of the femoral triangle. The pectineus muscle is easy to visualize medially as it looks like a triangle. Lateral to this muscle the anesthetist can identify the femoral vein and artery; further laterally the two bellies of the Sartorius can be identified. Medially to the Sartorius, the Rectus femoris can also be identified. The nerve is located craniolateral to the femoral artery and vein on the femoral triangle. Not that if the anesthetist is using US in conjunction to nerve stimulation, the needle needs to be placed dorsal to the Saphenous nerve, which is only a sensory nerve and won't provide muscle contraction, inducing great frustration on the anesthetist. The needle needs to be placed dorsally to the branches supplying the quadriceps muscles to elicit extension of the leg.

Iliopsoas Approach

Few authors have described this approach in various levels of the iliopsoas muscle. The potential advantage of this technique is that the femoral, obturator and lateral cutaneous femoral nerves run caudally within the iliopsoas muscle. Therefore targeting the femoral nerve in this location would improve spread of local anesthetic around the nerve, as well as, potentially blocking the obturator, but not the lateral cutaneous femoral nerve. A way that this author feels is easy to locate the femoral nerve on the Iliopsoas muscle, it is to start from the femoral triangle and follow the femoral artery cranially into the inguinal area where it joins the External iliac artery. Lateral and dorsal to the artery the operator is able to identify the Iliopsoas muscle and the potential femoral nerve. To make sure that the hyperechoic structure seen is the femoral nerve the operator can move the transducer on the dorsocaudal direction and follow the nerves trajectory. The femoral nerve enters the iliopsoas muscle on the level of L4 and L5 nerve roots dorsomedially and moves ventrolaterally during its trajectory caudally to the femoral triangle.

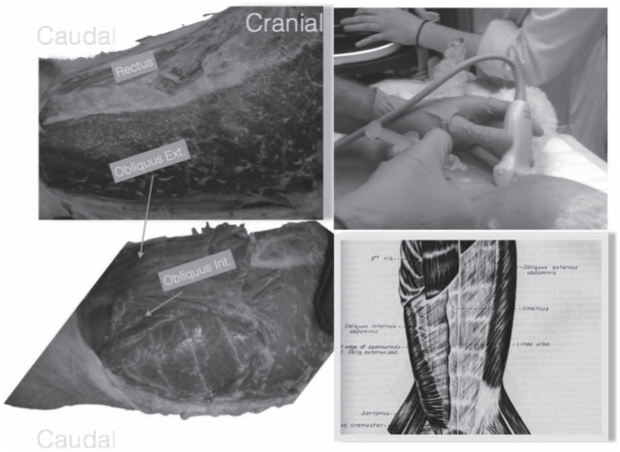
Sciatic Nerve

The Sciatic nerve can be visualized in several locations from the sacral area the mid femur. On the author's opinion, the easiest site to visualize and inject the sciatic nerve is on the lateral side of the limb just distal from the ischiatic tuberosity. The nerve can be visualized medial to the biceps femoris with the transducer placed transversely on the lateral portion of the limb under the fascia lata.



Transversus Abdominis Plane (TAP)

On the TAP technique, the needle is placed between the obliquus internus and the transversus abdominis muscles. The ventral branches of the cranial and caudal iliohypogastric nerves cross the aponeurosis of the transversus abdominis muscle and travel ventrocaudal until the mid of the abdomen where they have their cutaneous branches. The efficacy of the block is debatable. Two factors seem relevant, volume injected and injection sites, two sites (cranial and caudal) or one single cranial injection



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Tuesday 1st September | Room A | 13:50－14:50

L-3 Towards a better recognition of pain - differentiating emotional and sensory signs

○Daniel Mills
University of Lincoln, United Kingdom

Pain is an unpleasant sensory and emotional experience associated with the potential or actual threat of physical tissue damage. As such it involves more than mere sensation; it is a psychological state with three domains: sensory-discriminatory (intensity, location and duration of the pain), affective–motivational (emotional, unpleasantness and aversive aspects of pain), and cognitive–evaluative (evaluation of consequences of pain upon quality of life). In non-human animals the 'sensory-discriminatory' domain relates largely to bodily sensations associated with specific types of stimuli (e.g. pressure, temperature, burning, etc.). This is relatively easily provoked and the sensation is usually localised and therefore investigation of this can be relatively straightforward. By contrast the affective-emotional domain, which is usually most prominent in chronic situations, is more diffuse, but no less important if we are interested in protecting an animal's welfare. Although veterinary species cannot verbally self-report, recent innovations in the study of animal welfare mean this element is not inaccessible. However, exploration of the third domain is even more challenging, since it depends on the cognitive capacity of animals, and the study of processes such as metacognition and self-awareness which is in its infancy. However, it is important not to make the mistake of associating a lack of knowledge and hence evidence with an absence of these states. To understand the behavioural aspects of pain, we need to understand pain within this context, and as a starting point the distinction between emotional and sensory aspects of pain is fundamental. The emotional aspects of pain have an important influence on the self-report of pain perception in humans, but to date its importance in non-human animals has perhaps not been fully appreciated, because of difficulties with the study of emotions in these species. Recent developments in the study of animal behaviour however are beginning to shed more light on this topic.

Pain is one of the basic negative emotional states (alongside fear and frustration) which evolved early within the neural development of animals. In order to provide appropriate pain management, it is necessary to be able to first recognise and then assess the pain of an animal, before deciding on appropriate intervention. Since pain is an emotional response it is necessarily subjective and so cannot reliably be assessed simply from the environment or what has happened to the cat (although certain procedures will be obviously painful). This is particularly true in the case of chronic ongoing pain, such as occurs with chronic degenerative diseases like osteoarthritis. It is increasingly recognised that the assessment of pain can be made more reliable from the assessment of several measures and then using these scores to triangulate the evidence in order to make an inference. Behavioural approaches can be particularly useful as they are non-invasive and may not even involve disturbing the animal and potentially exacerbating its pain further, although in some situations provocation tests and physiological measures can add further valuable information. This approach has been used to develop pain scales, for example the UNESP-Botucatu Multidimensional Composite Pain Scale (UNESP-Botucatu MCPS) for cats see: http://www.animalpain.com.br/assets/upload/escala-en-us.pdf. This scale was the only one identified in a recent systematic review of pain assessment in this species (Merola and Mills 2015) to have published evidence of validity, reliability and sensitivity at the level of a Randomized Control Trial, but with a positive rather than placebo control, however it was developed for use within a specific context, i.e. post operatively in order to guide the use of analgesia, and as such, if adopted by veterinarians in practice might help ensure appropriate use of analgesia in the clinic hospital, but it is not so useful with regards to detecting pain as part of a presenting complaint. Similar problems, i.e. a lack of validation and limited context, exist with pain scales developed in other species.

Although this context is important, most pain and therefore welfare concern does not arise as a result of veterinary intervention, but rather as a result of chronic degenerative processes such as aging or wear and tear, which results in a more chronic (enduring) emotional change, and is often slow in onset, with no specific antecedent event. Developing a method to allow the recognition and assessment of pain without overt provocation or intrusion, before it becomes quite overt (by which time intervention options may be more limited) is a particularly challenging task. However, since the evolution of pain has an ancient lineage, it can be expected that basic observable features (often referred to as components in the literature- Scherer 1984) which define emotional responses will be present to a greater or lesser extent. These features are as follows:

1. Emotions involve a cognitive change, associated with the appraisal of stimuli, this means the response occurs in relation to stimuli having certain properties, and in the case of pain this means stimuli which have the potential to cause

actual bodily damage. However this is not sufficient for pain to be inferred, it is simply a necessary criterion.

2. Emotional responses involve a change in arousal. Physiological measures may be paricularly useful for assessing arousal, but behavioural correlates of the dominance of one part of the autonomic system over another are available, such as pupil dilation, visible ocular size, pilo-erection etc. It is important though to distinguish the arousal that occurs as a result of other contiguous activities, such as the specific sensory aspects of the painful stimulus from the more general emotional change. Arousal is often non-specific and difficult to quantify reliably. Nonetheless when making an assessment perhaps the important question is whether the direction of arousal is consistent with the prediction of pain. If the answer is "no" then we need to reject the hypothesis being tested, but not necessarily accept it, just because it is consistent- i.e. an appropriate change in physiological arousal is necessary but not sufficient to infer pain.
3. As a result of emotional arousal we also see a change in the behavioural tendencies of an individual. In the case of pain, this would include, protection of any specific pain focus but also more general strategies that avoid aggravating the pain, such as social withdrawal or in the case of highly social species with good social communication skills like dogs, care-solicitation from others.
4. The final component of emotional responses is their communication, this is typically done through facial expression. This has recently become a major area of interest in a range of species, as different forms of pain seem to be associated with reliable changes in the tone of the facial musculature. We are currently undertaking studies to see if we can build a self-learning computer programme that can detect these features and provide an initial prediction of the likelihood of pain from facial images. Initial results are very encouraging, but not sufficient on their own.

We have recently developed at Lincoln a systematic approach to the assessment of emotions in animals using this framework, as part of the need to develop a more evidence based approach in clinical animal behaviour. This has already revealed some interesting features of dogs in pain, presented for behaviour problems (Barcelos et al 2015) and started to apply it to develop better systems for the detection of pain in cats, with the support of an international panel of experts. At the same time we have also been critically appraising some of the fundamental concepts underpinning our approaches to the study of pain in non-human animals.

Using a modified Delphi approach we have identified reliable (i.e. sufficient) behavioural signs of pain in the cat, and their relationship with mild and more severe pain and the results will be presented for the first time at this meeting. This provides a model technique for elucidating this information for any species. We will then use this information to develop an instrument for the evaluation of pain by both veterinarians and owners and assess its quality (reliability, validity and sensitivity).

Our work using qualitative research methods has also demonstrated that the terms "acute" and "chronic" do not relate to reliable time courses as the etymology of the words might suggest, rather they refer to much more complex constructs extending beyond the duration of the pain. This includes its cause, intensity, potential to naturally heal and sensory-emotional impact on the subject.

In conclusion, out work shows that a multidisciplinary approach combining the skills of veterinary behaviour scientists and clinicians has the potential to not only help identify the specific signs of pain in the various species we deal with, but also (and perhaps more importantly) develop sound methodologies that can be translated across species easily.

Acknowledgments

I would like to thank the charity Feline Friends (Derbyshire) for supporting our work on feline pain that has allowed the developments reported here

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Tuesday 1st September | Room A | 14:50−15:50

L-4 Veterinary Anaesthesia - Past, Present and Future

○Dimitris Raptopoulos
Aristotle University of Thessaloniki, Greece

Introduction

The word 'anaesthesia' was originally been used by the ancient Greek philosopher Plato in the 4th century B.C. Plato used the word to mean the condition where the impulse is not transmitted to, or announced to the brain.

Anecdotal evidence exists that even from the ancient times various remedies from herbs were administered to animals in pain, especially to horses suffering from colic. During the 1830s it was from the observation that minor injuries were painlessly sustained during nitrous oxide or ether inhalation, during the nitrous oxide parties or the 'ether frolics', that the discovery of anaesthesia for surgical operations arose[1].

The history of veterinary anaesthesia can be said that it started in 29 January, 1847, when the earliest use of anaesthesia in veterinary practice was recorded. It was the first reported administration of ether to a horse, a few months after the first successful public demonstration in humans[1]. In 1876, the Cruelty to Animals Act in the UK required researchers to anaesthetise animals before experimentation involving the infliction of pain. And the Animals Anaesthetic Act of 1919 required animals to be anaesthetised for surgical operations.

Veterinary Anaesthesia

In small animals, ether and chloroform were commonly administered in the early part of the 20th century. However, general anaesthesia became more widely accepted after the discovery of barbiturates in the late 1920s. In the 1940s at the *Royal Veterinary College* in London endotracheal intubation was carried out[1]. But the modern era of veterinary anaesthesia begins in the 1950s when the concept of balanced anaesthesia in small animals was developed in the 1950's[2].

Until then, anaesthetic techniques consisted mainly of intravenous barbiturates and di-ethyl ether administered by semi-open masks. Many new drugs became available in the 50's, but the discovery of halothane in 1956 was the real stimulus to the development of inhalational anaesthesia not only for small but also for large animals, and it led to the development of equipment for that purpose[2].

The Specialty of Veterinary Anaesthesia

Since then, Veterinary Anaesthesia has made a tremendous progress, so that it has indeed changed from art to science and now has become a very dynamic specialty. The armamentarium of veterinary anaesthesiologists includes virtually all the drugs used in human anaesthesia, as well as purpose made, high quality, sophisticated anaesthetic machines and monitoring equipment. The combined subject of anaesthesia, pain management and intensive care has been introduced in the curriculum of all Veterinary Schools. In many Universities specialists were appointed, and positions of professorship in Veterinary Anaesthesiology were opened. Indeed some Veterinary Anaesthesiologists have reached the highest positions, and became Heads of Departments, Deans, Vice Rectors or Rectors of their Universities.

Veterinary Anaesthesiology, as a specialty in Europe, goes back to the early 1950's, when *Barbara Weaver* and *Leslie Hall* in England, endeavoured to close the gap between anaesthesia for animals and for humans[1].

Gradually, in 1964 the *Association of Veterinary Anaesthetists* (AVA) was established. In 1968, there were 46 members, and now there are more than 550.

In North America, the status of Veterinary Anaesthesiology, and the evolutionary needs for a specialty group, received casual interest during the early to mid 1960's, and began to make significant progress in the early 1970's. In 1970, the *American Society of Veterinary Anesthesia* was formed.

Postgraduate Education in Veterinary Anaesthesia

The specialty of Veterinary Anaesthesia offers many possibilities for post-graduate education. This includes studies for both academic, Master and PhD, and professional degrees, which include National Diplomas, and the Diploma awarded by the European and American Colleges of Veterinary Anaesthesia and Analgesia (ECVAA and ACVAA). The Diploma of Veterinary Anaesthesia (DVA) of the Royal College of Veterinary Surgeons, which started in the mid-60s, has been phased out in favour of the European College of Veterinary Anaesthesia and Analgesia Diploma.

In North America, in 1971 the *American Society of Veterinary Anesthesia* facilitated the establishment of the *American College of Veterinary Anesthesiologists* (ACVA), which in 1975 was approved by the *American Veterinary Medical Association*[3]. The College now (beginning of 2015) has a total of over 250 Diplomates, of whom over 220 are active.

In 1995, a further improvement was the establishment of the *European College of Veterinary Anaesthesia* (ECVA) and the development of the specialist Diploma, the Diploma of the European College of Veterinary Anaesthesia. To date (beginning of 2015) there are 150 Diplomates, of whom 135 are active.

The majority of Diplomates of both Colleges are in

academia, and a number of them work in specialty practices, as consultants, or in the pharmaceutical industry.

Veterinary anaesthesiologists are the specialists involved in the recognition and management of pain, both in research and veterinary practice. Therefore, analgesia was incorporated in the residency training programmes, and the ECVA was renamed to *European College of Veterinary Anaesthesia and Analgesia* (ECVAA) in 2007. Also recently the ACVA was also renamed to *American College of Veterinary Anesthesia and Analgesia* (ACVAA).

Apart from North America and Europe, specialist Associations are also found in other parts of the world. In Australia and New Zealand the *Australian and New Zealand College of Veterinary Scientists* was established in 1971. Within the College there are many Chapters, one of which is the Chapter of *Anaesthesia and Critical Care*, with more than 35 Members, 6 Fellows, and a small number of Associate Members. Members have a superior level of knowledge but not at the specialist level, while Fellowship was established as the specialist level.

In Japan, anaesthesiologists are members of the Japanese Society of Veterinary Anesthesia and Surgery with 1400 members, who are however, members of the unified Association without a distinction between the two disciplines. Five individuals work exclusively and 3 mainly on Anaesthesiology, all in academia. In other Asian countries, e.g. Thailand and Taiwan, there is also a small number of veterinarians working in Anaesthesiology.

In Brazil, the Brazilian College of Veterinary Anaesthesiology and Surgery started in 1972. However, a separate *Brazilian College of Veterinary Anaesthetists* was established in 2012. The College has now 150 members, of whom 16 are National Specialists, 8 ACVAA Diplomates, and 1 ECVAA Diplomate.

Veterinary Anaesthesiology is supported by a rich specialised bibliography. The first textbook for anaesthesia in animals by FTG Hobday, was published in 1915[4]. However, the foundations for modern veterinary anaesthesia were laid by JG Wright, who wrote what was for many years the only available textbook on the subject, the first edition appearing in 1941[5]. From the 1960s until very recently, a number of veterinary anaesthesia books have been published in various countries. Moreover, there is a specialised journal, the *Veterinary Anaesthesia and Analgesia* (VAA), published by Blackwell.

A number of veterinary anaesthesia meetings are organised every year. The first meeting was held in Cambridge, UK, in October 1964. Then, successful meetings of the AVA are held twice a year in Europe, with increasing international attendance. In 1970, the first meeting specifically on anaesthesia was held in USA and since then, it is organised once a year. In 1982, the first *International Congress of Veterinary Anaesthesia* (ICVA) took place also in Cambridge, UK. Since then, an International Congress takes place every third year, in various countries. It really is a World Congress, as participants come from many countries all over the world. Thus, in 1997, during the 6th ICVA in Greece, it was renamed to *World Congress of Veterinary Anaesthesiology* (WCVA).

Professional Veterinary Anaesthesia

In developed countries, the professional Associations like the *American Animal Hospital Association* have among their set of required standards for hospital accreditation, a set of requirements for anaesthesia practice and for pain management. Similar set of requirements for animal hospitals and practices have been set by the RCVS and the *British Small Animal Veterinary Association* (BSAVA) in the United Kingdom. In other countries too, the standards for veterinary practice, especially those for companion animals including horses, have been raised and keep on rising considerably.

However, in less developed countries the situation may be quite different. There are considerable problems concerning the availability of anaesthetic and ancillary drugs, and of anaesthetic and monitoring equipment. Training of veterinary surgeons is also a limiting factor. Factors like standard of living, education, and culture also play an important role, a situation that hopefully will improve.

Future developments will include improvements in anaesthesia in all species of animal, improvements in pain management, as well as improvements in education. Regarding the latter, efforts should be made for strong undergraduate teaching programmes, residency training programmes, continuing education programmes, including programmes for practitioners and technicians, and for the development of special instructional materials.

Acknowledgements

I particularly acknowledge BMQ Weaver, RS Jones, C Short, Y Moens, K Mama, L Cullen, S Luna, P Kronen, and R Nishimura who supplied their first hand information for this review.

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Tuesday 1st September | Room A | 14:50−15:50

L-4 History and Future of Veterinary Analgesia

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This brief excerpt elucidates some historical employments of analgesia. Clearly three different types of analgesic techniques at least stem from ancient times and were used by the ancient egyptians, greeks and chinese. Some parts of the historical use and development of opioid-, electro- and acupuncture-analgesia is discussed.

The history of newer analgesic drug classes as the local anaesthetics and the non-steroidal anti-inflammatory drugs is briefly elaborated.

More modern developments, such as alpha-2 agonist analgesia, dissociative analgesia, use of antidepressant and anticonvulsant drugs, implantable electrical stimulation devices, vanilliod-receoptor angostists/-antagonists, and most importantly combination therapy is discussed. Possible near-future molecular targets and application methods are also mentioned. Particularly, the different approaches to viewing pain over the ages seems an interesting topic to discuss and acute and chronic pain today and in the future even more create different necessities in veterinary practice. We are faced with special challenges in veterinary medicine when compared to human medicine and have to take this into account when trying to develop strategies for treatment. The World Congress of Veterinary Anaesthesiology seems particularly adept to discuss global scale developments in veterinary analgesia.

Tuesday 1st September | Room D | 10:20–11:20

L-5 Regulation mechanisms of TRPV1 and TRPA1

○Makoto Tominaga
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A wasabi receptor TRPA1 and a capsaicin receptor TRPV1 are two major receptors expressed in the small primary sensory neurons and involved in nociception activated by various chemical and physical painful stimuli. Their involvement in nociception has been proven using mice lacking TRPA1 or TRPV1. I would like to talk about our recent works regarding regulation mechanisms of TRPA1 and TRPV1.

We identified an alternative splice variant of the mouse *Trpa1* gene which we designated *Trpa1b* while full-length *Trpa1* was called *Trpa1a*. TRPA1a (full-length) and TRPA1b (splice variant) physically interacted with each other and TRPA1b increased the expression of TRPA1a in the plasma membrane. TRPA1a and TRPA1b co-expression significantly increased current density in response to different agonists without affecting their single-channel properties. Exogenous overexpression of *Trpa1b* gene in wild-type and TRPA1KO DRG neurons also increased TRPA1a-mediated allylisothiocyanate (AITC) responses. Moreover, expression levels of *Trpa1a* and *Trpa1b* mRNAs changed dynamically in the two pain models (complete Freund's adjuvant-induced inflammatory pain and partial sciatic nerve ligation-induced neuropathic pain models), and DRG neurons from the model mice showed increased responses to AITC. These results suggest that TRPA1 may be regulated through alternative splicing under these pathological conditions.

It is believed that cation influx through TRPV1 causes depolarization, leading to the activation of voltage-gated sodium channels, followed by action potential generation. We found that the capsaicin-evoked action potential could be induced by two components: a cation influx-mediated depolarization due to TRPV1 activation and a subsequent anion efflux-mediated depolarization via activation of anoctamin 1 (ANO1), a calcium-activated chloride channel, due to the entry of calcium through TRPV1. The interaction between TRPV1 and ANO1 was based on their physical binding. Capsaicin activated the chloride currents in an extracellular calcium-dependent manner in HEK293T cells expressing TRPV1 and ANO1. Similarly, in mouse DRG neurons, capsaicin-activated inward currents were significantly inhibited by a specific ANO1 antagonist, T16Ainh-A01 (A01) in the presence of a high concentration of EGTA, but not BAPTA. In addition, the generation of a capsaicin-evoked action potential was inhibited by A01. Furthermore, pain-related behaviors in mice treated with capsaicin, but not with α,β-methylene ATP, were significantly reduced by the concomitant administration of A01. These results indicate that TRPV1-ANO1 interaction is a novel pain-enhancing mechanism in the peripheral nervous system. Thus, inhibition of *Trpa1b* or TRPV1-ANO1 interaction would be an intriguing way to develop novel analgesic agents.

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Tuesday 1st September | Room D | 11:20–12:20

L-6 Neural mechanisms for pain-induced negative emotion

○Masabumi Minami
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Pain is an unpleasant sensory and emotional experience. The neural systems underlying the sensory component of pain have been studied extensively, but we are only beginning to understand those underlying its emotional component. The bed nucleus of the stria terminalis (BNST) has been implicated in stress responses and negative affective states, such as anxiety, fear, and aversion.

In the present study, we first examined the role of the neurotransmission via noradrenaline (NA) receptors within the ventral part of BNST (vBNST) in pain-induced negative emotion in male Sprague–Dawley rats. *In vivo* microdialysis demonstrated that NA release within the vBNST was significantly elevated by formaline-evoked noxious stimulus. We evaluated pain-induced negative emotion by a conditioned place aversion (CPA) test. Intra-vBNST injection of a beta-adrenoceptor antagonist timolol significantly suppressed formaline-induced CPA (F-CPA) without affecting nociceptive behaviors. Furthermore, we found that intra-vBNST injection of isoproterenol, a beta-adrenoceptor agonist, dose-dependently produced CPA even in the absence of noxious stimulus. These results suggest that noxious stimulus-induced NA release within the vBNST is involved in the pain-induced negative emotion.

Next, we examined the role of the CRFergic and NPYergic transmissions within the dorsolateral part of the BNST (dlBNST) in pain-induced negative emotion in rats. We observed the increased release of CRF within the dlBNST by intraplantar formalin injection. Intra-dlBNST injection of CRF receptor antagonists dose-dependently attenuated the F-CPA without reducing nociceptive behaviors. Intra-dlBNST injection of CRF dose-dependently produced CPA even in the absence of noxious stimulus. On the other hand, intra-dlBNST injection of NPY suppressed F-CPA. Co-administration of NPY inhibited CRF-induced CPA. These results suggest the opposing roles of CRF and NPY in pain-induced negative emotion.

In order to address cellular mechanisms for these effects of CRF and NPY, we examined the effects of CRF and NPY on neuronal activity in dlBNST neurons using whole-cell patch-clamp recordings. Whole-cell patch-clamp recordings from dlBNST slices revealed that CRF increased neuronal excitability specifically in type II dlBNST neurons, whereas NPY decreased it in these neurons. Excitatory effects of CRF on type II dlBNST neurons were suppressed by NPY. These results have uncovered some of the cellular mechanisms underlying pain-induced negative emotion by showing opposing actions of these peptides on neuronal excitability converging on the same target, type II neurons, in the dlBNST.

To clarify the neuronal circuits involved in pain-induced negative emotion, we characterized VTA-projecting BNST neurons using combined neurotracing and immunohistochemistry. The majority of BNST-VTA projections originates from GAD67-expressing GABAergic neurons in the BNST, and preferentially targets GABAergic interneurons in the VTA, suggesting the disinhibitory control of VTA dopaminergic neurons by BNST-VTA projection. I will discuss the neuronal circuits for pain-induced negative emotion.

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Tuesday 1st September | Room D | 13:50−14:50

L-7 Descending pain modulatory system and its activation by systemic alpha 2 agonist

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National Institute for Physiological Sciences, Japan

Behavioural responses to pain stimuli are well-known to be modified by arousal, attention and expectation possibly through activation of central nervous system (CNS) networks that modulate the transmission of nociceptive information. Noradrenergic descending system originating from the locus coeruleus (LC, a dense cluster of noradrenergic neurones) in the dorsal pons located either side of the floor of the fourth ventricle is one of the major central pain modulating pathways. The activity of noradrenergic neurons in the LC is thought to be controlled by the frontal lobe, amygdala and hypothalamus through the periaqueductal grey, and the neurons extend their descending axons to the spinal superficial dorsal horn to release noradrenaline and inhibit nociceptive information conveyed by the peripheral nociceptive primary afferents. They also send projections to most regions of the CNS. Therefore, the LC is implicated not only in pain modulation but also in the control of many homeostatic functions such as arousal and performance. The firing and subthreshold synaptic mechanisms of noradrenergic neurons in the LC have been studied in detail using brain stem slices and dissociated preparations. However, these types of in vitro study provide a limited insight into the integrated homeostatic functions of the LC networks including descending pain modulatory system.

Alpha-2 adrenoceptors are widely expressed in the CNS and the alpha-2 agonists are clinically used as sedative agents. Neurons in the LC and spinal superficial dorsal horn and their presynaptic terminals also express alpha-2 adrenoceptors. Previous studies using brain stem slices have suggested that the sedative action of alpha-2 agonists is primarily mediated by inhibition of the noradrenergic neuronal firings in the LC. Activation of alpha-2 adrenoceptors induces hyperpolarization through activation of GIRK potassium channels via $G_{i/o}$-proteins, and acts as an autoreceptor to reduce local noradrenaline release. In the spinal superficial dorsal horn, an alpha-2 agonist is reported to have a direct inhibitory action to hyperpolarize spinal superficial dorsal horn neurons to inhibit spinal nociceptive transmission. Little is known, however, how systemic alpha-2 agonist affects the noradrenergic descending system from the LC to the spinal cord.

In order to elucidate detailed characterization of the integrative mechanisms of descending inhibitory control of pain, we have developed in vivo patch-clamp recording techniques from neurons in the LC and spinal superficial dorsal horn which enable us to analyze the neuronal firings and subthreshold synaptic inputs in response to natural sensory stimulation under physiological conditions[1, 2]. Using the in vivo electrophysiological techniques in combination with an optogenetic approach to selectively activate noradrenergic neurons in the LC[3] (Figure 1A), we examined how descending noradrenergic system modified spinal nociceptive transmission[4], and further studied sedative and antinociceptive actions of systemic administration of an alpha-2 agonist, dexmedetomidine, mediated through the LC and descending noradrenergic neurons[5].

Under urethane-anesthesia, noradrenergic neurons in the LC of rats tested fired spontaneously in vivo. Cutaneous noxious stimuli applied to the contralateral hind limb transiently increased and then decreased the frequency of action potential discharges. Light stimulation applied to the noradrenergic neurons in the LC expressing channelrhodopsin 2 (ChR2), a light-activated nonselective cationic channel, increased the firing frequency, and even in deeply anesthetized animals with supplemental inhaled anesthetics, an optoactivation of LC was detected and the excitation was lasted during the light stimulation. In vivo patch-clamp recordings were made from spinal superficial dorsal horn neurons, and we first examined action of bath-applied noradrenaline on the spinal neurons. Noradrenaline superfused to the surface of the spinal cord induced a hyperpolarization in superficial dorsal horn neurons, and also elicited a barrage of inhibitory postsynaptic currents mediated by GABA and glycine. The noradrenaline-induced spinal hyperpolarization and enhancement of inhibitory synaptic transmission were mediated by alpha-2 and alpha-1 receptors, respectively. When noradrenergic neurons were optoactivated, the frequency of spinal inhibitory postsynaptic currents was drastically increased. However, hyperpolarization or any of slow postsynaptic currents were elicited in spinal superficial dorsal horn neurons. Low-dose dexmedetomidine applied through the femoral vein at doses below that shown to have sedative actions on the EEG or to produce loss of righting reflex dramatically enhanced spinal inhibitory transmission (Figure 1B) without eliciting any of membrane hyperpolarization. This was due to a paradoxical activation of the pontospinal descending noradrenergic system, and the enhancement of spinal GABAergic/glycinergic inhibitory transmission was mediated through alpha-1 adrenoceptors. Conversely, higher doses of

dexmedetomidine strongly inhibits LC neurons, probably producing the sedative effect of dexmedetomidine and simultaneously induced hyperpolarization of spinal superficial dorsal horn neurons via the direct alpha-2 activation which likely produces additional analgesic effects.

These results reveal a novel antinociceptive mechanism for systemic alpha-2 adrenoceptor agonists at low doses via the facilitation of spinal inhibitory synaptic transmission. This occurs at doses that are below the sedative range and may allow useful dissociation of the analgesia and sedation clinically and may also in part account for the known potent synergy between dexmedetomidine and anesthetics that potentiate inhibitory synaptic responses.

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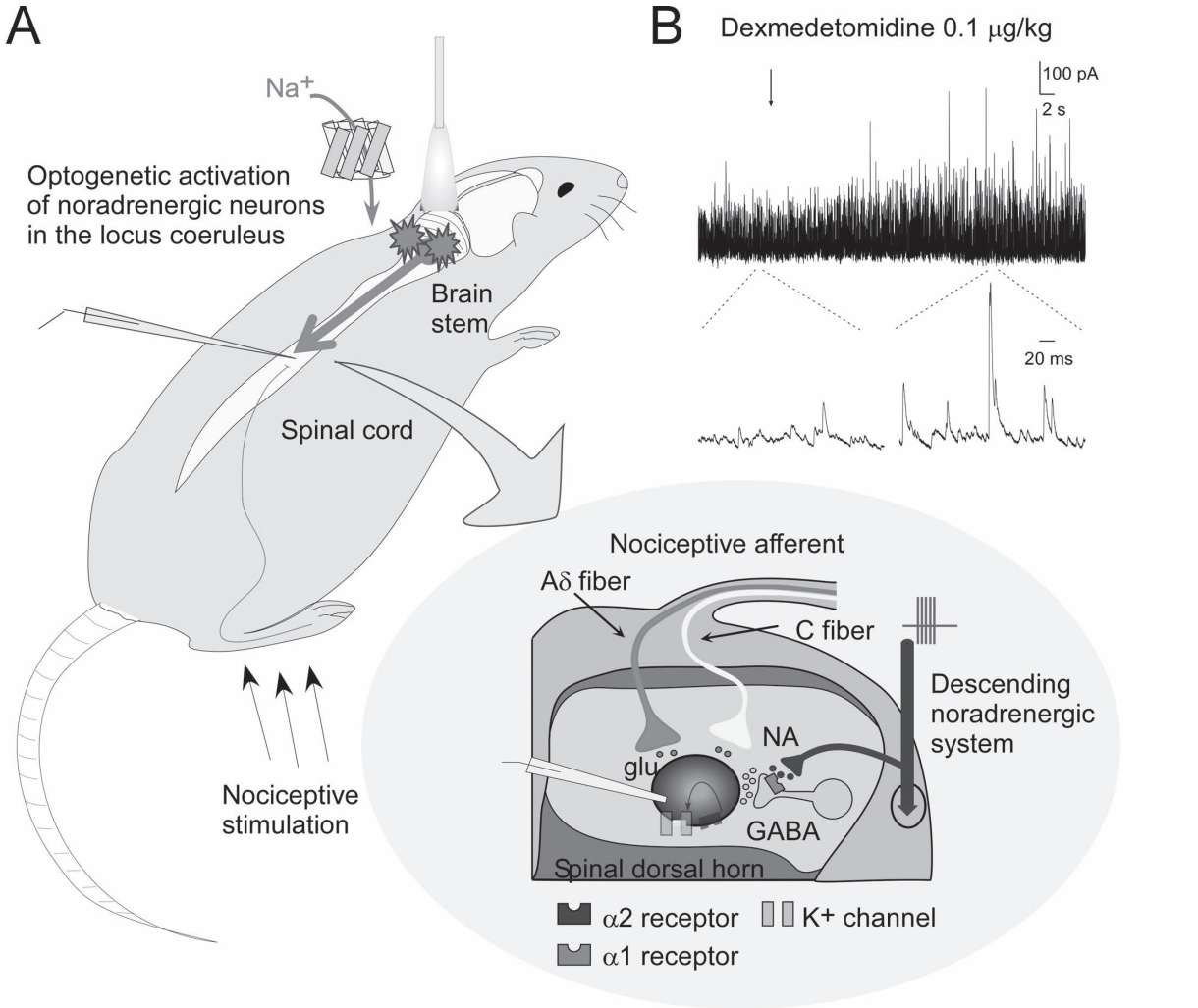
Legend

Figure 1 Schematic summarizing optactivation of noradrenergic neurons in the locus coeruleus in vivo and the descending control of pain in the spinal dorsal horn (A), and systemic action of dexmedetomidine showing an enhancement of spinal inhibitory postsynaptic currents (modified from Ref. 5) (B).



L-8 PK/PD integration and PK/PD modeling of NSAIDs in the cat: The example of Robenacoxib

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Nowadays, nonsteroidal anti-inflammatory drugs (NSAIDs) are extensively used for the relief of pain and inflammation in the cat, both perioperatively and for the control of pain associated with musculo-skeletal disorders. It is increasingly recognized that dosing regimens need be established based on studies performed in the target species and this observation certainly applies to NSAIDs in the cat (Toutain, 2002; Lees et al., 2004). Authors have previously shown that it was mainly cyclooxygenase-2 (COX-2) derived prostanoids that were involved in inflammation, pain and pyrexia (Zhang et al., 1997), whereas compounds associated with the greatest gastrointestinal side effects had the greatest cyclooxygenase-1 (COX-1) potency (Warner et al., 1999). These findings provided a rationale for the development of selective COX-2 inhibitory anti-inflammatory drugs (Mitchell and Warner, 1999). Several pre-clinical approaches have been used to evaluate the COX inhibition profiles of various NSAIDs and determine the appropriate NSAID dose for subsequent evaluation in clinical trials. These approaches will be presented using robenacoxib, a highly COX-2 selective drug, as an example.

Using pharmacokinetic/pharmacodynamic (PK/PD) integration with *in vitro* or *ex vivo* determined concentrations corresponding to submaximal inhibition of COX-2, it is possible to make preliminary proposals for clinically relevant doses of NSAIDs (Giraudel et al., 2005a; Warner et al., 1999).

With a refined whole blood assay, Giraudel et al (2009b) determined a robenacoxib potency inhibition ratio (COX-1/COX-2) of 502 (Table 1). In this work, several additional indices of selectivity were determined because the authors noted that, for some drugs, the ratio of COX-1 over COX-2 inhibition was profoundly influenced by the difference between the slopes of the COX-1 and COX-2 inhibition curves. It was therefore suggested that the comparison between COX-1 inhibition and COX-2 inhibition had to be established at what is believed to be therapeutically efficacious concentrations (eg inhibitory concentration $(IC)_{80}$ for COX-2) and that these indices improve the characterization of the pharmacodynamics of existing and novel compounds. Indeed, if it is confirmed that at drug concentrations corresponding to high levels of COX-2 inhibition (80% or higher COX-2 inhibition), the corresponding level of COX-1 inhibition is low, the drug can be considered highly selective and the COX-2 selectivity can be assumed to translate in an *in vivo* situation.

Table 1 - Three categories of indices describing the selectivity of robenacoxib in feline whole blood assays.

Indices*	Values
Classical selectivity ratios (IC_X COX-1 / IC_X COX-2):	
IC_{50} / IC_{50}	502.3
IC_{80} / IC_{80}	477.7
Other selectivity ratios (IC_X COX-1 / IC_Y COX-2):	
IC_{20} / IC_{80}	17.05
% Inhibition of COX-1 for a fixed % inhibition of COX-2:	
% Inhibition of COX-1 for IC_{50} COX-2	0.56
% Inhibition of COX-1 for IC_{80} COX-2	2.31

*Classical selectivity ratios are presented. Selectivity is also expressed as a suggested safety factor calculated as a ratio of a cut-off concentration corresponding to a level of COX-1 inhibition above which unacceptable side-effects might occur divided by a concentration producing a level of COX-2 inhibition considered to be required for therapeutic efficacy. The third category of indices gives the percentage by which COX-1 is inhibited for a given inhibition percentage of COX-2.

Because drug protein binding is taken into account in whole blood assays, an *in vivo* dose can be calculated using *in vitro* determined concentrations (eg IC_{50} or IC_{80} for COX-2 inhibition), provided the pharmacokinetic parameters of the drug are known

for the intended route of administration:

$$\frac{\text{Dose}}{\text{Dosing Interval}} = \frac{\text{Total Clearance} \times \text{Target Concentration}}{\text{F}}$$

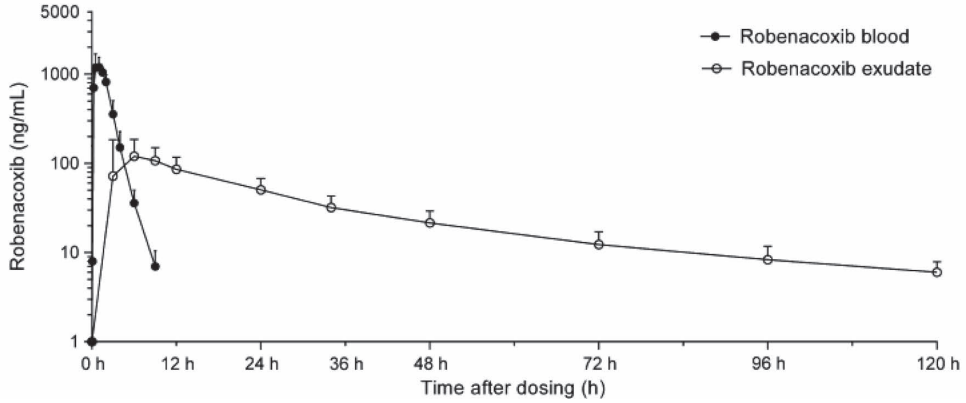
where Dose/Dosing Interval is the dose to be administered *in vivo* to give, in steady-state conditions, an average concentration over the dosing interval equal to the Target Concentration, Total Clearance is the total blood clearance of the test compound, F is the bioavailability and Target Concentration is the blood concentration to be achieved to obtain a desirable effect.

If the IC_{50} for COX-2 inhibition is taken as the target concentration to be reached and if the pharmacokinetic parameters of robenacoxib after subcutaneous administration in the cat are used (Giraudel et al., 2009b), the predicted dose of robenacoxib would be 0.3 mg/kg/24h. Previous authors have suggested that it is more relevant to use IC_{80} as the target concentration for an NSAID, because steady state plasma concentrations for commonly used NSAIDs often correspond to an IC_{80} for COX-2 inhibition (Warner et al., 1999). If the IC_{80} for COX-2 inhibition is taken as the target concentration to be reached, the predicted dose of robenacoxib would be 1.5 mg/kg/24h, which is very close to the recommended subcutaneous dose of 2 mg/kg.

An alternative to performing an *in vitro* whole blood assay followed by an *in vivo* pharmacokinetic study is to use an *ex vivo* approach where blood samples are taken from treated cats, at pre-determined times, in order to determine the blood robenacoxib concentration-time profile as well as measure *ex vivo* the time course of inhibition of COX-1 and COX-2 in whole blood assays. The advantage of such an approach is that it allows all of the parameters needed to calculate a preliminary *in vivo* efficacious dose using the equation presented above, to be determined in one experiment. An *ex vivo* experiment also takes into account some pharmacokinetic characteristics (eg accumulation of the active compound in the target cells, biotransformation leading to active metabolites) that can affect COX inhibition profiles. It is nevertheless required that the dose selected in the *ex vivo* experiment results in high enough NSAID concentrations to evaluate the entire drug concentration – COX-2 inhibition relationship.

A tissue cage model of acute inflammation based on the intracaveal injection of the mild irritant carrageenan provided additional insights into the pharmacokinetic and COX inhibition properties of robenacoxib. The authors measured the pharmacokinetic profile of robenacoxib both in blood and in the tissue cage and used serum TxB_2 and exudate PGE2 as surrogate markers for COX-1 and COX-2 activity, respectively (Pelligand et al., 2012; Pelligand et al. 2014). The objective of this work was to determine the COX inhibition profiles and the COX-2 selectivity of robenacoxib in situations that are more clinically relevant than *in vitro* studies, as well as to explore the selectivity of the drug for inflamed tissues. As in previous studies, the apparent blood clearance of robenacoxib was relatively rapid (0.68 L/kg/h) and the elimination half-life was relatively short (1.1 h) but the elimination half-life from exudate was approximately 41 h and the inhibition of the PGE2 synthesis in exudate was significant for up to 36 h (Pelligand et al. 2014), suggesting a longer duration of action in a clinical setting than what is predicted from the drug's blood clearance and elimination half-life (Figure 1).

Figure 1 – Robenacoxib concentrations in blood and inflammatory exudate after a 2 mg/kg subcutaneous administration to cats implanted with tissue cages.



Although it is well known that different experimental protocols and models can lead to different results in terms of IC_{50} values (Warner et al., 1999; Lees et al., 2004), it is interesting to note that the three very different approaches described above gave similar results, demonstrating consistently that robenacoxib is highly COX-2 selective and that this level of selectivity would lead *in vivo* to very low COX-1 inhibition levels. Using the classical whole blood assay, Schmid et al (2010) calculated an IC_{50} COX-1 / IC_{50} COX-2 ratio of 32, whereas this ratio was 171 in the tissue cage model (Pelligand et al., 2012). In this

latter model the IC_{50} COX-2 was 14 ng/mL, which is very close to the value of 19 ng/mL calculated by Giraudel et al (2009b).

Despite the usefulness of these approaches for NSAIDs, the measurement of COX-2 inhibition, whether it is *in vitro*, *ex vivo* or *in vivo*, has several limitations. Indeed, it is unclear what the exact level and duration of COX-2 inhibition needs to be in order to result in the expected clinical response, and it is difficult to measure COX-2 inhibition in the target tissues. COX-2 inhibition might also not be the only mechanism of action and other possible mechanisms of NSAID action have been described (inhibition of lipoxygenase, decrease in cytokine production, increase in inducible nitric oxide synthase production), which could result in *in vivo* efficacious doses being different from those predicted based on COX inhibition only. *In vivo* measurements of NSAID potency and efficacy for anti-inflammatory, analgesic and antipyretic effects are therefore necessary to select appropriate dose schedules for subsequent evaluation in clinical trials.

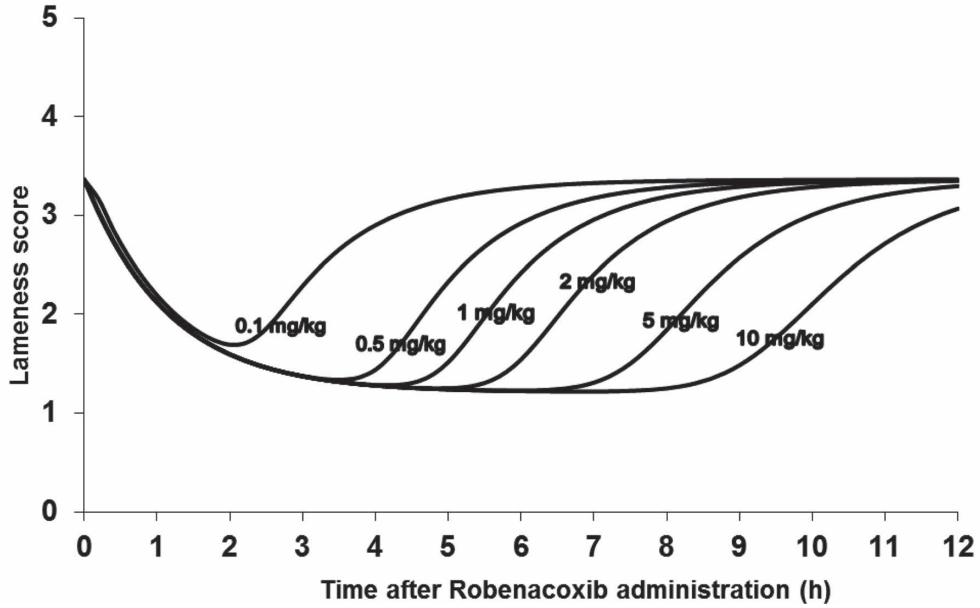
Preclinical dose determination studies may be based on the conventional dose titration approach but this approach has several disadvantages and limitations. As an alternative, PK/PD integration and PK/PD modelling may be used (Toutain, 2002) and it is increasingly accepted that PK/PD modelling is a powerful approach for predicting effective and safe dosage regimens for clinical use (Toutain, 2002; Lees et al., 2004). However, information on the relationship between blood/plasma concentration and analgesic or anti-inflammatory effect is limited for NSAIDs because most inflammation models do not permit PK/PD modelling to be conveniently performed. Another requirement for implementing PK/PD approaches is the availability of accurate quantitative measurements of clinically relevant endpoints or surrogate endpoints that reflect drug efficacy. An ethically acceptable *in vivo* model of inflammation and pain was developed by Giraudel et al (2005b and c) and different clinical and surrogate endpoints were selected to establish therapeutic efficacy of NSAIDs in the cat. The pre-clinical characterization of the pharmacodynamic profile of robenacoxib (determination of efficacy, potency, sensitivity and duration of drug response) was performed using this paw inflammation model and a PK/PD modelling approach (Giraudel et al., 2009a).

For skin and body temperature and climbing, lameness, pain and descending scores clear drug responses were consistently obtained after robenacoxib administration. The mean time of peak response was similar for all endpoints, occurring between 2.6 and 3.5 hours after drug dosing. Mean minimum body temperature after robenacoxib administration (38.3°C) was similar to mean baseline temperature (38.6°C) before kaolin injection, indicating that complete suppression of hyperthermia was achieved with a 2 mg/kg dose of robenacoxib. Climbing, descending and pain scores also returned to baseline levels after robenacoxib administration.

Because the onset of robenacoxib responses was very rapid, the total duration of response was considered to correspond to the time between drug administration and disappearance of drug response. Statistical analyses comparing values of each endpoint after drug administration with pre-treatment values (obtained just before robenacoxib administration) demonstrated that duration of drug response ranged from 4.6 hours (descending time) to 8.1 hours (lameness score), with an average of approximately 6 hours. The relatively high inter-animal variability observed for most endpoints translated into a high variability for the model and drug parameters (e.g. CVs for potency ranged from 48 % (body temperature) to 86 % (descending score)). For most parameters there were also differences depending on the endpoint considered. This was especially true for potency, with mean values ranging from 39 ng/ml (lameness score) to 168 ng/ml (skin temperature difference).

Data sets for which acceptable PD fittings were obtained and for which drug and model parameters were estimated with adequate precision, were used to simulate average drug response profiles for several dosage regimens. Figure 2 illustrates for the lameness score the simulated average drug response profiles for doses of robenacoxib ranging from 0.1 to 10 mg/kg. It is predicted that the lowest dose (0.1 mg/kg) would give only a very small drug response, 0.5 mg/kg would provide nearly maximal efficacy but drug response would be transient, whilst a 2 mg/kg dose would provide good efficacy during 5 to 7 hours. Moreover, for a dose of 10 mg/kg robenacoxib, the duration of drug response would be extended, but only to 8 to 11 hours.

Figure 2 - Simulated time profiles of lameness score for single dose administrations of 0.1, 0.5, 1, 2, 5 and 10 mg/kg robenacoxib.



Using *in vitro* results obtained with robenacoxib in feline whole blood assays (Giraudel et al 2009b), predicted COX-1 and COX-2 inhibition levels for different dosage regimens of robenacoxib were calculated to provide information on the clinical relevance of the COX-2 selectivity of this drug (Table 2). Potencies for *in vitro* COX-1 and COX-2 inhibition were also compared with potencies obtained after PK/PD modelling and the potencies for clinical response (EC50 or Effective Concentrations achieving 50% of the maximal drug response) corresponded to concentrations inhibiting COX-2 by 79% to 94%, which is line with the observation by Warner et al (1999) that high levels of COX-2 inhibition are usually required to achieve the desired clinical response.

Table 2 - Predicted inhibition percentages of COX-1 and COX-2 for different single dose administrations of robenacoxib. Blood concentration vs. time profiles were simulated with average pharmacokinetic parameters obtained after subcutaneous administration of 10 cats with 2 mg/kg robenacoxib. ICs (concentrations producing different levels of COX-1 and COX-2 inhibition) were obtained in feline whole blood assays (Giraudel et al., 2009b).

Parameter	Value
% inhibition of COX-1 corresponding to the average blood concentration[a]	5.1
inhibition of COX-2 corresponding to the average blood concentration	89.8
% inhibition of COX-1 corresponding to the maximal blood concentration	19.6
% inhibition of COX-2 corresponding to the maximal blood concentration	97.5
Time above IC_{50} for COX-2 (h)[b]	6.5
Time above IC_{80} for COX-2 (h)	4.1
Time above IC_{10} for COX-1 (h)	2.0
Time above IC_{20} for COX-1 (h)	0.0

[a]Predicted level of COX-1 inhibition (%) corresponding to the average robenacoxib concentration achieved over the first 12 hours following a single SC administration of robenacoxib

[b]Predicted time (h) during which the robenacoxib blood concentrations exceed a concentration equal to the IC_{50} for COX-2 i.e., the time during which COX-2 would be inhibited by more than 50 %.

IC_{50} and I_{C80} for COX-2 are 18.9 and 104.9 ng/mL, respectively. IC_{10} and IC_{20} for COX-1 are 674.8 and 1788.8 ng/mL, respectively.

The pre-clinical data described in this manuscript have been used to select a dose rate and dosing interval for robenacoxib in the cat for subsequent evaluation in clinical trials. These trials were designed to establish the relief of pain and inflammation associated with surgery and acute musculoskeletal disorders. Although some of the presented pre-clinical data may suggest that twice daily dosing would be a more suitable dosing regimen, clinical findings have established good efficacy with once daily dosage of 1-2 mg/kg. No efficacy advantage was in fact detected with robenacoxib at 1-2.4 mg/kg BID compared with robenacoxib at 1-2.4 mg/kg SID (Giraudel et al., 2010). Once daily dosing also provided efficacy over the 24 hour dosing interval in cats undergoing combined orthopaedic and soft tissue surgery (King et al., 2012). The ultimate step of drug development, namely the clinical trials, remains therefore important for the determination of an efficacious dosing regimen in a clinical setting.

It is concluded that *in vitro* and *ex vivo* whole blood assays as well as pre-clinical PK and PD data provide an invaluable basis for initial dosage determination of NSAIDs.

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Wednesday 2nd September | Room A | 10:50−11:50

L-9 Buprenorphine in cats: from the research lab to the clinical setting

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Buprenorphine is a partial mu agonist and kappa antagonist of opioid receptors. The drug is one of the most popular opioids used in small animal practice (Hunt et al. 2015). Buprenorphine has drug market authorization in several countries and commonly produces analgesia, euphoria, mydriasis with minimal adverse effects when administered to cats. A recent study has reviewed the use of buprenorphine in cats (Steagall et al. 2014). This review provides a summary of the pharmacokinetic and pharmacodynamic studies using thermal and mechanical threshold testing while revisiting the thorny issue of routes of administration and clinical application of buprenorphine in cats. In addition, this review article suggests guidelines for clinical use of this drug in this species.

This presentation highlights important aspects of the aforementioned review study and revisits some scientific evidence of research and clinical studies of buprenorphine in cats. A discussion on the onset and duration of action, interaction with other opioids, dosage regimens, routes of administration and novel formulations of buprenorphine in feline practice is presented. Important updates on the subject will be shown (Bortolami et al. 2012; Warne et al. 2014; Kirk & Brown 2015; Simon et al. 2015) including the novel FDA-approved high-concentrated formulation of buprenorphine (Simbadol® 1.8 mg/mL). The latter has been launched in the USA and according to the drug's label, it may provide postoperative analgesia in cats for up to 3 days when administered by the subcutaneous route every 24h. This formulation has been shown to be safe in cats (Sramek et al. 2015) and provide antinociception for prolonged periods of time (Taylor et al. 2015). New data will be presented (Doodnaught et al. 2015).

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Wednesday 2nd September | Room D | 9:50−10:50

L-10 Total intravenous anaesthesia and alfaxalone

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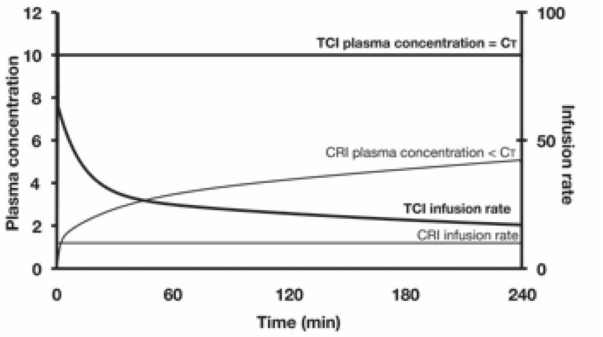
Typically the modus operandi for anesthetising veterinary patients is to premedicate with single or multiple drugs, perform induction with a registered injectable drug(s) and then maintain anaesthesia in the patient with an inhalant anaesthetic. Another less frequent but certainly viable means of performing induction and maintenance of anaesthesia is to replace the inhalant anaesthetic with an injectable anaesthetic which equates to total intravenous anaesthesia (TIVA). The intravenous anaesthetic provides hypnosis and muscle relaxation. Analgesia can be provided by the administration of an opioid, alpha-2 adrenergic agonist, ketamine, lidocaine or a combination thereof. Anaesthesia can be maintained by intermittent boluses but continuous rate infusion (CRI) produces a more stable plane of anaesthesia with less variation in haemodynamic, respiratory and central effects and thus is safer for the animal. CRI can also be administered with manual adjustment (i.e. stepped or variable rate infusion [VRI]) with or without a loading dose. The loading dose (LD) is calculated as LD = target plasma concentration of injectable anaesthetic (C_p) x volume of distribution of the central compartment (V_c). The maintenance dose for the CRI = C_p x total body clearance (Cl_B). Cl_B is calculated from a good quality pharmacokinetic study(ies) of the injectable anaesthetic; ideally using compartmental modelling. Compartmental modelling will also yield the micro constants (V1, k10 ± k12 & k21± k13 & k31), necessary to perform Target Controlled Infusion (TCI) calculations.

The concept of TCI was first described by Krüger-Thiemer in 19681. The first theoretical model of TCI was by Schwilden et al[2] and called the computer-assisted total intravenous anaesthesia system (CATIA). Since that time a number of different computer programs have been developed for TCI including the STANPUMP (Stanford University), the STELPUMP (University of Stellenbosch), RUGLOOP from Ghent University and the Diprifusor System (first commercial system for propofol)[3]. The distinct advantage of TCI over CRI is that with TCI the "effect site concentration" is reached quickly while slowly increasing drug in the peripheral compartment(s) until the concentration of anaesthetic in all compartments equals the targeted effect site concentration. Figure 1 shows the conceptual difference between rate and plasma drug concentration for CRI and TCI.

Figure 1. Comparison of CRI and TCI*



*Pypendop B. Pharmacokinetic principles for the design of intravenous infusions. Pain Management in Veterinary Practice. Edited by Egger C, Love L and Doherty T. Pages 125-130.

Calculation of the effect site concentration 50% (EC50) for an injectable anaesthetic is roughly performed in the same manner as a minimum alveolar concentration (MAC) study except the TCI infusion pump replaces the vaporiser. Both studies are designed to calculate the lowest drug concentration preventing movement in response to a maximal noxious stimulus in 50% of a population.

Alfaxalone, like propofol, is a drug that has attributes necessary for TIVA. It theoretically has a short context sensitive half-life (unpublished data) and does not appear to pharmacokinetically or pharmacodynamically accumulate during infusion at clinically recommended dose rates. Alfaxalone in 2-hydroxypropyl-β-cyclodextrin has been successfully used for TIVA or partial intravenous anaesthesia (PIVA) in dogs[4-10], cats[11-18], horses[19-20], ponies[21-22], pigs[23], sheep[24-26], goats[27], monkeys[28], rabbits[29] and rats[30-32]. This lecture will discuss the principles of TIVA, CRI and TCI as they apply to alfaxalone and cite case examples where appropriate.

Acknowledgement

The author would like to thank Professor Bruno Pypendop (University California, Davis) for his assistance in understanding the concepts and mathematics of TCI.

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Wednesday 2nd September | Room D | 10:50−11:50

L-11 Application of Alfaxan® in Species other than Dogs and Cats

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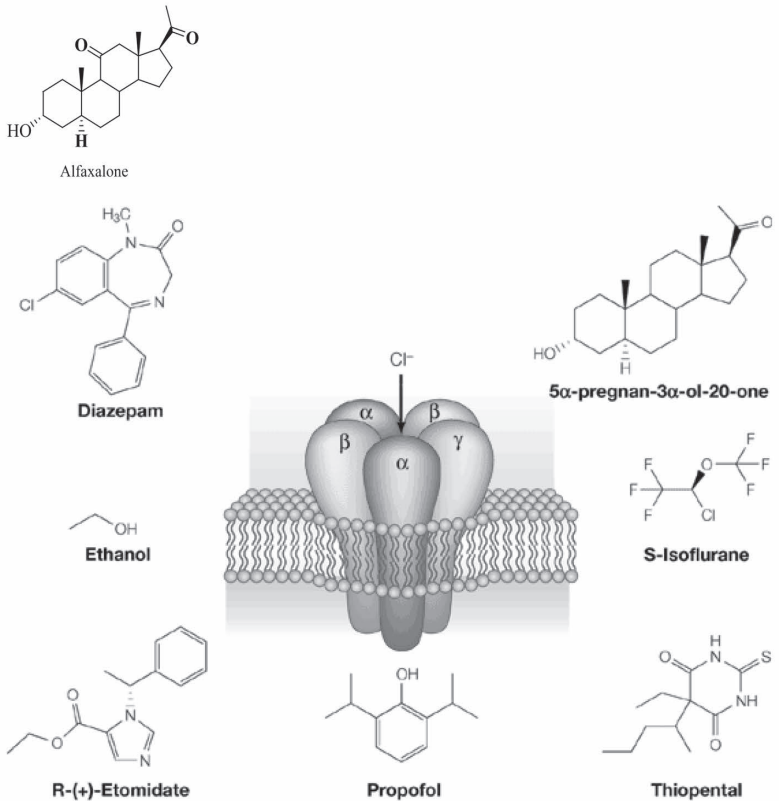
Jurox Pty Ltd, Australia

The anaesthetic properties of steroids have been known for more than 70 years. In the 1940s the Hungarian born endocrinologist Hans Selye showed that reversible unconsciousness could be produced in rats administered intraperitoneal injections of large quantities of steroid hormones[1]. Of the steroids injected desoxycorticosterone acetate, a pregnanedione, was the most potent and devoid of hormonal activity[2]. In 1955 P' An and colleagues reported that a close structural analogue of pregnanedione, hydroxydione, was more potent and safer than the thiobarbiturate thiopentone[3]. However, hydroxydione was not the ideal anaesthetic induction agent in that it produced a delayed anaesthetic induction of up to 3 minutes and it had to be solubilised in an alkaline pH causing venous thrombosis. Further structure activity relationship on this neurosteroid showed that manipulation of the 3 and 21 carbon positions altered anaesthetic potency[4,5]. Eventually, the active molecule 3 α -hydroxy-5 α -pregnane-11,20-dione (alfaxalone) was discovered by the Glaxo UK Pharmacology Department. Similar to the barbiturates, benzodiazepines, propofol and isoflurane it is thought that the main mechanism of action is through the gamma-aminobutyric acid type A ($GABA_A$) receptor which belongs to a superfamily of ligand-gated, pentameric ion pore-forming cell surface receptors found in neurons and other excitable cells (see Figure 1) [6].

Figure 1: $GABA_A$ receptor and known ligands



Alfaxalone was later combined with alfadolone (21-acetoxy-3 α -hydroxy-5- α -pregnane-11,20-dione), Cremophor® EL (B.A.S.F.) and sodium chloride to yield formulation CT1341. The alfadolone was placed in the formulation to improve the solubility of the alfaxalone[7]. Child et al performed a battery of pharmacological tests on CT1341 in laboratory animals and found it offered significant advantages over the other injectable anaesthetics in that it had a higher margin of safety, it was non-irritant to tissues including veins, it was compatible with the adjuvant and pre-anaesthetic drugs, it did not accumulate and it produced a pleasant anaesthetic experience for the patient[8]. In the early 1970s, CT1341 was introduced as an intravenous (IV) anaesthetic induction agent for humans (Althesin®) and as an IV and intramuscular anaesthetic (Saffan®) for cats and monkeys. Saffan® was not licensed in dogs because in dogs polyoxyethylated emulsifying agents

like Cremophor® EL cause histamine release and potential anaphylaxis[9]. In an effort to remove the side effects observed with drug carriers such as Cremophor® EL, groups like Brewster et al found that alfaxalone and other drugs could be solubilised in safe carriers like 2-hydroxypropyl cyclodextrins (2-HPCD) [10,11].

Since 2000, alfaxalone in 2-HPCD (Alfaxan®) has been commercially available as an anaesthetic for intravenous injection. The product is registered and labelled for the induction and maintenance of anaesthesia in dogs and cats in multiple countries. However, the formulation has been administered in many other species by different routes of administration to produce sedation or anaesthesia. By definition *the actual use or intended use of a drug in an animal in a manner that is not in accordance with the approved labeling* is **extralabel** drug use. This includes, but is not limited to:

1. use in species not listed in the labeling,
2. use for indications (disease or other conditions) not listed in the labeling,
3. use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and
4. deviation from the labeled withdrawal time based on these different uses.

In most cases the extralabel administration of Alfaxan® is used for:

1. Clinical Reasons - there is no approved sedative or anaesthetic approved in the species and Alfaxan® is rationalized as a good choice.
2. Research – the properties of Alfaxan® are being researched in a non-approved species or Alfaxan® is being used in an experimental model of research in a non-approved species.

An internal corporate search and an external search (i.e. PubMed, Google Scholar etc.) of Alfaxan® administration to species other than dogs and cats yielded numerous studies. Routes of administration included IV, IM, IP, SC and topical routes of administration. Some studies were corporate sponsored internal studies, drug in kind or collaborations[12-29], however, most of these studies were independent studies (i.e. there was no corporate knowledge that the study was being performed) cited in refereed journals[30-72]. This lecture will be an in depth discussion of the extralabel use of Alfaxan® in species other than dogs and cats.

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The author would like to thank Dr Brad O' Hagan (Jurox Pty Ltd) for his assistance in preparation of this manuscript.

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L-12 Comparative Respiratory Physiology - Gas Exchangers and Metabolic Demand for Oxygen

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Oxygen delivery required for steady-state aerobic metabolism in vertebrates is influenced by many factors. In terms of the O_2 demand of the tissues – the quantity of O_2 needed for oxidative metabolism – the primary determinants are body temperature and body size, the effects of which are called scaling or allometry. Higher body temperature increases chemical reaction rates according to the Q_{10} effect, increasing (or decreasing) them, and hence metabolic rate, in most vertebrates by a factor of approximately 2.3-fold per 10 ℃ change in body temperature. Across the range of vertebrate body temperatures (0-43 ℃) Q_{10} can alter the metabolic rate (= O_2 consumption) by nearly 35-fold. An even larger effect on metabolic rate is caused by allometric differences in body size. Considering just mammals (although the same relationship holds for other vertebrate classes), the smallest mammal (Etruscan shrew) weighs 1.5 g, while the largest blue whale weights 150 T, 10^8 times larger. As mammals become larger in size, their mass-specific (per kg) rate of oxygen consumption decreases by a factor of 10 for every 10^4 increase in body mass. This means that across the entire size range of mammals O_2 consumption per kg differs by 100-fold (10 x 10).

In terms of how much O_2 is delivered to metabolizing tissues, the two major determinants are the structure of the heart and cardiovascular system and the design of the gas exchanger that obtains O_2 from the environment. In general, vertebrates show an evolutionary trend toward increasing the number of chambers in the heart over the simple two chambers found in fish hearts. Because of the Q_{10} effect, birds and mammals, the two homeothermic classes of vertebrates that maintain relatively high and constant body temperatures, also have the highest metabolic demand for O_2; for a given body mass, they are very similar. Both classes have evolved completely divided hearts that enable them to have high systemic vascular pressures and flows and to utilize variation in vascular resistance to direct blood flow where needed. In contrast, their pulmonary circulations function with lower pressures that reduce the likelihood of edema formation due to Starling forces. It is notable that some reptiles, e.g., varanid (monitor) lizards, achieve dynamic functional separation of their ventricles during systole enabling them to have higher vascular pressures, blood flow, O_2 delivery and metabolic rates than other reptiles.

The structures of vertebrate gas exchangers are largely dictated by the medium in which the animal lives. Fish live in an aquatic medium with low O_2 availability due to its low solubility coefficient and a high energy cost to pump water through the gills due to its high density and viscosity compared with air. As a result, fish have evolved the most efficacious of all vertebrate gas exchangers in terms of extracting the maximal quantity of O_2 from a given volume of water that passes through the gills. This gas exchanger, called a counter-current flow exchanger, maximizes the extraction of O_2 from the water by orienting the flow of blood through the gill lamellae in the opposite direction to the flow of water that is passing through the gills as a result of pumping by buccal and opercular pumps. By creating a counter-current flow, a partial pressure gradient difference for O_2 between water and blood is maintained at every moment along the length of the exchanger as water flows past the blood. The reason for this is that as O_2 diffuses from water with a higher partial pressure of O_2 than the adjacent blood, the water's O_2 partial pressure decreases, but it immediately flows into contact with blood that has not had as much O_2 diffuse into it, hence, that blood has an even lower O_2 partial pressure than the adjacent water and diffusion continues to occur until nearly all of the O_2 has been extracted from the water. A counter-current gas exchanger allows the water that is expired from the gills to have a much lower O_2 partial pressure than the arterial blood that is circulated to the body. However, an important consequence of aquatic gas exchangers is that because of the much higher solubility coefficient for CO_2 than O_2 in water, aquatic breathers (fish and amphibians) cannot retain CO_2 in their bodies and must regulate their ventilation based on hypoxic drive rather than on a buildup of CO_2 as do terrestrial quadrupeds.

Amphibians metamorphose and must balance requirements for aquatic and aerial gas exchange. Larval stages obtain O_2 with external gills that are not actively ventilated, whereas, adults may utilize a combination of cutaneous (surrounded by water) and pulmonary ventilation. The lungs of frogs are relatively simple saclike structures, and because frogs lack ventrally attached ribs they cannot create subatmospheric intrapleural pressures and must utilize a positive pressure buccal pump to ventilate their lungs. Salamanders in the family Plethodontidae, called the lungless salamanders, obtain O_2 by diffusion through their skin and the lining of their mouths. These animals tend to be small in size and to live in cold streams. A consequence of small body size is that due to allometric relationships, small animals have

relatively greater body surface area than larger ones, hence, providing greater surface area for O_2 uptake. The consequence of living in a cold environment with low body temperature is the Q_{10} effect reduces metabolic rate and the demand for O_2.

Reptiles exhibit increasing complexity of both cardiovascular and pulmonary structures as they evolved to have greater aerobic capacities and metabolic scopes. All reptiles have ventrally attached ribs and can generate subatmospheric pressues to ventilate their lungs. The simplest form of reptilian lung, found in most families of lizards and the New Zealand tuatara, is called unicameral, having a single undivided central lumen and with respiratory surfaces being formed by partitions of the lung wall. A second type of lung found in chameleons and iguanas is called paucicameral, with a few large septa subdividing the lung and increasing its surface area. The most active reptiles – crocodiles, monitor lizards and turtles – have multicameral lungs, subdivided into many pockets that can be quite heterogeneous in size and shape. The gas exchange regions of these lungs may be faveolar, in which muscular ridges on the inner lung surface form a honeycomb appearance and increase surface area for gas exchange. Faveolar lungs occur in active species with unicameral lungs, e.g., snakes. In turtles, a postpulmonary septum evolved to separate the lungs from the coelomic cavity, and the lungs adhere dorsally to the carapace. Monitor lizards and crocodiles also have postpulmonary septa separating the pleural and peritoneal cavities. In varanid lizards and crocodiles, the lungs are attached to the dorsal body wall as in turtles. In crocodiles, there is an additional posthepatic septum, and attached to its margins are striated muscle originating from the pelvic girdle. Contraction of these muscles retracts the posthepatic septum and inflates the lungs; this may be an adaptation for crocodiles to ventilate forcefully at the surface when wrestling with prey underwater.

The two homeothermic classes of vertebrates, birds and mammals, maintain the highest demand for and delivery of oxygen because of their high body temperatures and have both evolved divided circulations that allow high systemic and low pulmonary vascular pressures. However, these two taxa have evolved fundamentally different respiratory gas exchange system designs, with mammals subdividing the lungs relatively homogeneously into alveoli of similar size, whereas, birds subdivide their system heterogeneously with lungs of small volume that are formed of small parallel tubes through which air flows unidirectionally, called parabronchi, and large air sacs that make up the majority of respiratory system volume. The avian respiratory system may occupy 20% of a bird's body, whereas, mammalian lungs are approximately 7% of its volume. The large avascular air sacs of a bird may extend into pneumatic bones but do not participate in gas exchange; that occurs exclusively in the lungs, which are about half the size of those of a mammal of similar size and metabolic rate. However, the small avian lungs can extract more O_2 from air flowing through them than can a mammal's lungs. The reason for this is that the orientation of the parabronchi with air flowing through them is at a right angle to the flow of blood undergoing gas exchange, thus creating a cross-current flow gas exchanger. The effect of this orientation is that as the air's O_2 partial pressure is reduced as it passes through the parabronchus it nevertheless keeps encountering blood with a lower O_2 partial pressure, that of mixed-venous blood. As a result, the arterial O_2 partial pressure exiting the lungs is higher than the expired O_2 downstream, hence, the bird removes more of the available O_2 than is possible in the mammalian lung, in which arterial and expired O_2 partial pressures can at best be equal. Although the avian cross-current flow exchanger can extract more O_2 than can the mammalian lung, it does not extract as much as the counter-current flow exchanger of fish. The ability of birds to extract more O_2 from inspired air than can mammals may partially explain how birds can perform heavy exercise (flight) at high altitudes where oxygen partial pressure is low.

L-13 Lung pathophysiology in the perioperative patient

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This session will focus primarily on the pathophysiology of respiratory failure syndromes. It is assumed that this will be of most use to the audience as less severe derangements are likely of lesser consequence and more readily addressed with standard supportive measures. The discussion will utilize many case examples from the author's practice and highlight how the pathophysiology dictated the therapeutic approach taken.

Etiology/Pathophysiology

Acute respiratory failure occurs when an insult to the respiratory system that is sudden in onset or short in duration results in levels of alveolar ventilation or pulmonary oxygen transfer (or both) that are insufficient to maintain vital metabolic processes and homeostasis. This term does not imply that more chronic respiratory compromise may not be present concurrently. In a subset of cases, the acute exacerbation of a chronic process or the sudden development of a secondary complication (e.g. respiratory tract infection) may lead to signs of acute deterioration in clinical status. Similarly, chronic pulmonary compromise may lead to fairly abrupt fatigue of the muscles of respiration and provoke an acute crisis. The proximate cause of the acute crisis in such a case is the suddenly inadequate ventilatory capacity; however, the ultimate underlying cause may be an unsustainable workload due to a chronic disease process (e.g. progressive dynamic airway collapse, parenchymal fibrosis, etc.).

Categorization schemes for acute respiratory failure are typically multi-tiered in their organization. The first level of differentiation is often based on the predominant arterial blood gas alteration. With this approach one often finds acute respiratory failure divided into three main sub-categories: (1) hypercapneic respiratory failure, (2) hypoxemic respiratory failure, and (3) mixed respiratory failure.

Hypercapneic respiratory failure

Hypercapneic respiratory failure includes those conditions that result in a severe, sustained reduction in alveolar ventilation. By definition, a respiratory acidosis is present. One must bear in mind that this does not mean that all such patients will be acidemic. The retention of excessive quantities of carbon dioxide is a process that will tend to acidify a living system; thus, it is an acidosis. Acidemia, or a reduction in blood pH, may or may not be present concurrently depending on a host of other factors such as the current capacity of the extracellular hydrogen ion buffering systems. Generally in acute hypercapneic respiratory failure, inadequate time has passed to allow for generation of maximal compensatory responses and acidemia is present more often than not. Indeed, some definitions of acute hypercapneic respiratory failure require that acidemia be present as a pre-requisite indicator of the abrupt onset of the condition. Such definitions fail to take into account patients that may have had a pre-existing alkalosis (e.g. long term diuretic usage). Regardless of whether the definition used incorporates acidemia or not, all such approaches universally rely on the identification of hypercapnia. The cut-off value at which hypercapneic respiratory failure is deemed to be present varies, but is typically in the 60-70 mmHg range when arterial or end-tidal exhalate sampling is utilized. A P_aCO_2 of greater than 60 mmHg is often listed among the indications for mechanical ventilation in the veterinary literature, which can thus serve as *de facto* evidence of respiratory failure in many instances. In the post-operative setting, this guideline requires substantial modification. Re-intubation of all patients with a P_aCO_2 of greater than 60 mmHg would lead to an epidemic of mechanical ventilation cases. In recently extubated patients whose respiratory efforts seem appropriate, moderate hypercapnia should be treated more conservatively as sub anesthetic doses of anesthetic agents have often only transiently altered chemoreceptor sensitivities. The passage of time and greater clearance of anesthetic agents is often the only required course of action. However, if respiratory effort is exaggerated then more aggressive therapy is warranted.

Hypercapneic respiratory failure (and hypercapnia in general) is the result of one or more of the following circumstances: (1) inadequate or inappropriate ventilatory drive, (2) insufficient ventilatory capacity, or (3) an excessive mechanical or chemical load imposed on the respiratory system. Inadequate or inappropriate ventilatory drive results from intracranial disease, medications/anesthetics/sedatives, or extracranial encephalopathies. The respiratory centers reside in the medulla with inputs from both pons and cerebrum. Diseases resulting in compromise of these pontine and medullary centers may lead to marked alterations in respiratory pattern (e.g. Cheyne-Stokes breathing, apneusis, etc.) or alternatively a reduction in respiratory rate and/or tidal volume with little alteration in pattern of breathing. In the setting of hypercapneic respiratory failure due to intracranial disease, hypercapnia may be both a result and a cause of elevated intracranial pressure and imminent herniation. Inadequate or inappropriate respiratory drive is typically identified in the laboratory setting by

determining the relationship between minute ventilation and P_aCO_2 or P_aO_2. This relationship is rarely defined quantitatively in the clinical setting, however. Qualitatively, a clinician may note that a hypoxemic patient has failed to hyperventilate as would be expected in those circumstances. Such a finding would suggest altered ventilatory drive or inadequate ventilatory capacity. An alternative approach to defining respiratory drive is to measure the drop in airway pressure that occurs 0.1 sec after transient occlusion of a patient's breathing circuit (termed P100 for the drop in pressure observed 100 ms after occlusion). P100 has been used to assess respiratory depression due to anesthetic agents as well as to predict ventilator weaning success. The dog has long served as a model in studies of the impact of various factors on P_{100}, but data is more limited from cats. Both a reduced as well as an increased P_{100} can signify altered respiratory drive (normal being on the order of 1-2 cm H_2O).

Insufficient ventilatory capacity is the second general mechanism for hypercapneic respiratory failure and is typically the result of compromise of the respiratory muscles or the neural input to them. Respiratory drive may be sufficient (although it is difficult to assess in this setting), while the transmission or end-effector systems are dysfunctional. The problem may lie anywhere along the myoneural axis. High cervical myelopathies (cranial to the C5 spinal segment) can disrupt transmission at a level cranial to the formation of the phrenic nerve roots. Low cervical myelopathies may impair the intercostals nerves while sparing phrenic nerve transmission (which is usually sufficient on its own to maintain ventilatory status). The nerve roots may be impacted by disease as is seen in polyradiculoneuritis (Coon Hound paralysis). Similar forms of ascending paralysis (tick paralysis, botulism, some snake envenomations) may result in hypercapneic respiratory failure that appears quite similar in nature albeit occurring via different mechanisms. The phrenic nerve itself may become compromised (phrenic neuropathy) due to trauma (surgical or external), demyelinating diseases, disruption by tumor growth, or idiopathic causes. Unilateral phrenic neuropathy is often well tolerated, while bilateral dysfunction can require mechanical ventilatory support.

Disorders of the neuromuscular junction can lead to hypercapneic respiratory failure. Junctionopathies may be sub-classified as pre-synaptic, synaptic, or post-synaptic in nature. Pre-synaptic disorders include those that increase (e.g. low serum magnesium and some envenomations such as Black Widow spider bites) as well as decrease (e.g. hypocalcemia, botulism, tick paralysis, aminoglycoside antibiotics) acetylcholine release into synaptic clefts. Synaptic cleft disorders include diseases that alter the removal of acetylcholine from this site (e.g. cholinesterase inhibitors, organophosphates). Post-synaptic disorders can include forms of myasthenia gravis and well as administration of depolarizing and non-depolarizing muscle relaxants (e.g. succinylcholine).

Myopathies are a potential cause of reduced ventilatory capacity as well. Specific myopathies of the respiratory muscles are quite rarely diagnosed in veterinary patients except for traumatic myopathies. Traumatic diaphragmatic herniation or avulsion is perhaps the most frequently recognized myopathic process leading to hypercapnia and respiratory failure. Another uncommon, but well recognized, myopathy of small animals that may profoundly reduce ventilatory capacity is potassium depletion polymyopathy of cats. While hypokalemic myopathies are more fully characterized in cats than dogs, it should be noted that profound hypokalemia also may result in hypoventilation in dogs. In fact, the proximate cause of death in older studies of prolonged starvation in dog models is respiratory failure associated with muscle weakness. Other causes of diaphragmatic myopathies reported in humans are rarely reported in veterinary species, seldom associated with respiratory failure, or limited to select lines of highly inbred animals (e.g. Duchenne's muscular dystrophy, thyrotoxicosis, myxedema, hyperadrenocorticism, systemic lupus erythematosis). Severe abnormalities of the sternum or chest wall may compromise diaphragmatic function by placing it at an unfavorable orientation or resting length.

An excessive mechanical or chemical load imposed on the respiratory system is the third general mechanism of acute hypercapneic respiratory failure. In this case, the respiratory system may be functioning at a high level, but has been required to perform its duties in the face of a mechanical or chemical load that would exceed the capacity of any healthy respiratory system. Mechanical loads that are excessive may be the result of reductions in compliance of the chest wall or pulmonary parenchyma, increases in respiratory system resistance, or both. Reductions in compliance can result from alterations in the biomechanical properties of the structural elements themselves or due to alterations in surface tension forces. In the former instance, such alterations are typically the result of chronic disease processes and excessive fibrosis. However, acute changes can be superimposed iatrogenically in the form of tight wraps on the trunk at either the thoracic or abdominal level (e.g. Spica splints, etc..). Elevated intra-abdominal pressure (intra-abdominal hypertension, abdominal compartment syndrome) can secondarily result in reduced respiratory system compliance and can develop acutely in the setting of hemoabdomen or other forms of rapid peritoneal fluid accumulation. Likewise, pleural filling disorders can compromise the tidal volume that is achieved with a given degree of respiratory muscular effort. A given volume of air may reduce tidal volume to a larger degree than an identical volume of fluid in the pleural space. Unlike fluid, air can expand and such expansion during inspiration can compromise tidal volume beyond the effect that results

from disruption of pleural contact forces alone. Acute reductions in the compliance of the pulmonary parenchyma and interstitium are often seen concurrently with disruption of surface tension forces in inflammatory and edematous lung diseases. Pulmonary edema, pulmonary hemorrhage, near-drowning, pneumonitis, and pneumonia all may lead to reduced pulmonary compliance both via tissue edema formation and increased surface tension due to surfactant dilution and alveolar collapse. While these effects are important, each of the diseases mentioned in this context are far more likely to cause hypoxemic respiratory failure than the hypercapneic form. Acute hypoventilation often occurs only once respiratory muscle fatigue develops or the airway becomes occluded with exudate, serosanguinous fluid, or foam.

Increased airway resistance is another important cause of hypercapneic respiratory failure due to an excessive mechanical load. Many commonly diagnosed diseases in small animal practice can lead to excessive airway resistance. It is important to distinguish airway resistance from tissue resistance. Tissue resistance is a term used to describe and quantify the forces that must be overcome in order to deform and displace tissues. In the section above, each of the edematous/inflammatory diseases mentioned would typically be associated with increased tissue resistance to deformation. This section is instead focused on airway resistance, which is the resistance to the flow of gases during inhalation and exhalation. Airway resistance is not a meaningful factor when flow is absent or nearly absent, whereas tissue resistance can still be of importance during no flow states as the lung is still being deformed (i.e. stretched). Airway resistance can impact both total gas flows into the system as well as intrapulmonary redistribution of gas after bulk flow has ceased (pendelluft). Many common diseases in small animal practice can cause life-threatening increases in airway resistance at the level of the extrathoracic (e.g. laryngeal paralysis, brachycephalic syndrome) or intrathoracic (e.g. feline asthma, tracheobronchial malacia) airways. These conditions are often chronically active with sudden deterioration resulting from additional factors such as increased environmental temperatures, inhaled particulates and antigens, respiratory tract infections, or atypical activity/exertion. Alternatively, disease progression may have lead to a new manifestation that represents an intolerable burden (e.g. the onset of new, or higher grade, laryngeal or pharyngeal collapse).

Focal/localized intrathoracic airway narrowing or collapse typically needs to be quite proximal to significantly impair ventilation (e.g. tracheal or lobar bronchial collapse). Diffuse collapse or narrowing of large intrathoracic airways can severely impair ventilation and limit expiratory flow substantially. Narrowing or collapse of smaller intrathoracic airways generally needs to be diffuse in nature to significantly impair ventilation. Feline asthma and bronchiolitis in dogs (e.g. secondary to canine adenovirus infection) may serve as examples of diseases encountered in small animal practice that result in diffuse small airway narrowing. Bronchiolitis in puppies raises several important points that remain unknown in veterinary pulmonology. In humans, it is known that diffuse lower airway disease can compromise ventilation far more severely in children than in adults. In human infants and young children, the contribution of the peripheral airways to overall airway resistance is much larger than it is in adults (50% versus 20%). Further, collateral ventilation (via pores of Kohn and Lambert) between adjacent alveoli are not fully developed until later in life predisposing alveoli to collapse when flows via respiratory bronchioles and alveolar ducts are not patent. The impact of these developmental issues is that children develop far more ventilatory compromise from bronchiolitis (e.g. respiratory syncitial virus infection) than would be seen if an adult's lung suffered from a similar degree of pathology. Whether such factors are contributing to more severe respiratory compromise in puppies and kittens relative to adult animals of the same species remains undetermined.

Increased alveolar deadspace ventilation also represents a form of excessive mechanical load. In this setting, an atypically high proportion of respiratory muscular work is being devoted to ventilating alveolar units that are not participating in gas exchange. The effective alveolar ventilation is reduced although total minute ventilation may be normal (or more likely increased). This reduction in alveolar ventilation is identified (and defined) by the accompanying rise in alveolar and arterial carbon dioxide tensions. However, end-tidal concentrations become dissociated and reduced. This increase in the gradient between arterial and alveolar carbon dioxide tensions is due to the simultaneous emptying of those alveolar units that did and those that did not participate in gas exchange. Thus deadspace gases dilute the carbon dioxide in the exhalate from perfused alveoli. Increased alveolar deadspace may result from pulmonary vascular occlusion (e.g. pulmonary thromboembolism) or from decreased pulmonary capillary hydrostatic pressures in hypovolemia and other forms of severe cardiovascular impairment. These diminished intraluminal vascular pressures result in the formation of greater numbers of persistently non-perfused alveoli (i.e. West Zone I units) when intraluminal pressures are below alveolar pressures (i.e. extraluminal pressures exceed intraluminal pressures).

An excessive chemical load on the respiratory system can also manifest as hypercapneic respiratory failure. In this context, the high chemical load is in the form of excessive carbon dioxide and this CO_2 burden exceeds that which any healthy respiratory system might be able to eliminate. An excessive CO_2 load can be the result of an abrupt and marked increase in carbon dioxide production ($VdotCO_2$) as is seen in malignant hyperthermia or status epilepticus. Alternatively, the excessive CO_2 load can be the result

of rebreathing exhaled carbon dioxide. Rebreathing may occur in several clinically relevant settings such as a maintaining a patient in a poorly ventilated, confined space (e.g. anesthetic induction box), excessive apparatus deadspace (e.g. end-tidal monitoring and other devices attached to orotracheal tubes in very small patients), or exhausted soda lime in a rebreathing anesthetic circuit. The greater density of carbon dioxide relative to other oxygen and nitrogen has raised concerns that a gradient may develop over time when animals are delivered supplemental oxygen via an oxygen hood. Convention is often to place the venting site upwards (12 o' clock) to that heat may readily escape; however, periodic shifting of the vent site to a downward location (6 o' clock) may be useful to reduce carbon dioxide accumulation. Typically patient movement is sufficient to periodically shift the vent orientation without clinician intervention, but active repositioning may be required in moribund patients.

Hypoxemic respiratory failure

Respiratory failure that is categorized as hypoxemic largely results from venous admixture in various forms. Venous admixture is a term for the co-mingling of deoxygenated venous blood with arterialized blood during flow from the right heart to the left heart. Some authors prefer to use the term *true venous admixture* to describe right-to-left shunting through an abnormal anatomic conduit (e.g. right-to-left patent ductus arteriosus). In such frameworks, the mixing of deoxygenated venous blood with arterialized blood that occurs in the pulmonary veins in conditions such as increased ventilation-perfusion mismatching is termed *venous admixture-like* in nature. Such distinctions offer little advantage in the author's opinion. A more clinically relevant approach might be to define venous admixture as those conditions which produce hypoxemia with an accompanying increase in alveolar-to-arterial PO_2 gradient (A-a gradient). The predominant mechanisms resulting in hypoxemia are listed in Box 1.

Box 1: Mechanisms of hypoxemia

1) Associated with a *normal* A-a gradient (no venous admixture)
   - Hypoventilation
   - Decreased P_IO_2
2) Associated with an *increased* A-a gradient (venous admixture)
   - Right-to-left shunting (anatomic shunting)
   - Perfusion of non-ventilated alveoli (no V/Q; physiologic shunting)
   - Ventilation-perfusion mismatching (low V/Q)
   - Diffusion impairment

Hypoventilation results in hypoxemia by reducing alveolar oxygen tensions. The retention of carbon dioxide within the alveolar spaces reduces the partial pressure of oxygen via dilution to a degree, but it is ultimately the failure to provide adequate inflow of oxygen to replace what has been taken up that reduces P_AO_2. For this reason, hypoxemia due to hypoventilation may be readily corrected by restoring appropriate levels of alveolar ventilation, by increasing the proportion of inspired gas that is oxygen (i.e. F_IO_2), or both. Hypoventilation is thus best considered as a form of hypercapneic respiratory failure than a truly hypoxemic form. Hypoventilation is an implausible mechanism of hypoxemia in patients receiving supplemental oxygen if one excludes complete apnea from the discussion.

Decreased P_IO_2 is an often incorrectly or incompletely categorized cause of hypoxemia. Many authors will list decreased F_IO_2 instead of P_IO_2 as the mechanism. A truly decreased fraction of inspired oxygen is quite rare as the proximate cause of hypoxemia and would generally only be encountered if a patient were on a rebreathing circuit with inadequate fresh gas inflow. One would hope that this is a rare occurrence. Low P_IO_2 in contrast is quite common and occurs anytime an animal is taken significantly above sea level unless they are maintained in a suitably pressurized environment such as an aircraft. The hypoxemia that develops at elevation is the result of a decrease in P_IO_2 with a normal F_IO_2 (i.e. the atmosphere is still 21% oxygen, but total pressures and thus all partial pressures are decreased). Thus, decreased P_IO_2 is more correct as it accounts for reduced inspired oxygen fraction (rare) as well as reduced barometric pressure (more common). For a patient breathing room air at sea level, decreased P_IO_2 is not a reasonable differential diagnosis for hypoxemia. In the case of both hypoventilation and decreased P_IO_2 the hypoxemia that is observed is due to a decrease in P_AO_2. This decrease in P_AO_2 is accompanied by a proportional decrease in P_aO_2 and thus the A-a gradient remains within the normal range.

As mentioned above, causes of hypoxemia that are associated with an increased A-a gradient are those that fall under the overarching category of venous admixture. Venous admixture includes all mechanisms by which blood passing from the right heart to the left heart fails to be properly oxygenated despite an adequate alveolar partial pressure of oxygen (P_AO_2).

Right-to-left shunting (anatomic shunting) is a relatively uncommon cause of hypoxemia in veterinary practice relative to other forms of venous admixture. Tetralogy of Fallot is perhaps the most common congenital defect in which right-to-left shunting occurs routinely. In many other conditions, a potential shunting conduit may be present, but right-to-left shunting does not occur unless cardiac pressures on the right side exceed those on the left (e.g. septal defects). Similarly, pathology involving the great vessels such as patent ductus arteriosus would not be expected to result in right-to-left shunting unless significant pulmonary hypertension, profound systemic hypotension, or both were present. In such cases, differential cyanosis may alert the clinician to the presence of this pathology. When significant anatomic right-to-left shunting is present, hypoxemia may become refractory to correction with supplemental oxygen. The iso-shunt diagrams developed by J.F. Nunn and colleagues and published in 1973 provide a graphic depiction of the response to supplemental

oxygen with increasing proportions of shunt flow. When shunt flow reaches 30% of cardiac output, hypoxemia is largely unresponsive to supplemental oxygen and with no improvement expected at all with shunt flows approaching 50% of total blood flow. The shunt equation may be used in two ways. First it may be used to estimate the shunt fraction (percent of cardiac output) in patients with anatomic or physiologic (see below) right-to-left shunting. Alternatively, in patients with other forms of venous admixture the shunt equation may be used to determine the "equivalent amount of right-to-left shunting" that would be required to produce a comparable level of hypoxemia as that observed. The shunt equation is shown in **Box 2**. Note that while central/mixed venous and arterial oxygen content may be measured, pulmonary capillary oxygen content must be estimated by first estimating alveolar PO_2 with the ideal alveolar gas equation and then using that PO_2 value to estimate capillary blood saturation based on the oxyhemoglobin equilibrium curve. If the P_AO_2 is suitably high (>120 mmHg) then 100% saturation of pulmonary capillary blood may be assumed. The shunt equation is slightly cumbersome and a clinically useful shortcut is to estimate 5% extra shunting (5% is normal so this is *additional* shunting added to the 5% baseline value) for every 100 mmHg that the P_aO_2 is below the expected value for that F_IO_2. For example, if a patient has a P_aO_2 of 200 mmHg on 100% oxygen then one would estimate the shunt fraction to be 20% (expected P_aO_2 is 500 mmHg on 100% oxygen). Mechanical ventilation may result in minimal improvement in hypoxemia due to anatomic shunting. Distension of the lung with positive pressure may reduce the resistance in extra-alveolar vessels while increasing the resistance in pulmonary capillary beds. The end result in some cases may be a net rise in pulmonary vascular resistance and an increase in shunting.

Box 2: The Shunt Equation

$$\frac{Q_s}{Q_T} = \frac{C_c'O_2 - C_aO_2}{C_c'O_2 - C_vO_2}$$

Qs/Qt = shunt flow as a fraction of cardiac output
$Cc'O_2$= pulmonary end-capillary oxygen content
CaO_2 = arterial oxygen content
CvO_2 = mixed or central venous oxygen content

Physiologic shunting occurs when perfusion is maintained to non-ventilated alveoli. This situation could be considered a failure of hypoxic pulmonary vasoconstriction. Inflammatory mediators and drug agents can compromise the function of both the sensing and effector arms of this response system. As alveolar oxygen tensions drop, the expected response is that the local vascular resistance to those alveoli will increase, thus diverting flow to better-ventilated alveoli. In the case of zero alveolar ventilation the optimal response would be to reduce perfusion to that region as well. Failure to do so results in physiologic shunting. The effect is the same as if the lung were not there at all and the blood was passing through an anatomic shunt. This mechanism explains why obstruction of ventilation to a lung lobe during lung lobectomy (e.g. during one-lung ventilation for thoracoscopic lung lobectomy) results in hypoxemia, but the subsequent lung lobectomy itself does not. Removal of an excessive amount of lung tissue (e.g. all of the lung lobes on the right side) can result in hypoxemia, however this is due to ventilation-perfusion mismatching (excessive perfusion relative to ventilation) in the remaining lung lobes rather than physiologic shunting. Much as is observed with anatomic shunting, physiologic shunting when excessive can result in hypoxemia that is unresponsive to oxygen supplementation. In this setting, the clinical priority is to restore ventilation to the non-ventilated alveoli, which often mandates mechanical ventilation with positive end-expiratory pressure (PEEP).

Ventilation-perfusion (V/Q) mismatching is perhaps the most common cause of hypoxemic respiratory failure in small animal practice. Aspiration pneumonia, cardiogenic edema, and non-cardiogenic edema are commonly encountered causes of hypoxemia in small animal patients and can each result in respiratory failure. Pleural filling disorders can result in ventilation-perfusion mismatching as well as hypoventilation. Atelectasis and pulmonary thromboembolism each result in V/Q mismatching as well albeit by vastly different mechanisms. Pulmonary hypertension is increasingly recognized as a major health concern in veterinary species and can result in substantial V/Q abnormalities. In the ideal lung, ventilation and blood flow would be delivered proportionally to alveoli. An increase in ventilation relative to blood flow (high V/Q ratio) is akin to deadspace ventilation and does not directly cause hypoxemia. The blood flowing to such alveoli encounters alveolar oxygen tensions that are normal or slightly above typical values. Perfect 1-to-1 matching likewise produces conditions that are favorable for pulmonary capillary and alveolar oxygen tensions to reach equilibrium assuming blood flow rates are not excessive (and they rarely are except in extreme circumstances). It is in those alveolar units in which perfusion is disproportionately high relative to ventilation that hypoxemia develops. In this setting, blood encounters atypically low alveolar oxygen tensions and saturation is sub-maximal. The mixing of this poorly arterialized blood with the blood draining high and normal V/Q regions results in systemic hypoxemia. The shape of the oxyhemoglobin equilibrium curve precludes the high V/Q regions from "compensating" for the low V/Q regions. The flat portion observed at high PO_2 values prevents an increase comparable to the decrease observed at lower PO_2 values (the steep portion). Moreover, the low V/Q regions may be of that nature because of high flow (not

just low ventilation) and are thus contributing a disproportionately high volume to the final mixture. Likewise, the high V/Q regions may represent areas with normal ventilation but lower perfusion and are thus contributing relatively less volume to the final mixture.

As with physiologic shunting, V/Q mismatch may be considered a failure of hypoxic pulmonary vasoconstrictive responses in many settings. Inflammatory mediators are often vasoactive in nature and may directly impair pulmonary vasoconstrictive responses that might otherwise have been generated to maintain V/Q matching appropriately. Whether the problem arose due to a reduction in ventilation or an increase in perfusion, adaptive compensatory adjustments would be expected in any otherwise healthy animal. In other circumstances, inadequate hypoxic pulmonary vasoconstriction may not be primarily responsible for the V/Q inequality. In massive pulmonary thromboembolism (PTE), the portion of the lung to which blood flow is compromised in now a high V/Q region. It has become physiologic deadspace and is not directly responsible for hypoxemia (high V/Q regions provide well oxygenated blood). In this setting, if cardiac output does not fall substantially then the remaining lung is now over-perfused and represents a large region of low V/Q alveolar units. In this way, hypoxemia can result indirectly. This explanation seems insufficient to explain clinical experiences with this disease process, however. Surgically removing a similarly sized region of lung would presumably produce the same level of over-perfusion, but does not typically result in hypoxemia. The missing portion of the mechanism for hypoxemia in this setting is likely to be altered bronchomotor tone. It was first demonstrated in 1942 that pulmonary thromboembolism (or external mechanical occlusion of a pulmonary artery) results in bronchospasm in the dog. The hypoxemia seen in PTE, but not following lung lobectomy, is likely the result of over-perfusion combined with regional decreases in ventilation. Relief in sensations of dyspnea in humans is reported following theophylline administration. This may be due to a reduction in bronchospasm or reduced activation of pulmonary C-fibres via adenosine receptor antagonism.

Diffusion impairment is a common contributor to hypoxemia in small animal patients, but rarely a sole or primary cause of such. Fick's Law of Diffusion details the major contributing factors to gas or solute flux via diffusion: (1) concentration or partial pressure difference, (2) length of the diffusion pathway, and (3) surface area available for diffusion. With these factors in mind, both hypoventilation and low P_IO_2 represent a reversible form of diffusion impairment. Many of the diseases listed above under ventilation-perfusion mismatch result in alveolar flooding or collapse. This represents a loss of surface area for diffusion. In a similar manner, PTE results in the formation of excessive alveolar deadspace, which also represents a loss of surface area for diffusion. Among the diseases common to small animal practice, chronic congestive heart likely represents the best example of increased diffusion distance. Remodeling of the alveolar epithelial-capillary endothelial interface in chronic congestive heart failure can result in thickening of this barrier and an increased diffusion distance.

Despite these many examples of means by which common disease processes can compromise the process, diffusion limitation is considered to be a primary cause of hypoxemia on only rare occasion. In human medicine, emphysema can result in a massive sustained loss of surface area and diffusion limitation is considered a more significant cause of hypoxemia in that species. The limited role of diffusion limitation in producing hypoxemia in small animal species is perhaps best illustrated in the setting of chronic congestive heart failure. In this syndrome, some degree of diffusion limitation is likely chronically present yet hypoxemia is rarely noted in the absence of pulmonary edema with alveolar flooding and V/Q mismatch. Pioneering work by Norman Staub has previously demonstrated in acute models of canine congestive heart failure that interstitial pulmonary edema is insufficient to produce hypoxemia in the absence of alveolar flooding in this species. Many clinicians have reported the experience of managing congestive heart failure patients in which clinical signs of respiratory distress improve markedly despite persistence of radiographic evidence of interstitial pulmonary edema. Such experiences may reflect resolution of hypoxemia prior to clearance of excessive fluid accumulation in the pulmonary interstitium.

Diffusion impairment may be overcome by increasing the partial pressure gradient by raising P_AO_2 or instead by recruiting additional surface area (or both). The recruitment of additional surface area can involve both recruitment maneuvers (breath hold) and the application of PEEP.

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L-14 Avian physiology: Implications for anesthesia

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Birds represent the only clade of dinosaurs to have survived the Cretaceous–Paleogene extinction event 65.5 million years ago. Taxonomically, birds comprise the Class Aves consisting of 27 Orders, 168 Families and approximately 10,000 species worldwide and inhabit every continent on this planet, living in a wide range of environmental niches, some inhospitable to humans. Emperor penguins (*Aptenodytes forsteri*) live in the Antarctic, Ruppell's griffon (*Gyps rueppelli*) can soar at extreme altitude (11,485 m; 37,900 feet), wandering albatrosses (*Diomedea exulans*) spend most of their life in flight, landing only to breed, and the burrowing owl (*Athene cunicularia*) nests underground. Birds also vary in size. Bee Hummingbirds (*Mellisuga helenae*) measure 5-6 cm (2-2.4 inches) in length and weigh 1.6-2 grams while the ostrich (*Struthio camelus*) has a height of 2.75 m (9 feet) and weighs up to 145 kg.

For millennia humans have been fascinated with birds because of their ability to fly and their feathered beauty. Flight is the ability to produce lift, to accelerate, and to maneuver at various speeds. In terms of energy expenditure, it is the most demanding form of locomotion in animals and exerts the most demands on the respiratory system; its energetic demands are beyond those attainable by non-flying animals. For example, a pigeon running on a treadmill consumes oxygen at 27.4 mL/min, but while flying at 19 m/s, oxygen consumption is 77.8 mL/min. However, at high speeds the distance covered per unit of energy expended is less than that of other forms of locomotion, thus it is the most efficient form of locomotion.

Smaller, agile passerine birds can attain speeds of 15–40 kph, while swifts, pigeons and loons can attain speeds of 90–150 kph (56–93 mph), and falcons have been clocked at more than 180 kph (≥112 mph). Although these flight speeds may seem slow by comparison to commercial jet flight, we gain a different perspective when speed is scaled to body size. A Boeing 747-400 jet has a length of 71 m and cruises at 963 kph or 268 m/s, thus traveling 3.8 times its own length in 1 s. By comparison, a swift flying at 40 kph covers 100 of its body lengths in 1 s. An athletic human covers five body lengths in 1 s; the cheetah, the fastest land mammal, covers 18 body lengths per second.

Humans have also had a practical interest in birds as a source of food. But in domesticating and selecting for desirable production characteristics, such as rapid weight gain or high egg laying capability, a number of structural and functional changes have occurred in domesticated species that are not seen in their wild counterparts. For example, turkeys selected for rapid weight gain have lower lung volume and gas exchange surface area compared to turkeys not so selected. Layer chickens have a smaller lung volume relative to body weight, a lower oxygen diffusing capacity, and a greater blood:air capillary volume ratio than their wild ancestor, the Red Jungle Fowl (*Gallus gallus*). Thus when studying avian physiology, especially cardiorespiratory physiology, one must keep in mind that important physiological differences exist between wild and domesticated birds.

Gas Exchange

Avian respiratory system specific volume (respiratory gas volume per unit of body mass) is between 100 and 200 mL/kg, but the volume of gas in parabronchi and air capillaries accounts for only 10% of the total specific volume. By comparison, a dog's specific volume is 45 mL/kg, and pulmonary gas volume in the mammalian lung is 96% of the total specific volume.

A tertiary bronchus (parabronchus) and its mantle of intertwined air and blood capillaries is the basic unit of gas exchange in birds. Gas exchange surface area varies from a low of ~10 cm^2/g body weight in chickens to a high of 87 cm^2/g in hummingbirds. Bats, the only flying mammal, have a surface area of 63 cm^2/g, while in shrews and humans it is 33 and 18 cm^2/g, respectively. Thickness of the blood–gas barrier is also important; the most meaningful estimator of diffusing capacity (conductance) of the blood–gas barrier is harmonic mean thickness, which in domestic chickens and hummingbirds is 0.318 and 0.099 μm, respectively; in bats, shrews and humans it is 0.219, 0.338, and 0.620 μm, respectively. The greater surface area and thinner mean harmonic thickness of the avian lung make it an extremely efficient gas exchanger, more so than the mammalian lung.

The efficiency of the avian lung becomes apparent when considering what happens to the partial pressures of carbon dioxide (PCO_2) and oxygen (PO_2) both in respired gas as it flows through the lung and in blood as it perfuses the lung. Gas flowing along a parabronchus receives CO_2 and gives off O_2 so that at the inflow end of the parabronchus gas has the lowest PCO_2 while gas at the outflow end has the highest PCO_2; the reverse is true for PO_2. The overall result is that the partial pressure of CO_2 in end-parabronchial gas (P_ECO_2) can exceed the partial pressure of CO_2 in arterial blood (P_aCO_2), and the partial pressure of O_2 in end-parabronchial gas (P_EO_2) can be lower than the partial pressure of O_2 in arterial blood (P_aO_2).[1-3] This potential overlap of blood and gas partial pressures for both CO_2 and O_2 demonstrates the high gas exchange efficiency of the avian lung.[1, 2, 4]

Gas exchange in awake, healthy birds occurs through a process involving a wide range of integrated pulmonary and extra-pulmonary factors that operate sub-maximally (a broad-based low-keyed strategy),5 but the efficiency of which is obvious when one considers the altitudes at which some avian species fly. Bar-headed geese (*Anser indicus*) serve as a model. These birds have been documented to fly over the Himalayas at altitudes of up to 7290 m (~24,000 feet); most fly over the Himalayas at 5500 m (~18,000 feet).4 At this altitude the atmospheric pressure is ~390 mmHg or 51% that at sea level, and the PO_2 in the cold dry air is 82 mmHg. Assuming a bar-headed goose maintains constant body core temperature of about 41C, and inhaled air is warmed to body temperature and fully saturated with water vapor, the PO_2 in the air reaching the air capillaries is ~72 mmHg!! Flapping flight is metabolically demanding and requires sustained high rates of O_2 consumption that are 10 to 15 times above resting levels in a wind tunnel at sea level; bar-headed geese are able to meet this metabolic demand in air that severely limits aerobic metabolism in many lowland animals.[4]

Gas exchange efficiency of the avian lung is not the sole reason why birds can fly at extreme altitudes or dive into the ocean's depths. Although not part of the respiratory system, hemoglobin is crucial for transporting oxygen by blood from the lungs to all tissues of the body.

Birds possess two types of hemoglobin, each with different oxygen affinities; as a result erythrocytes have a greater range of oxygen partial pressures over which oxygen can be bound and released, an advantage for avian species that must cope with large variations in the partial pressure of oxygen. For example, high-altitude flying birds and penguins encounter hypoxic conditions, but their conditions differ: high-altitude flyers, such as bar-headed geese, contend with prolonged hypoxia during sustained metabolically-powered flight whereas penguins experience transient but frequent hypoxia during dives. The P_{50} of hemoglobin, the partial pressure of oxygen at which hemoglobin is 50% saturated with oxygen, is lower in birds living at extreme altitudes and in diving birds such as penguins than birds in general.[6] A low P_{50} means that the hemoglobin has a high affinity for oxygen thus favoring the uptake of oxygen in the lungs, an obvious advantage under hypoxic conditions. The hemoglobin–oxygen affinity in emperor penguins (*Aptenodytes forsteri*) (P_{50} = 28 mmHg, pH 7.5) is similar to that in bar-headed geese (*Anser indicus*) (P_{50} = 27.2 mmHg).[6] In emperor penguins this P_{50} allows increased oxygen at low blood PO_2 during dives and more complete depletion of the respiratory store of oxygen.

The tremendous diversity in form, function and mode of life that exists across avian Orders, and between wild and domesticated species, poses challenges to our anesthetic management of birds, a challenge that can be lessened by considering and applying basic principles of avian physiology. Indeed, the avian cardiorespiratory system seems far superior to that of mammals, but it often poses challenges to designing and implementing anesthetic protocols for birds. This talk focuses on these two systems and their implications for anesthetic management.

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L-15 Applying pathophysiologic and pharmacological principles to anesthesia management of ruminants and camelids

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Due to the extensive nature of this topic the focus for this manuscript and accompanying lecture will be to highlight a few aspects of ruminant and camelid pathophysiology and pharmacology as they apply to clinical management. While local and regional techniques are briefly mentioned, emphasis will be on sedation and general anesthesia management. Veterinarians responsible for anesthesia care of food producing ruminants should be aware of regional, national and international regulatory considerations.

Special considerations for general anesthesia of ruminant and camelid species

1) Salivation, regurgitation and bloat
   a) Ruminants (up to 50 L/day for cattle and 16 L/day for sheep) and to a lesser extent camelids, salivate copious amounts and as they cannot swallow during anesthesia, there is a potential loss of buffering capacity.
   b) Anticholinergics may reduce secretions briefly but also have potential to increase thickness of both salivary and airway secretions in these species
   c) Ruminants and camelids frequently regurgitate, and ruminants may bloat (albeit less likely if fasted). A 'bloat' tube may be placed to relieve gas distention during extended anesthesia periods and administer medications if the need arises.
   d) A 24 – 48 hour food fast, 12 – 18 hour water fast is recommended for adult ruminants and camelids if environmental conditions allow. May also help allay V/Q abnormalities. Nursing animals may continue to nurse (solid feed should be withheld) until just prior to general anesthesia
2) Oxygenation
   i) Llamas are adapted to high altitude
      (a) RBCs contain more hemoglobin (MCHC ~ 40%)
      (b) Hemoglobin has high oxygen affinity (P_{90} ~ 50 mm Hg)
      (c) Packed cell volume often low compared to other species (25 – 32%)
      (d) Ventilation / perfusion matching seems fairly good
   ii) Sheep do not oxygenate well
      (a) Hemoglobin has low oxygen affinity (P_{90} ~ 72 mm Hg)
      (b) Ventilation / perfusion mismatch is common
      (c) Xylazine activates PIMs, leading to damage to capillary endothelium and alveolar type-I cells, intra-alveolar hemorrhage, and pulmonary edema and hypoxemia
   iii) Ventilation perfusion abnormalities observed in recumbent cattle
      (a) This has shown to be exacerbated by xylazine
      (b) Septate or lobed lungs, with little to no collateral ventilation. Bronchus to right lung lobe at approximately level of 3rd rib (similar in small ruminants)
      (c) Hypoxic pulmonary vasoconstriction notable (clinical implications broader reaching than for anesthesia management)
      (d) Respiratory pattern designed to accommodate rumen (rate of approximately 20 breaths per minute and smaller tidal volume than comparably sized horse)
3) Venous catheterization
   i) Llamas
      (a) Jugular vein preferred
      (b) Thick skin; vein difficult to visualize or palpate - Make pilot hole with blade
      (c) Recommend site higher on neck
   ii) Ruminants
      (a) Jugular vein in cattle; jugular, saphenous, cephalic or auricular veins in small ruminants
      (b) Skin not as thick in ruminants as camelids over jugular vein, but pilot hole helpful during catheterization of cattle
4) Endotracheal intubation
   a) Anatomy
      i) Long narrow jaws that do not open very wide
      ii) Thick tongue
      iii) Long soft palate
      iv) Sharp teeth
      v) Short neck in ruminants
      vi) Right apical (tracheal) bronchus must be considered in ET tube placement
   b) Technique
      Camelids and small ruminants
      i) Local anesthetic to desensitize arytenoids
      ii) Mouth gag or gauze ties to hold jaws apart
      iii) Long laryngoscope blade
      iv) Long ET tube
      v) Stylet used as guide
      vi) Nasotracheal intubation an option in llamas/alpacas
      Larger ruminants and camels
      i) Manual intubation – essential to have good holder and mouth gag
      ii) First palpate the epiglottis and arytenoids, and then guide the ET tube between the

arytenoids into the trachea
iii) Guide tube may be used
iv) Sternal recumbency if possible to minimize regurgitation
v) Appropriate anesthesia plane (balance active and passive regurgitation)

5) Post-anesthetic upper airway obstruction (llamas)
i) Preferential nasal breathers
ii) Prone to dorsal displacement of soft palate
iii) Exacerbated by nasal congestion after head-down positioning
iv) Lavage of nasal passages has been suggested prior to recovery and extubation

6) Restraint, moving, padding and positioning
i) Requires specialized equipment (e.g., chute/tilt table) or a lot of physical effort / personnel for large ruminants and camelids. Small ruminants and camelids may be halter trained, hobbled and blindfolded to facilitate minor procedures (e.g., catheter placement)
ii) Superficial nerves such as the radial nerve are subject to trauma and resulting paresis especially in larger animals
iii) Myopathies may occur with poor padding and/or hypotension

7) Blood pressure
i) Tends to be elevated in adult cattle during inhalation anesthesia
ii) Drug protocol influences blood pressure in non-domesticated ruminants/camelids

8) Medications
i) Most notable is sensitivity to xylazine among these species. Ruminants require about $1/10^{th}$ of standard route specific equine doses; approximately $3/10^{ths}$ for camelids. This sensitivity is not reported with detomidine, medetomidine.
ii) Analgesic responses to opioids are variable among these species. Ileus and behavioral side effects may be observed
iii) NSAID medications such as aspirin can be administered orally whereas others are given IV

9) Ocular (eye) considerations during anesthesia
i) Eye signs are not reliable in camelids; both globe movement and a palpebral response may be observed variably throughout anesthesia. Eyelid aperture has however been correlated with anesthesia depth in at least one study.
ii) Due to the prominent position of the globe in llamas and alpacas, lubrication and protection is key to prevention of trauma and subsequent ulceration.
iii) Globe position is associated with changing planes of anesthesia in cattle; the globe rotates ventrally with increasing depth and a medial ventral eye is thought to be appropriate for surgical anesthesia. A dorsal rotation suggests a deeper plane. Nystagmus is not common in cattle but may be associated with a changing plane of anesthesia.

10) Recovery from anesthesia
i) Ruminants and camelids tend to recover well following general anesthesia
ii) Oxygen should be supplemented until extubation (after swallowing is observed)
iii) Sternal positioning of ruminants will facilitate eructation

Anesthesia Techniques (Selected suggestions included as information)

Regional Anesthesia

Many procedures are performed in standing cattle with only regionally administered local anesthetics. Due to complications associated with recumbency these methods are selected because they facilitate surgical intervention and minimize the need for administration of drugs with systemic effects. Regional techniques are also be used in the sedated or anesthetized patients to provide analgesia or anesthesia.

Individual nerve blocks and regional anesthetic administration as for example the paravertebral n. block are described in cattle and camelids. Epidural techniques are also described for ruminants, camelids and pigs. Lidocaine (0.22 mg/kg) and xylazine (0.17 mg/kg) have been used to facilitate diagnostic and surgical procedures involving the rectum, vagina and perineum in llamas. The onset of anesthesia is 3-4 minutes following either lidocaine or xylazine and lidocaine, but the duration varies significantly lasting about 1 hour with lidocaine and 6 hours if using both drugs. Analgesia following xylazine alone is evident after about 20 minutes and lasts 3 hours. Mild sedation is reported in animals receiving xylazine. Epidural morphine at doses (0.05 – 0.2 mg/kg) similar to those used in other species may provide longer term analgesia and may have value for post-operative analgesia for procedures involving the hind limbs or caudal abdomen and perineum. Note that in sheep spinal administration of morphine frequently results in pruritis; similar side effects can be observed in other species.

Sedation and Injectable Anesthesia Techniques in Cattle

Xylazine 0.05-0.2 mg/kg IM for in light to heavy sedation/recumbency
Xylazine 0.2 mg/kg IV can provide conditions suitable for intubation
Detomidine 2.5 – 10 μg/kg IV or IM for sedation
Butorphanol 0.02 to 0.05 mg/kg IV for light sedation
Butorphanol may be combined with xylazine 0.01-0.03 mg/kg, or acepromazine 0.02-0.03 mg/kg for moderate to heavy sedation
Diazepam 0.05-0.1 mg/kg IV for 5 – 10 min of restraint
Acepromazine 0.05-0.2 mg/kg IM or 0.05 mg/kg IV for mild tranquilization
Ket Stun (IM or SQ)
Xylazine 0.02 to 0.05 mg/kg
Butorphanol 0.01 to 0.025 mg/kg or Morphine 0.02

to 0.05 mg/kg
Ketamine 0.04 – 0.1 mg/kg
For standing procedures in adult cattle a recommended starting combination is X 10 mg, B 5 mg and K 20 mg. Recumbency is observed with higher doses notably xylazine

Guaifenesin (GG) 50-100 mg/kg + ketamine (1-2 mg/kg) IV 10 – 20 min recumbency
Can mix 1 L 5% GG with 1-2 gm ketamine and administer "to effect"
Diazepam 0.1 mg/kg + ketamine 2-5 mg/kg IV for 15 – 30 min recumbency
Mix guaifenesin (1 L 5% 50 mg/mL) + xylazine 100 mg (0.1 mg/mL) + ketamine 1-2 gm (1-2 mg/mL) IV only aka 'Triple drip' for cattle: Loading dose 0.5 mL/kg; maintenance dose 0.7-2.2 mL/kg/hr
Xylazine (0.05-0.1 mg/kg) + ketamine (1-2 mg/kg) IV for recumbency of ~ 20 min
Xylazine (0.03-0.05 mg/kg) + diazepam (0.1 mg/kg) + ketamine (2 mg/kg) IV for recumbency of ~ 30 min

Sedation and Injectable Anesthesia Techniques in Sheep
Butorphanol 0.1-0.5 mg/kg IV for mild sedation and approximately 1 – 2 hours of analgesia.
Diazepam 0.25-0.5 mg/kg IV for short term sedation
Xylazine 0.05-0.2 mg/kg IV or IM for sedation
Detomidine 2.5 – 10 μg/kg IV or IM for sedation
Diazepam 0.1-0.2 mg/kg + ketamine 2-5 mg/kg IV for 5 – 15 min of recumbency
Guaifenesin 25 – 100 mg/kg + ketamine 2-5 mg/kg for 5 – 15 min of recumbency
Diazepam 0.1-0.2 mg/kg + propofol 2 mg/kg IV for 5 – 10 min of recumbency
Dr. Larue Johnson's (prior CSU faculty) small ruminant "cocktail":
Mix: Ketamine 1000 mg (10 mL) with Xylazine 100 mg (1 mL) and
Butorphanol 10 mg (1 mL) for a total volume of 12 mL
Dosed at 0.01 ml/lb
Variable duration of recumbency – can last 30 – 45 minutes; hypoxemia notable.

Sedation and Injectable Anesthesia Techniques in Goats
Xylazine 0.05-0.1 mg/kg IV or 0.1-0.2 mg/kg IM – Sternal recumbency observed in 5 –10 min, sedation can last 20 – 90 min and recovery is frequently prolonged lasting 60 – 240 min
Medetomidine 15-30 μg/kg IM for recumbency up to 75 min in duration
Diazepam 0.1 -0.2 mg/kg IV + Butorphanol 0.1 mg/kg IV for sedation
Diazepam 0.1-0.2 mg/kg + ketamine 2-5 mg/kg IV for 5 – 15 min of recumbency
Xylazine 0.1-0.2 mg/kg + ketamine 11 mg/kg IM (combined) for 40 – 45 min of recumbency. Recovery can take 90 – 120 min

NOTE: Alpha-2 agonists (e.g., xylazine) provide good sedation (albeit as in other species, individual animals may temporarily arouse during stimulation) and analgesia, but are associated with marked cardiovascular and respiratory depression in ruminants. Hypoxemia is marked with these drugs in all ruminant species. Xylazine has been associated with third trimester abortions in cattle and so should be used cautiously in that situation. Antagonists for xylazine: tolazoline 0.2 to 2.2 mg/kg) IV or IM (smaller cattle require higher dosage/kg; yohimbine 0.13 mg/kg IV or IM

Sedation and Injectable Anesthesia Techniques in Camelids
Diazepam (or Midazolam) 0.02-0.1 IV mg/kg for sedation in cria's
Butorphanol 0.01-0.04 mg/kg for mild sedation and possibly analgesia
Xylazine 0.05-0.3 mg/kg IV or IM for sedation and possibly recumbency for 30-45 min
Ketamine 2.5-5 mg/kg + diazepam 0.1-0.2 mg/kg IV for 10-15 min recumbency
Xylazine 0.25 mg/kg IV (or IM) + ketamine 2.5 mg/kg IV (or 5 mg/kg IM) for 30-60 min recumbency
Dr. Larue Johnson's (prior CSU faculty) camelid "cocktail":
Mix: Ketamine 1000 mg (10 mL) with Xylazine 100 mg (1 mL) and
Butorphanol 10 mg (1 mL) for a total volume of 12 mL
Administered at 1 ml/40 lb for alpacas and 1 ml/50 lb for llamas.
Results in approximately dose of Xylazine 0.3-0.4 mg/kg + Butorphanol 0.03-0.04 mg/kg +
Ketamine 3-4 mg/kg IM and provides 20 (alpacas) to 60 (llamas) min recumbency
Guaifenesin 50 mg/mL 1 liter + ketamine 2 mg/mL 2 gram + xylazine 0.2 mg/mL 200 mg titrated to effect aka triple drip for camelids (care to not exceed 100 mg/kg guaifenesin within a 60 minute period)

Following sedation or anesthesia induction with aforementioned techniques, anesthesia may be maintained with inhalation anesthetics or with a combination of inhaled and injectable agents (e.g., ketamine, morphine, etc). These adjunct drugs may be used to provide peri-anesthetic analgesia which while not the focus of this talk, are an important consideration in food animals and limited study supports an improvement in productivity. Many analgesics have been suggested for use in ruminants and camelids including NSAIDs (e.g., aspirin 100 mg/kg PO q 12 hours or phenylbutazone 5-10 mg/kg PO or IV q 24 – 48 hours in cattle, Flunixin meglumine at 1 – 2 mg/kg, IV or IM in all these species), and opioids (e.g., fentanyl 2 microgram/kg/hour in sheep, morphine 0.1 – 0.3 mg/kg in camelids or sheep IV or IM, butorphanol 0.05 – 0.1 mg/kg IV or IM in all these species).

References provided upon request

Friday 4th September | Room A | 9:50−10:50

L-16 Errors in veterinary anesthesia

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In August 1950, Dr. J. Edwards Deming lectured on statistical process control and concepts of quality improvement to the Japanese Union of Scientists and Engineers.[a] Amongst those attending was Dr. Kaoru Ishikawa who subsequently became a driving force in Japan's quality improvement processes (QIP); his name is internationally recognized today because of his contributions to QIP.

Forty-nine years later in November 1999 the Institute of Medicine published "To Err is Human: Building a Safer Health System" documenting in-hospital deaths in US hospitals each year due to preventable medical errors.[1] The patient safety movement that has developed as a result of that report uses many of the quality improvement processes and tools developed by Dr. Ishikawa. Error and patient safety are major topics in human medicine, but what about in veterinary medicine?

It's a busy night of emergencies and a new intern's first night on duty. He is assisting with a German shepherd dog with GDV. After initially stabilizing the dog, it is anesthetized and intubated (ETT) to facilitate passing a stomach tube. Without further instructions the intern is told to attach an oxygen insufflation hose to the ETT. He inserts the hose into the ETT instead of attaching it to a flow-by device; oxygen flow is set at 5 L/min. The error goes unnoticed because the team is focused on decompressing the dog's stomach; within minutes the dog has a cardiac arrest. During CPR the team recognizes that the dog has a pneumothorax and its source is quickly identified.

How should this situation be handled? When a patient under our care suffers a life threatening injury or dies, it's natural to look for something or someone to blame; usually it's the person who "made the mistake." This is a normal response. Subsequently we may reprimand or terminate the individual who caused the accident thus assuming we have prevented from ever occurring again. Unfortunately, such is not the case. This approach fails to take into account two realities: 1) all humans, without exception, make errors;[2] and 2) errors are often due to latent conditions within the organization, conditions probably present long before the person who erred was hired. We can either acknowledge these realities and take steps to learn from errors and accidents, or we can deny them out of fears of criticism or litigation, and condemn ourselves to make the same errors over and over again.[2-9]

There are two approaches to thinking about human fallibility and the making of errors: the person approach and the systems approach.[6] The person approach focuses on individuals and their errors, and attributes their errors to aberrant mental processes, such as forgetfulness, inattention, poor motivation, carelessness, negligence, and recklessness.[6] Those who follow this approach often use countermeasures such as naming, blaming and shaming the individual who erred.[6] They also tend to treat errors as moral issues because they assume bad things happen to bad people, what psychologists call the just world hypothesis.[6]

In contrast, the systems approach recognizes that humans always have and always will make errors, a reality we can not change.[7] But the conditions under which people work can be changed so as to build defenses within an organization to prevent errors or mitigate their effects.[6] Adherents of the systems approach strive for a comprehensive management program aimed at several different targets: the person, the team, the task, the workplace, and the institution as a whole.[6]

Some have misgivings about the systems approach because they believe it will lead clinicians to behave irresponsibly and not take responsibility for their errors.[5] These fears are unfounded because they tend to confuse the making of an error with misconduct.[5] Misconduct is never to be tolerated in healthcare. Dr. Lucian Leape contends that the systems approach increases a clinician's responsibilities: when an error does occur the clinician has an obligation to future patients to ask how the error could have been prevented and questions the system with all of its component parts. The majority of errors—95% or more—are made by well-trained, well-meaning, conscientious people who are trying to do their job well, but who are caught in faulty systems that set them up to make mistakes thus becoming "second victims."[5]

Error origination: The organization

A human factors-based model uses a four-tiered framework for categorizing causes of errors: 1) unsafe acts or the actual actions of the healthcare provider leading to the incident; 2) preconditions for unsafe acts; 3) supervision or management actions affecting the healthcare provider; and 4) organizational influences.[10] This model delineates the elements involved in error generation and makes explicit the role of organizational factors in error causation. Error generation is often due to latent factors inherent in the organization;[7, 11-14] they exist as a result of defensive gaps, weaknesses, or absences unwittingly created within a system as the result of earlier decisions made by the designers, builders, regulators, managers and supervisors of the organization or system.

Error origination: The individual

Unsafe acts are those actions taken by individuals that cause errors. Actions taken are preceded by

cognitive processes that we must understand in order to prevent errors. A widely accepted cognitive model posits that the human mind functions in two modes:[8, 15] 1) a schematic control mode that is automatic, fast-responding and in which the mind has unconscious mental models composed of old knowledge¬¬—schemata—activated by very little conscious thought or by sensory inputs which the mind interprets from earlier experiences; and 2) an attentional control mode that is a controlled, conscious, analytical mode of cognition requiring effort that is difficult to sustain; it uses stored knowledge and is used when one encounters a new situation or the schematic control mode has failed.

Within this cognitive model there are three levels of human performance:[8, 15] 1) skill-based (SB) level performance governed by stored patterns of pre-programmed instructions—schemata—that are largely unconscious, highly routinized, and occur in familiar circumstances; skill-based performance relates to technical performance and proper execution of tasks;[14] 2) rule-based (RB) level performance consists of actions or solutions governed by stored rules of the type "if...then"; rule-based performance relates to supervision, training and qualifications, communication, and interpretation;[14] and 3) knowledge-based (KB) level performance that occurs when synthetic thought is used for novel situations; it requires conscious analytical processing and stored knowledge.

Conceiving of and executing an action sequence involves three stages: planning, storage (memory), and execution. Errors may occur within any of the three stages; the types of errors that may occur are: slips, lapses, and mistakes. There are many types of slips, but in general the actual action is wrong even though the intended action may have been correct. Slips are usually observable and often occur as a result of any number of factors that divert one's attention from the task at hand. Absent-minded slips increase the likelihood of making errors of omission.[15]

Lapses involve failures of memory that occur when one's attention is distracted or preoccupied; they are usually apparent only to the person who experiences them.[15] Thus, slips are execution failures while lapses are storage failures; both occur at the skill-based level.[15]

Mistakes occur when a plan is inadequate to achieve its desired goal even though the actions may run according to plan; mistakes occur at the planning stage of both RB and KB levels of performance.[16, 17] They are errors of conscious thought that can be affected by the same physiological, psychological and environmental factors that produce slips. An RB error (mistake) occurs when a good rule is misapplied because the individual fails to interpret the situation correctly, or applies a bad rule that exists in memory.[17]

Knowledge-based errors (mistakes) are complex because it is difficult to identify what an individual was thinking at the time of an error. The usual scenario is that a novel situation is encountered for which the induvidual does not possess pre-programmed solutions (no schemata) and an error arises for lack of knowledge, or because the problem is misinterpreted.

What strategies can we implement to prevent errors? A crucial prerequisite is to recognize that most errors are due to human actions and humans will always make errors. Everything else follows from this reality. Healthcare givers then need to be aware of factors in the environment that may cause errors, including self (current state of the individual(s) in the organization), context (nature of the environment in which the 'self' and 'task' interact), and task.[7] This state of awareness, referred to as "mindfulness," requires that we "know" the nature of our work environment with all its pitfalls and hazards. Specific methods for gaining knowledge of the work environment include: voluntary reporting and logging of errors;[18] effectively using M&M rounds for identifying and dealing with errors by promoting open dialogue; using human factors analyses, root cause analysis, causal trees, reality charting, Ishikawa diagrams, mind maps and systems walks; all are meant to uncover truths/realities or existing factors that promote or detract from effective performance of a task.

Using case examples this talk will elaborate on the concepts of error generation and prevention.

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Friday 4th September | Room A | 10:50−11:50

L-17 Recent advances in monitoring and treatment of the respiratory system in anaesthetized animals

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Examination of the distribution of ventilation has been the target of many research projects because it is an important determinant of ventilation / perfusion inequality and hypoxemia. Historically it was examined by invasive and cumbersome methods that do not allow repeated measurements.

There is an exponentially increasing interest for a novel monitoring device (Electrical Impedance Tomography) in human medicine that may also be applicable for animals. Electrical Impedance Tomography (EIT) is a non-invasive, radiation-free, easily applicable and repeatable method for examining the aeration of the lungs. Its operation is based on measuring voltages between electrodes placed around the thorax while a small electrical current is injected between two of these electrodes. A two dimensional impedance map can be reconstructed from these voltage data representing mostly the distribution of air at the EIT electrode plane. Creating such images at high repetition rate (e.g. 50 Hz) provides a video image in which the distribution of air (movement of lungs) can be observed in real time. The resolution of EIT images is relatively low but EIT images were favourably compared to those obtained by other methods such as dynamic CT, SPECT, PET, hyperpolarized He MRI and Xe CT in different species. However, the applicability of EIT on domestic animals has not yet been established. Many studies are currently in progress.

In order to provide anatomically plausible EIT images there is a need for a pre-defined electronic image, so called mesh. Such mesh resembles the contour of the object to be examined (e.g. the thorax of a horse) and contains assumptions about internal organ location. Each mesh is species specific and represents an average subject (animal or human patient); therefore, the mesh cannot accommodate to individual anatomical or pathological variances. Additionally, the fact that the locations, sizes and shapes of organs change during respiration but the mesh is static may further increase uncertainty of the model.

The next step is to project the impedance data onto this mesh (typically 32x32 pixels) that defines the resolution of an EIT image. Many different and complex mathematical algorithms are being used for this purpose. However, there is no single good solution for this mathematical problem. It means that a single set of voltage measurements (e.g. collected during an experiment) may be used to generate multiple impedance maps (EIT images). That's why it is important to input initial guesses into the algorithm (e.g. this is the purpose of the mesh) to end up with more anatomically appealing images. For the same reason it is also possible that small artefacts may have large impact on the EIT image. Therefore, EIT images should not be regarded as absolute accurate calculations of impedance but rather as approximations. Since both the algorithm and the mesh are defined by the manufacturer (or data interpreter) the final appearance of EIT images may also be influenced by the manufacturers' "policy". The question is: "do we get an image that is accurate or do we get the one we would like to see?" There is no good answer for this question. Either way there will be a bias.

During the process of image projection different types of spatial and temporal filters are applied that have substantial influence on the resulting EIT image. The user (experimenter) may have a choice to change some properties of these filters. In spite of this fact, there is no general recommendation on the type of filter to be applied and none of these are considered being right or wrong. This amount of freedom may increase subjectivity in generating and interpreting EIT images and may lead to investigator bias.

On the resulting EIT video image each single pixel is a signal that consists of the relative impedance change (ΔZ) over time compared to a common reference value of that individual pixel. The reference impedance was calculated, for each pixel, as the average impedance (Z) value for the first 300 frames of each EIT recording and ideally includes at least one full respiratory cycle. Since an EIT signal represents relative impedance changes but air volume changes in the lungs are absolute values there is a discrepancy between the tool we are using and our expectations to accurately measure air volume changes. This is probably not so important when the lungs are well inflated but may play a role when atelectatic or underinflated lung areas are used for the reference impedance signal. This effect may artificially increase impedance for example when atelectatic lung areas open during an alveolar recruitment manoeuvre (ARM).

The generation of an EIT video image (dynamic EIT image) was discussed above. From these dynamic EIT images functional EIT images can be generated to allow further analysis. Functional EIT images represent a summary of information over time. Typically, the standard deviation (SD) of each pixel signal over time would be used but there are other methods such as those using the slope or the Pearson

"r" for the regression of each pixel signal and a reference ventilation signal. There are many published methods for analysing functional EIT images, among those would be calculating left to right ratio, geometric centre of ventilation (COV) or global inhomogeneity (GI) index. Comparing these numbers using appropriate statistical methods allows defining trends in a population of subjects (during an experiment).

Applying EIT on animals is not always straightforward because of anatomical differences among species. In our previous study for example, we identified an area on thoracic EIT images of horses where inverse respiratory signals were located. This area was located ventrally, where the heart was assumed to be. When reviewing computer tomographic images of anesthetized ponies it appeared that relatively large amount of intestinal gas was located a few cm caudally from the cardiac apex. Since EIT images are not so narrow slices such as CT images but EIT depicts a wider area of impedance. Therefore, it is logical to assume that this abdominal gas pocket may have caused the inverse respiratory signals in horses. Such large amount of abdominal gas near the thoracic cavity appearing consistently at the same location is typical for horses and it is not present in humans or dogs.

The most common use of EIT is to examine the distribution of ventilation in the lungs at the plane of the EIT belt. However, there are methods to depict the distribution of pulmonary perfusion too. The pulsatility signals are embedded in the EIT signal superimposed on the much larger ventilation signals. Different methods exist to separate the pulsatility and ventilation components. It is important to mention though, that EIT may detect expansion of space (blood volume) but not forward blood flow. Additionally, the signal-to-noise ratio for the weak pulsatility signal is much lower than that of the ventilation signal. Studies showed that pulmonary blood flow distribution estimated by EIT does not compare well with reference methods.

Alveolar Recruitment Manoeuvre

Anaesthetised horses often develop pronounced disturbance of gas exchange. This is typically represented by a large intrapulmonary shunt fraction with little or no perfusion of low V/Q regions irrespective of body positioning and mode of ventilation. Pulmonary atelectasis seems to be the chief mechanism in development of intrapulmonary shunt in anaesthetized horses. So far, the only proven method to reverse pulmonary atelectasis during anaesthesia is to perform an ARM and continue mechanical ventilation with an individually defined positive end-expiratory pressure (PEEP) to prevent re-collapse of alveoli (open lung concept). Such an ARM typically consists of two consecutive PEEP titrations. During the first PEEP titration the "optimal" PEEP is determined and during the second one the lungs are re-opened and continued to be ventilated at the previously determined PEEP.

Clinical recruitment manoeuvres are therapeutic interventions aiming to pose only minimal cardiovascular risk on the patients. For this goal to be achieved, the duration of recruitment and the airway pressures used have to be restricted to the minimum. Current techniques for performing ARM are mostly focusing on defining individual PEEP. In this presentation, elements of an ideal ARM will be proposed to aid discussion. The questions are: "Where are we today and were shall we go?"

Elements of an ideal ARM

- Establish meaningful inclusion / exclusion criteria before performing an ARM
- Determine minimum but effective Peak Inspiratory Pressure (PIP) individually
- Determine minimum duration of time individually when PIP should be applied
- Determine most effective inspiratory flow pattern
- Determine ideal PEEP individually
- Establish safe endpoints (quit ARM to avoid accidents) using appropriate monitoring techniques.

L-18 Monitoring the circulatory system: Monitoring of the peripheral perfusion

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An important goal of hemodynamic monitoring is early detection of inadequate tissue perfusion and oxygenation not only during anaesthesia but also at the ICU. A large number of measurement-techniques are used to measure the peripheral flow.

In circulatory failure blood flow is diverted from less important tissues (skin, subcutaneous, muscle) to vital organs (heart, brain). Thus monitoring perfusion in these less vital organs could be an early marker of vital tissue hypoperfusion.

I. **Clinical assessment**

During circulatory failure cutaneous circulation is deprived of autoregulation, and the sympathetic neurohumoral response predominates, resulting in a decrease in skin perfusion and temperature in these conditions.

a. *Capillary refill time (CRT)*

CRT has been validated as a measure of peripheral perfusion with significant variation. Several clinical studies have reported a poor correlation between CRT, heart rate, blood pressure, and cardiac output. However, prolonged CRT has been found to be a good predictor of dehydration and increased blood lactate levels.

b. *Skin temperature*

Distal extremity skin temperature has also been related to the adequacy of the circulation. Patients with cold periphery (including septic patients) had lower cardiac output and higher blood lactate levels as a marker of more severe tissue hypoxia. In another the presence of a cold and clammy skin was a predictor of 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction.

c. *Temperature gradients*

Body temperature gradients have been used as a parameter of peripheral perfusion. In the presence of a constant environmental temperature a change in skin temperature is the result of a change in skin blood flow. The temperature gradients peripheral-to-ambient (ΔTp-a) and central-to-peripheral (ΔTc-p) can better reflect cutaneous blood flow than the skin temperature itself. Considering a constant environment condition, ΔTp-a decreases and ΔTc-p increases during vasoconstriction. Experimental studies have suggested a Tskin-diff threshold of 0°C for the initiation of vasoconstriction, and a threshold of 4°C for severe vasoconstriction in anesthetized patients.

II. **Optical monitoring**

Optical methods apply light with different wave lengths directly to tissue components using the scattering characteristics of tissue to assess various states of these tissues. At physiological concentrations the molecules that absorb most light are hemoglobin, myoglobin, cytochrome, melanins, carotenes, and bilirubin. These substances can be quantified and measured in intact tissues using simple optical methods. The assessment of tissue oxygenation is based on the specific absorption spectrum of oxygenated hemoglobin (HbO_2), deoxygenated hemoglobin (Hb) and cytochrome aa 3 (cytaa3).

a. *Peripheral perfusion index*

The peripheral perfusion index (PFI) is derived from the photoeletric plethysmographic signal of pulse oximetry and has been used as a noninvasive measure of peripheral perfusion in critically ill patients.

The principle of pulse oximetry is based on two light sources with different wavelengths (660 nm and 940 nm) emitted through the cutaneous vascular bed of a finger or earlobe. The Hb absorbs more light at 660 nm and HbO_2 absorbs more light at 940 nm. Using a two-wavelength system the nonpulsatile component is then discarded, and the pulsatile component is used to calculate the arterial oxygen saturation.

The overall hemoglobin concentration can be determined by a third wavelength at 800 nm, with a spectrum that resembles that of both Hb and HbO_2. The resulting variation in intensity of this light can be used to determine the variation in arterial blood volume (pulsatile component). The PFI is calculated as the ratio between the pulsatile component (arterial compartment) and the nonpulsatile component (other tissues) of the light reaching the detector of the pulse oximetry, and it is calculated independently of the patient's oxygen saturation. A peripheral perfusion alteration is accompanied by variation in the pulsatile component, and because the nonpulsatile component does not change, the ratio changes. As a result the value displayed on the monitor reflects changes in peripheral perfusion. A PFI of 1.4 has been found to be correlated best with hypoperfusion in critically ill patients using normal values in healthy adults. The inclusion of PFI into the pulse oximetry signal is a recent advance in clinical monitoring. However, more studies are needed to define its clinical utility.

b. *Near-infrared spectroscopy*

Near-infrared spectroscopy (NIRS) offers a technique for continuous, noninvasive monitoring of tissue oxygenation. NIRS has a greater tissue penetration than pulse oximetry and provides a global assessment of oxygenation in all vascular compartments (arterial, venous, and capillary).

Using the venous and arterial occlusion methods NIRS can be applied to measure regional blood flow and oxygen consumption by following the rate of HbO_2 and Hb changes. In the venous occlusion method a pneumatic cuff is inflated to a pressure of approximately 50 mmHg. Such a pressure blocks venous occlusion but does not impede arterial inflow. As a result venous blood volume and pressure increase. NIRS can reflect this change by an increase in HbO_2, Hb, and total hemoglobin. In arterial occlusion method, the pneumatic cuff is inflated to a pressure of approx. 30 mmHg greater than systolic pressure. Such a pressure blocks both venous outflow and arterial inflow. Depletion of local available O_2 is monitored by NIRS as a decrease in HbO_2 and a simultaneous increase in Hb, whereas total Hb remains constant. After release of the occluding cuff a hyperemic response is observed. Blood volume increases rapidly, resulting in an increase in HbO_2 and a quick washout of Hb.

Despite the potential clinical applications of NIRS, some limitations still exist. There is no a gold standard to which NIRS data can be directly compared, and one of the reasons is that a variety of NIRS equipment is commercially available with different working systems.

In both small- and large-animal models of hemorrhagic shock and resuscitation NIRS has demonstrated sensitivity in detecting skeletal muscle and visceral ischemia. The potential to monitor regional perfusion and oxygenation noninvasively and online makes clinical application of NIRS technology of particular interest in intensive care.

c. *Orthogonal polarization spectral*

Orthogonal polarization spectral (OPS) is a noninvasive technique that uses reflected light to produce real-time images of the microcirculation. Light from a source passes through the first polarizer, and it is directed towards the tissue by a set of lens. As the light reaches the tissue, the depolarized light is reflected back through the lenses to a second polarizer or analyzer and forms an image of the microcirculation on the charge-coupled device, which can be captured through a single videotape.

OPS can assess tissue perfusion using the functional capillary density (FCD), i.e., the length of perfused capillaries per observation area (measured as cm/cm_2). FCD is a very sensitive parameter for determining the status of nutritive perfusion to the tissue and it is an indirect measure of oxygen delivery. OPS produce excellent images of the sublingual microcirculation by placing the probe under the tongue. Movement artifacts, semiquantitative measure of perfusion, the presence of various secretions such as saliva and blood, observer-related bias, and inadequacy of sedation to prevent patients from damaging the device are some of the limitations of the technique.

d. *Sidestream dark-field (SDF) imaging*

A further development of OPS is SDF imaging. Light-emitting diodes arrange a ring formation at the tip of the light guide emit green light with a wavelength of 540 nm, which directly illuminates the tissue microcirculation.The illuminating light source is optically isolated from the emission light path in the core of the light guide. SFD technology provides improved resolution and clarity of the images compared to OPS imaging but with the limitation that only tissues with a thin epithelial layer can be examined (mucosal layer of GT).

e. *Laser Doppler flowmetry*

Laser Doppler flowmetry (LDF) is a noninvasive, continuous measure of microcirculatory blood flow, and it has been used to measure microcirculatory blood flow in many tissues including neural, muscle, skin, bone, and intestine. The principle of this method is to measure the Doppler shift - the frequency change that light undergoes when reflected by moving objects, such as red blood cells. As a result LDF produces an output signal that is proportional to the microvascular perfusion.

A major limitation of this technique is that it does not take into account the heterogeneity of blood flow as the velocity measurements represent the average of velocities in all vessels of the window studied. No current laser Doppler instrument can present absolute perfusion values (e.g., ml/min per 100 g tissue) and measurements are expressed as perfusion units, which are arbitrary.

III. **PO_2 and PCO_2 transcutaneous measurements**

a. *Transcutaneous measurements of PO_2 and PCO_2*

Continuous noninvasive measurement of oxygen and carbon dioxide tensions is possible because both gases can diffuse through the skin, and thus their partial pressures can be measured in transcutaneous tissue. The correlation between transcutaneous oxygen partial pressure ($PtcO_2$) and PaO_2 gives information about peripheral blood flow.

When blood flow is adequate, $PtcO_2$ and PaO_2 values are almost equal, and the tc-index is close to 1. During low flow shock the $PtcO_2$ drops and becomes dependent on the PaO_2 value, and tc-index decreases.

Transcutaneous carbon dioxide partial pressure ($PtcCO_2$) has been also used as an index of cutaneous blood flow. Differences between $PaCO_2$ and $PtcCO_2$have been explained by local accumulation of CO_2 in the skin due to hypoperfusion. Because of the diffusion constant of CO_2 is about 20 times greater than O_2, $PtcCO_2$ has been showed to be less sensitive to changes in hemodynamics than $PtcO_2$.

One of the main limitations of this technique is the

necessity of blood gas analysis to obtain the tc-index and $PaCO_2$. In addition, the sensor position must be changed every 1–2 h to avoid burns. After each repositioning a period of 15–20 min is required for the next readings, which limits its use in emergency situations.

b. *Gastric (pHi) tonometry*

Measurement of the tissue-arterial CO_2 tension gradient has been used to reflect the adequacy of tissue perfusion. The gastric and ileal mucosal CO_2 clearance is been the primary reference for measurements of regional PCO2 gradient during circulatory shock. The regional PCO_2 gradient represents the balance between regional CO_2 production and clearance. In low flow states CO_2 increases as a result of stagnation phenomenon.

Gastric tonometry is a technique that can be used to assess the adequacy of gut mucosal blood flow to metabolism. The methodological limitations of gastric tonometry required a search for a tissue in which PCO_2 can be measured easily in a noninvasive approach.

c. *Sublingual capnometry*

Comparable decreases in blood flow during circulatory shock have been also demonstrated in the sublingual tissue PCO_2 ($PslCO_2$).

The instrument uses fiberoptic technology to transmit light through the sensor placed between the tongue and the sublingual mucosa. Carbon dioxide diffuses across a semipermeable membrane of the sensor and into a fluorescent dye solution. The dye emits light that is proportional to the amount of CO_2 present. This light intensity is analyzed by the instrument and displayed as a numeric $PslCO_2$ value.

Several studies have suggested that $PslCO_2$ is a reliable marker of tissue hypoperfusion. As the $PslCO_2$ is influenced by $PaCO_2$, the gradient between $PslCO_2$ and $PaCO_2$ ($Psl\text{-}aCO_2$) is more specific for tissue hypoperfusion. One limitation of this technique includes the necessity of blood gas analysis to obtain $PaCO_2$. In addition, normal vs. pathological $Psl\text{-}aCO_2$ values are not well defined.

Friday 4th September | Room D | 9:50－10:50

L-19 Feline post-operative complications. The case of post-anesthesia blindness in cats.

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General anesthesia in cats has a mortality that has been historically larger than in dogs. The overall risk of mortality for cats has recently been documented at 0.24%, whereas in dogs it was 0.17%. In cats, over 60% of deaths occurred in the early postoperative period, during the first 3 hours following the end of anesthesia. The large study by Brodbelt showed that in cats, 5% of deaths were of neurological origin, which included seizures or failure to regain consciousness. While this number may appear unimpressive at first sight, it approximates the incidence of death from cardiovascular causes (6%), and it is superior than deaths arising from renal causes (only 3%).

Several reports of neurological deficits in cats, following general anesthesia can be now be found in the literature. Both cases of blindness with or without other more severe neurological deficits have occurred. In some cases, vision loss has been regained after a short interval, while in others, lack of improvement resulted in the euthanasia of the animal. The reason for neurological deficits following general anesthesia had historically been attributed to decreases in cardiovascular function, resulting in insufficient perfusion/oxygenation to the brain. This was further supported by some cases where cardiac arrest had occurred, and the patient had recovered with neurological deficits. However, cats recovering with neurological deficits despite uneventful anesthesia have also occurred and have put into question the relationship between poor neurological outcomes and cardiovascular function. Recent research projects have help elucidate a possible cause for these problems; the key appears to relate to unique anatomical characteristics of this species.

Isolated case reports of these problems can be found sporadically over the past decade. A cat that recovered blind from a seemingly uneventful anesthesia was reported in 2001. The issue, however, was only recently studied in more detail. In 2012 Stiles et al showed data of 20 cases of either blindness or more generalized neurological deficits in cats, following general anesthesia. Those authors revised medical records of cats that presented blind – with or without other neurological deficits – after anesthesia, but that did not have such findings prior to being anesthetized. A total of 20 cases were identified, who had been anesthetized at different practices, including a College of Veterinary Medicine. They found 3 cats with blindness only, and 17 who had other neurological deficits, in addition to vision loss. Those abnormalities included circling, ataxia, head tilt, weakness, decreased conscious propoception and abnormal mentation. Interestingly, two cats were completely blind only on one side. The majority of the cats regained vision during the following six weeks. At least 1 cat was euthanized after a month due to unresolving abnormalities. Evidently, regarding the incidence of permanent negative outcomes, blindness with or without neurological deficits in cats following general anesthesia, can result devastating for the animal, the owner and the veterinarian.

Stiles et al examined the anesthesia records of the subject, but no association with particular drugs or even time of anesthesia could be identified as responsible for the deficits. Moreover, dissections could not determine if lesions to the vasculature existed.

The majority of the cats in that report had been anesthetized for dental procedures, or endoscopy. In such procedures, a spring-loaded mouth gag had been used to keep the mouth open. The authors speculated that overstretching of blood vessels could occur during that maneuver.

A more intimate link between the use of the spring-loaded mouth gag and the development of blindness (and other neurological deficits) was later investigated in a prospective study. Cats were anesthetized and their mouth was opened with a spring-loaded gag. Electroretinography (ERG) was measured before and during mouth opening. In two animals, the ERG was decreased when the mouth was opened, indicating that retinal or cerebral ischemia had occurred. Additionally, in one animal, the brain auditory evoked response (BAER) was also decreased. Computed tomography and magnetic resonance was also used to investigate blood flow through the maxillary arteries. Indicators of blood flow were decreased in several animals when the mouth was opened maximally. Taken together, these findings strongly suggested that maximal opening of the oral cavity can, in some cats, decrease or even interrupt maxillary artery blood flow. In some cases, the decrease was sufficient to alter functioning, as evidenced by the decreased ERG and BAER tests.

A second study was conducted to further investigate this phenomenon. It was speculated that only maximal opening of the mouth would result in the interruption of maxillary artery blood flow, but that submaximal opening would not have negative outcomes. Cats were anesthetized and both the ERG and MRI were performed with mouth closed, maximally opened (spring-loaded gag) and opened at intermediate

distances, using plastic gags. Maximal mouth opening produced a flat ERG in one cat, and decrease maxillary artery blood flow as indicated with MRI, in 4 cats. No reductions in blood flow indicators were observed with intermediate gags, except in one cat, where the MRI signal was reduced. In that cat, a plastic gag of the same length as the cap of a hypodermic needle was used. This length was investigated as needle caps are often use to keep mouths opened during dental procedures. It was concluded that while negative results were more often seen with the spring-loaded gag, even smaller gags could – in some cats – reduce maxillary artery blood flow.

The cat's anatomy and the problem with mouth gags.

A radiological study also investigated this phenomenon. Both computed tomography (CT) and digital subtraction angiography were used to evaluate changes when a spring-loaded mouth gag was used in anesthetized cats. During CT, it was observed that the maxillary artery coursed between the medial aspect of the angular process of the mandible, and the lateral wall of the tympanic bulla. The distance between these boney structures was significantly decreased as the mouth was opened. As a result, the maxillary artery can be compressed by the soft tissue contained in that space, as the mouth is opened maximally. During subtraction angiography, the passage of contrast media through the carotid arteries, maxillary arteries, the retia mirabilia and the cerebral arterial circle was observed. When the mouth was opened, there was reduced and delayed passage of contrast rostral to the level of the angular process, that is, the level where the maxillary arteries can become compressed between the mandible and the tympanic bulla. These findings suggest that the maxillary arteries might in fact become compressed between boney structures (and the soft tissues contained between them) as the mouth is opened maximally.

Compression of maxillary arteries in cats can be of serious consequences. The brain receives perfusion through 4 pairs of arteries that arise from the cerebral arterial circle and by the basilar artery. However, there are species differences in how blood flow reaches the cerebral arterial circle. The cerebral circle might receive blood flow from internal carotid arteries, maxillary arteries, or basilar artery. The internal carotid arteries in cats are either absent or vestigial. Blood in the basilar artery in cats, flows away (in a caudal direction) from the brain. As a result, perfusion to the arterial circle (and the brain) in cats, relies in blood flow through the maxillary arteries via the retia mirabilia. The caudal part of the medulla oblongata, which is perfused by vertebral arteries. As a result of this unique vascular anatomy, occlusion of maxillary arteries prevents (or reduces) blood flow to most of the brain. Maximal opening of the mouth by using a spring-loaded mouth gag can occlude maxillary artery blood flow, and hence, result in brain ischemia.

The data presented by different investigators, and summarized here, provides strong evidence that this might be the cause of blindness in cats recovering from an otherwise uneventful anesthesia. Care should be used when using mouth gags; gags that do not open the mouth to its maximum extent might be safer.

Friday 4th September | Room D | 10:50−11:50

L-20 Management priorities in perioperative sepsis

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Bacterial sepsis is a major cause of morbidity and mortality in both veterinary and human medicine. Varied terminology can contribute to the confusion regarding recognition and treatment. For this session, the author will conform to the following definitions: (1) the systemic inflammatory response syndrome (SIRS) refers to persistent signs of systemic inflammation including, but not limited to, leukocytosis or leukopenia, a left-shifted leukogram with immature granulocytes evident, tachycardia (or bradycardia in cats), tachypnea, and altered body temperature (fever or hypothermia), (2) sepsis is SIRS with a known or suspected infectious etiology, (3) severe sepsis is sepsis with evidence of remote organ dysfunction (i.e. excluding the organ in which the infection originated), and (4) septic shock is sepsis with persistent hypotension that cannot be alleviated solely with fluid therapy alone. Persistence is an important part of these definitions. Without a requirement that the signs continue for an extended period of time, then any cause of tachypnea and tachycardia (e.g. exercise) would cause a patient to be incorrectly assigned the problem of SIRS. Formal criteria for diagnosis of SIRS and sepsis are also limited in that absolute criteria cannot be established that are meaningful, sensitive, and/or specific for all patient types. For example, a heart rate that one might consider to be tachycardic for a 70 kg Great Dane may be both normal and appropriate for a 1 kg Chihuahua. Despite these limitations, the SIRS criteria do serve an important function. They are excellent exclusion criteria with reasonably high negative predictive value. That is to say that it's quite unlikely that an immunocompetent patient with SIRS or sepsis will fail to have abnormalities in 2-3 of the categories. Another approach to sepsis diagnosis is one that was long championed by Steve Haskins at UC Davis. Dr. Haskins relatively straight-forward approach could be summarized as follows: "*If the patient is far sicker than one can explain based on the disease processes that are known to be present, then the patient is likely septic.*" While clearly a more subjective approach, the utility of this method is that septic patients are rarely missed by the clinician. This WCVA2015 session will focus on current recommendations for the management of septic patients in the perioperative period.

Sepsis can be a particularly challenging disease process for the anesthesiologist to tackle. The inflammatory mediators that drive the process are often vasoactive and can produce inappropriate vasoconstriction and vasodilation. Vasomotor tone is no longer tightly matched to tissue metabolic rates (i.e. intrinsic or autoregulation of perfusion) in this setting. As many anesthetic agents have a similar effect on vasomotor tone, profound hypotension and tissue hypoperfusion can be anticipated in septic patients that are anesthetized. Moreover, splanchic hypoperfusion, reduced glomerular filtration rate (GFR), and capillary hyperpermeability all may contribute to altered pharmacokinetics and pharmacodynamics of anesthetic agents. Critical illness-related corticosteroid insufficiency (CIRCI) may exacerbate this situation by producing relative vasoplegia. [1] In addition, excessive nitric oxide production can also lead to oxidation of catecholamines and altered sensitivity to endogenous and exogenous pressors.[2-3]

The key management priorities in septic patients that will be discussed herein are as follows: (1) fluid therapy, (2) vasopressor agents, (3) antibiotics, (4) transfusion triggers, (5) anesthetic agents, and (6) goal-directed resuscitation strategies.

Fluid therapy*Crystalloids versus colloids*

Perhaps no other area in sepsis management has undergone as much careful reconsideration recently as has fluid resuscitation strategies. Fluid therapy remains the cornerstone of sepsis supportive care, but the optimal approach remains a subject of heated debate. A body of work can be cited to advance the concept that colloids provide superior volume support to that of crystalloids in animals during general anesthesia with volatile anesthetics. [4-6] For these reasons and others, it might seem ideal to use colloids preferentially in septic small animal patients under general anesthesia. However, an alarming number of studies continue to identify synthetic colloids as independent risk factors for the development of acute kidney injury (AKI) in septic human patients. In 2008, the results of the VISEP trial were published after the study had been stopped prior to completion. [7] This report (n=537) raised significant concerns about potential causal links between hydroxyethyl pentastarch administration and AKI in septic patients. Both the incidence of AKI and the need for renal replacement therapy (RRT) was greater in the group that received pentastarch. Hydroxyethyl starch solutions with lower substitution ratios (i.e. tetrastarches) gained greater popularity after the VIESP results were published. However, in the intervening years three major trials have raised similar concerns about tetrastarch solutions (CRYSTMAS, 6S, and CHEST). [8-10] These studies and those like them suggest that the improvement in hemodynamic parameters with HES solutions is minimal in septic patients compared to resuscitation with crystalloids while the increased risk of AKI is

substantial. Native colloids such as albumin concentrates may offer a reasonable alternative to synthetic colloids. The SAFE trial resutls would suggest that albumin concentrates do not carry the same risks as HES solutions. [11] However, the greater cost and the potential antigenicity of the product may preclude its routine use in all but the most dire of circumstances. [12-15]*Balanced electrolyte solutions versus 0.9% saline*

Normal saline is the most widely used fluid in human intensive care. [16] However, saline is beginning to fall out of favor due to concerns raised in several cohort studies. [17-18] In particular, a concern that has been raised is that the excessive chloride content of saline leads to impaired tubuloglomerular feedback (TGF) and predisposes patients to inappropriate vasoconstriction of the afferent arteriole of glomeruli. [18] In septic patients, a balanced electrolyte solution such as Lactated Ringer's solution or Plasmalyte 148 would appear to be a superior crystalloid selection in many instances.

Fluid balance

The hemodynamic instability of septic patients often drives clinicians to administer large amounts of intravenous fluid support. A positive daily fluid balance is quite common in this setting. Whether positive fluid balance (i.e. in's > out's) is detrimental to septic patients remains another area of active debate. The results of the SOAP study would suggest that positive fluid balance carriers with it greater rsik of mortality in the critically ill. [19] However, the later VASST trial would appear to suggest that a positive fluid balance at 12 hrs post-admission is associated with the best outcomes. [20] At this point, no definitive conclusions can be reached other than that under-resuscitation and needless overhydration can both negatively impact outcomes.

Vasopressors

In years past, both dopamine and norepinephrine have been considered "first line" agents for vasopressor support in septic patients. [21] However, in recent years norepinephrine has gained greater support while dopamine has largely fallen out of favor. In the most recent (2012) Surviving Sepsis Campaign guidelines, dopamine is now considered a 4th choice vasopressor (after norepinephrine, epinephrine, and vasopressin) due to it's greater association with arrhythmias in criticall ill humans. [22]

Meta-analysis of six separate trials has also identified dopamine administration as an independent risk factor for mortality in septic humans. While dopamine remains a popular choice of pressor in veterinary anesthesia, it's usage is declining in veterinary intensive care units.

Antibiotics

Early administration of appropriate antibiotic therapy has been shown to reduce sepsis mortality in some, but not all clinical trials and retrospective studies. [23-24] Based on the available data, the spectrum of coverage of the antibiotics may be more crucial than the precise timing in determining sepsis outcomes. Monotherapy with cefazolin is suitable for prevention of wound infections in stable surgical patients, but is unlikely to achieve optimal outcomes in the majority of septic small animal patients. Monotherapy with meropenem is effective in human patients, but is generally reserved for patients with a clearly demonstrated need in veterinary practice. Combinations of a beta-lactam and a fluoroquinolone remain widely used combinations. Selections should be based on an up-to-date antibiogram generated by each facility.

Transfusion triggers

The optimal hematocrit for septic patients remains undetermined and is unlikely to be uniform in all settings. Sepsis does interfere with the autonomic nervous system (central regulation) and local regulation of blood flow distribution. This macro- and microcirculatory dysfunction increases the point at which oxygen delivery drops below the anaerobic threshhold (DO2crit). On this basis, a fairly liberal transfusion strategy could be endorsed. However, the recently published results of the TRISS trial (comparing liberal versus conservative transfusion protocols in septic patients) identified no mortality benefit in the group that received more blood products. [25]

Anesthetic agents

As mentioned above, CIRCI is an important cause of decreased vasoreactivity to pressors in septic patients. This acquired form of adrenocortical insufficiency may be addressed with physiologic doses of corticosteroids (hydrocortisone 0.5 mg/kg IV q 12hrs). Another important cause of transient inadequacy of adrenal gland function is etomidate administration. Etomidate usage would seem to be a preferred agent due to its minimal cardiovascular depressive effects, however its usage has been associated with greater mortality risk in septic humans. [26] Also, propofol may compromise leukocyte function and the soybean oil vehicle is known to exacerbate hypertriglyceridemia and hypocholesterolemia. Ketamine has several properties that may make it a preferred induction agent in the setting of sepsis although there is no robust data set from a clinical trial on which to base such a recommendation.

Goal-directed therapy

The last topic that will be addressed in this session is the role of goal-directed therapy in perioperative care of septic small animal patients. The landmark paper by Rivers et al established the important gains in reducing sepsis mortality that can be achieved by optimizing hemodynamics prior to ICU admission in humans. The application of the Rivers algorithm has

been shown to reduce perioperative mortality in humans, but necessitates the placement of a fiberoptic central venous hemoglobin saturation probe that can prove burdensome in many settings. Subsequent studies have shown that standard approaches using point-of-care lactate testing can achieve similar goals and are non-inferior. The key is not *in vivo* saturation monitoring, but rather timely and attentive interventions to optimize oxygen delivery.

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L-21 Perioperative Acute Kidney Injury (AKI) : Management Priorities

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Acute kidney injury (AKI) is characterized by an abrupt and persistent decrease in the glomerular filtration rate (GFR). It is a common disorder in companion animals and is associated with high morbidity and mortality (as well as great expense to the owner). In humans, AKI is predominantly a disease of hospitalized patients whereas in companion animals AKI is most often acquired in the out-of-hospital environment. Four phases are currently recognized in AKI which have been termed: (1) initiation, (2) progression, (3) maintenance, and (4) recovery. Blood urea nitrogen and serum creatinine are the two most widely used biochemical markers of azotemia. However, when these two markers are used the disease is typically recognized only in the maintenance phase. At this stage the disease is well established and the clinical signs are overt. More than 80-90% of the kidney function is already lost by the time this stage is reached.

In spite of advances in AKI therapy including extracorporeal therapy (e.g. CRRT, hemodialysis) the mortality rate among both human and animal patients remains quite high. Mortality rates of human patients with AKI in the intensive care units have remained as high as 70% for nearly half a century.[1] Delayed recognition of the disease likely contributes to the poor outcomes observed. The recently adopted shift in terminology (i.e. from ARF to AKI) is intended to emphasize the importance of early recognition prior to overt renal failure. Delayed identification of the disease unfortunately affords clinicians only a very narrow window of opportunity for therapy before irreversible renal failure develops. The need for early and reliable identification of AKI is thus of paramount importance. This is particularly true in veterinary medicine In veterinary medicine because extracorporeal therapies are not readily available to the extent that they are in human medicine.

Serum creatinine concentration remains a very widely used biochemical marker, but has many major limitations. Large changes in GFR may be associated with only minor changes in serum creatinine concentration for several days following initiation of AKI. In critically ill patients, each of the determinants of serum creatinine concentration (sCr) are frequently unstable and highly variable themselves and thus substantial delay may occur before sCr levels stabilize and AKI becomes apparent. This delay also inhibits the ability to accurately estimate timing of injury, to assess the severity of dysfunction, and to properly and accurately identify causal relationships. Even relatively small Increases in sCr (~0.5 mg/dL) have been associated with increased mortality. [2] Increases in sCr need not be sustained to have a significant impact on patient outcomes. It has been reported that even a transient (24-72 hrs) rise in sCr can be associated with an increase in both in-hospital mortality as well as the need for chronic dialysis in the years that follow. [3-4]

Risk Factors for AKI

As mentioned above, in humans AKI is largely a disease of hospitalized patient populations and occurs in 1-5% of all hospital admissions. [5-6] Surgery remains a major cause of AKI in this patient population. This increase in AKI risk has been most widely studied in populations undergoing cardiac bypass in which up to 15% of all patients will develop AKI. One seventh of those patients will require renal replacement therapy of some type. For non-cardiac surgery patient the risk is still substantial with 1% of major non-cardiac surgery patients developing AKI. Overall, in a large cohort of human patients surgery is the second leading cause of AKI in humans (following only septic shock). [5]

Box 1. Common risk factors for AKI

1. Major surgery
2. Chronic kidney disease
3. Advanced age
4. Heart failure
5. Liver disease
6. Nephrotoxic drugs
    a. NSAIDS
    b. Aminoglycosides
    c. Radiocontrast agents
7. Hypotension
    a. Hypovolemia
    b. Cardiac disease
    c. Drug-induced
8. Sepsis
9. Diabetes mellitus

Three major classification schemes have been developed to aid in the early recognition of AKI in humans (RIFLE, AKIN, & KDIGO). [7-9] All of them are based on GFR (or sCr) and urine output (UOP) indices. Many of these have been modified for use in veterinary patients, however these veterinary schemes have not yet been evaluated with truly large, robust prospective data sets. The recently proposed Veterinary Acute Kidney Injury (VAKI) staging system is based entirely on alteration in sCr without

consideration of the presence or absence of oligoanuria. [10] In the report that describes the development of that staging system, the majority of dogs that developed AKI had undergone anesthesia. This suggests that canine and human risk factors for AKI may be similar in this regard. Additional risk factors for AKI are listed in Box 1.

Prevention and treatment priorities

AKI is often a predictable and preventable event. In humans, it has been found that AKI could have been prevented in as many as 20% of the patients that develop and die from it. [11] Several health care systems have suggested prevention measures that could easily be adapted to the veterinary practice environment.

1. Have a client education plan for patients at risk
   a. The owners of patients with chronic diseases that carry increased AKI risk (e.g. diseases managed with aminoglycosides or NSAIDS, CKD, diabetes, CHF, etc…) should be informed that prompt veterinary care should be sought if the patient develops vomiting, diarrhea, polyuria or another condition that can result in extracellular fluid volume contraction.
2. Hospital policies
   a. All staff that care for patients in acute hospital settings should have competencies in monitoring, interpretation of results and provision of prompt response to acutely ill patients appropriate to the level of care that they provide. With regard to AKI, nursing staff must be competent in recording of fluid balance and doctors in assessing volume status, interpreting fluid-balance charts, and delivering appropriate intravenous fluids.
3. Twice daily case review by senior staff members
   a. Several lines of evidence suggest that frequent input from more senior clinic staff can reduce AKI incidence and severity. In the UK, it was found that the quality of care was greater when senior staff were the one's admitting patients. It was also found that those that had AKI on admission received better care than those that developed it while hospitalized. These two findings together suggest that delayed recognition and under treatment contribute to AKI burden.
4. Making use of technology
   a. The advantages of automatic clinician notification of abnormal creatinine values by the clinical laboratory has been demonstrated in human healthcare settings. [13-14] Automated electronic notification can result in more rapid recognition of AKI and in greater avoidance of nephrotoxic agents in patients at risk.
5. AKI management guidelines
   a. Evidence- and consensus-based guidelines for AKI management continue to evolve. Ultimately the management of AKI is highly dependent on the underlying cause. However, initial supportive care should include clinical assessment of volume status, appropriate fluid resuscitation and detailed medication review. Nephrotoxic medications should be stopped and appropriate dose adjustments made for medications metabolised and/or excreted by the kidneys. While this may sound self-evident, data from human hospitals indicates that even these basic measures are routinely not implemented in a timely manner.
6. High quality case transfers
   a. The finding that a significant number of AKI cases are preventable suggests that continuity of care has an important role to play in prevention strategies. Case transfer within the hospital (e.g. ER => Anesthesia => ICU => Wards) can result in data loss including data on volume status and renal values. Personnel should be instructed to emphasize these parameters during case transfer discussions.
7. Correct recognition
   a. A growing body of experimental and clinical evidence support the concept that even relatively small increases in sCr are associated with significant mortality risk. Recognizing and acting on increases in serum creatinine that are ~50% above baseline values even when the values are still within the reference interval is advised.
8. Appropriate fluid therapy
   a. This presentation will devote the majority of the allotted time to discussion of AKI fluid therapy guidelines. Many veterinarians were trained with a "*fluids are the answer, not the problem*" mindset when it comes to AKI. A growing body of evidence suggests that the converse may, in fact, be true. Overhydration can play a significantly detrimental role in AKI cases. Excessive fluid administration can contribute to renal intersitial edema, disruption of tubuloglomerular feedback, reduced renal perfusion pressures, and increased need for positive pressure ventilation (itself a risk factor for AKI). Monitoring and therapy strategies designed to reduce these adverse effects will be discussed at length.
   b. The evidence that chloride-rich crystalloid fluids interfere with tubuloglomerular feedback mechanisms will be discussed at length. The administration of high, non-physiologic chloride containing fluids (e.g. 154 meq/L in normal saline) markedly increases chloride flux in the renal tubules. This flux is monitored and used to adjust renal hemodynamic parameters. Excessive chloride filtration leads to detrimental changes in renal arteriolar tone.
   c. Colloid-induced nephropathy is largely associated with the administration of synthetic colloids patients that are septic. However, a smaller body of published work suggests that

other patient populations are also at risk. The current state of knowledge of synthetic colloids' contributions to AKI risk will be discussed.

Summary

AKI is a devastating and common condition in veterinary practice. A significant portion of AKI in human patients is avoidable. Veterinarians should be proactive in implementing measures to reduce AKI risk in their own practice setting. Overhydration and excessive fluid administration should be avoided with the same diligence as is afforded to nephrotoxic agents in at-risk patient populations.

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Panel discussion

Panel discussion Takeuchi Memorial Panel Discussion
Pain management education in Asian countries

Tuesday 1st September | Room A | 16:10−18:10

PD-1 Pain management education in Asian countries

○Inhyung Lee
Seoul National University, Korea

There are 10 veterinary schools located in South Korea; nine are National universities and one is a private university. The Doctor of Veterinary Medicine (DVM) is a 6-year program. The first two years consist of pre-vet courses, where students study basic sciences and literature. The next 4 years consist of the main veterinary courses. Each year, approximately 500 students graduate from the 10 veterinary schools and begin their work as new veterinarians.

Most veterinary schools in South Korea teach veterinary anesthesiology as a component of veterinary surgery during 3rd or 4th year of the main DVM curriculum. Among the 10 veterinary school hospitals, Seoul National University Teaching Hospital is the only clinic that has a separate anesthesiology department. At other university hospitals, anesthesia is performed together by the surgery department.

At Seoul National University, the anesthesiology course is provided to 3rd year students, and consists of 32 hours of lectures and 8 hours of practical training. Lectures consist of an introduction into veterinary anesthesiology (2 hours), patient evaluation and preparation (2 hours), preanesthetic medication (4 hours), intravenous anesthetics (2 hours), inhalation anesthetics (2 hours), local anesthetics (2 hours), anesthetic machines and breathing systems (2 hours), intubation and ventilation (2 hours), patient monitoring (2 hours), anesthetic procedures of dogs and cats (2 hours), anesthetic procedures of laboratory animals (2 hours), anesthesia of patients with specific diseases (4 hours), anesthesia of the critical patients (2 hours), and tests (2 hours). Practical training consists of anesthetic planning, injectable anesthesia, inhalation anesthesia and monitoring for small animal practice.

Among the lectures, students showed some difficulties when making anesthetic plans and when selecting sedatives, analgesics, as well as induction and maintenance agents. Therefore, a simple classification method was developed to help students memorize and understand the characteristics of each premedication agent. Also, a simple mnemonic was made so that students would not forget the essential agents needed to make an efficient anesthetic plan. Particularly, during the 1st semester of 2015, Seoul National University's Center for Teaching and Learning (CTL) video-recorded the lectures so that students would be able to review them online both during their years as a student and after graduation.

During 4th year, students get first-hand experience in small animal anesthesiology and pain medicine through a two-week intensive course during clinical rotations. Every morning at 8:30 am, the anesthesiology team performs clinical rounds. During this time, students evaluate the history and diagnostic test results of anesthetic cases to be performed that day, and propose an anesthetic plan that is best suitable for those patients. Under the supervision of the professor in charge and the anesthesiology team, students perform anesthesia and monitor patients. Especially, a variety of analgesic techniques, including systemic, regional and local analgesia are actively performed using narcotic analgesics to provide the most effective pain management for our patients. During the two-week rotation period, students are evaluated on their ability to perform safe anesthesia on patients. Students who do not demonstrate this ability are encouraged to participate in another two-week rotation period.

Even after graduation, graduates have opportunities to receive supplementary education in their desired fields of study. Seoul National University's Center of Continuing Veterinary Medical Education provides various programs for continuing education of veterinarians. Especially nowadays, veterinarians are showing an increased interest in pain management and are requesting information on the use and management of narcotic analgesics. In addition, the Korean Veterinary Emergency & Critical Care Society (KVECCS) is sharing information on effective pain management to all veterinarians who are interested in small animal critical care.

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Tuesday 1st September | Room A | 16:10–18:10

PD-2 Pain management education in Asian countries (Taiwan)

○Hsien-Chi Wang
National Chung-Hsing University, Taiwan

This study was to investigate the medications used for premedication, induction and maintenance from randomly selected 162 veterinary clinics in Taiwan in 2014. In general, opioids were used only in 3% of the veterinary clinics, while analgesics was included for premedication in approximately 34% of the veterinary clinics. Because opioids were strictly controlled by Taiwan government, most of the veterinarians were reluctant to use opioids, and prefer to use un-controlled anesthetics, such as Zoletil.

Panel discussion **Takeuchi Memorial Panel Discussion**
Pain management education in Asian countries

Tuesday 1st September | Room A | 16:10–18:10

PD-3 Pain management education in Thailand

○Sirirat Niyom
Kasetsart University, Thailand

Pain is defined by International association for the study of pain (IASP) as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain mechanisms serve as a natural protective function of organisms against noxious stimuli by changing the physiology and behavior to reduce or avoid further damage, and promote recovery. However, if the pain is uncontrolled the patient will be suffering and facing life-threatening condition. Pain induces physiological changes and has a negative impact on multiple systems of the body, for example, cardiovascular, respiratory and immune systems. In the severe case, mistreated postoperative pain can cause sudden death during perioperative and recovery periods. Furthermore, freedom from pain is one of considerations in Animal Welfare that ensuring animals are well-being, not caused unnecessary pain or suffering when they are used for food, in animal testing, as pets, or in other ways.

Despite consequences and harmful effects of pain have been demonstrated, animal pain is often undiagnosed or under-diagnosed and may be undertreated. Veterinarians may not administer analgesics to animals for several reasons. The possible reasons are lack of knowledge of physiological pain and analgesics, fear of toxic side-effects of analgesics, failure to recognize and assess pain in animals, belief that animals do not feel pain and ignorance of deleterious effects of pain (Hugonnard et al., 2004). The continuing education of veterinary pain management is, therefore, necessary for veterinarians and animal health technologists to provide adequate pain control.

In Thailand, mostly, basic of pain physiology and management has been educated in veterinary schools as a small part of surgery or anesthesiology course. This possibly means that Thai vet students have been studied animal pain treatment two to five hours in lecture and laboratory with cadavers in the veterinary schools. The short period of study time may reflex that University veterinary programs is insufficient for train veterinary students in the recognition and treatment of animal pain. The data from one survey study also demonstrates that ninety six percent of Thai veterinarians wanted the undergraduate veterinary school teach more about pain management in animals. Eighty eight percent of Thai veterinarians used to fail to control pain in their animal patients at least once. Forty seven percent felt their knowledge in the area of assessment of pain need to be improved, forty five percent wanted to learn more about physiology of pain, forty six percent interested in update of analgesic drug information, and forty two percent would like to enhance their pain management practices.

The continuing education regarding on basics to advances of pain management in animals tends to play an important role to provide the adequate knowledge of pain control to Thai veterinarians. Workshops and conferences have been established more often in the past three years. Professors and experienced veterinarians from both local and other countries were invited to give animal pain treatment presentations to Thai veterinarians and veterinary students. This indicates high level of concern with pain management in animals of Thai veterinarians.

Panel discussion **Takeuchi Memorial Panel Discussion**
Pain management education in Asian countries

Tuesday 1st September | Room A | 16:10−18:10

PD-4 Pain management education in Japan

○Yamashita Kazuto
Rakuno-Gakuen University, Japan

Pain management in animals becomes indispensable care for current veterinary practice in Japan. We can effectively reduce pain in animals by administering analgesics with concepts of preventive and multimodal analgesia. This present status in Japan is brought about by pain management education to veterinary practitioners and students and development of many analgesics approved for animal use during the last 20 years. In this panel discussion, I will look back at progress made in veterinary pain management and its education during the last 20 years and introduce the current situation of the veterinary pain management education in Japan.

1. Continuing education in veterinary pain management

In the late 1990s, pain management in animals began to attract attention and to be taken enthusiastically in veterinary referral practice in Japan. Then, many continuing education programs on veterinary pain management were held all over Japan in the early 2000s. In particular, the Japanese Society of Veterinary Anesthesia and Surgery (JSVAS) and the Japanese Society for Study of Animal Pain (JSSAP) have been playing important roles in enlightenment of the pain management in veterinary practice for the past 20 years. The JSVAS started as a society for the study of veterinary anesthesia in 1970 and has organized a special committee for veterinary anesthesia and analgesia (JSVAS-VAA) since 2003. The JSVAS-VAA has coordinated continuing education programs in the field of veterinary anesthesia and analgesia in every academic meeting of JSVAS held twice a year. The JSVAS-VAA has also promoted intensive training course in veterinary anesthesia and analgesia, "Anesthesia Boot Camp", every year since 2010. In addition, the JSVAS-VAA devised and announced guidelines for peri-operative pain management adopting concepts of preventive and multimodal analgesia in companion animals in 2012.

The JSSAP was founded in 2003 to push forward scientific studies and to aim at enlightenment of understanding and treating pain in animals with the veterinary industry. The JSSAP has coordinated continuing education programs in the field of veterinary pain management in the annual academic meeting of Animal Clinical Research Foundation. In addition, the JSSAP had dispatched its working group (JSSAP-WG) consisting of Japanese experts in the field of veterinary pain management to many study meetings held in various parts of Japan to provide veterinary pain management lectures for veterinary practitioners for 5 years from 2003 to 2007. The JSSAP-WG conducted an attitude survey of Japanese small animal practitioners toward pain management in dogs and cats in 2003 and 2008. The results of this survey showed an improvement in their attitude toward pain management, for instance, the proportion of veterinary practitioners who administered analgesics to dogs and cats peri-operatively increased from 73.6% in 2003 to 88.9% in 2008. The JSSAP-WG also developed Canine Acute Pain Scale in 2006 and Canine Chronic Pain Index in 2014 (these are written in Japanese) to enhance pain recognition by veterinary practitioners, technicians, and owners in Japan.

Recently, both the JSVAS-VAA and JSSAP-WG introduced "Guidelines for recognition, assessment and treatment of pain" devised by the World Small Animal Veterinary Association Global Pain Council (WSAVA-GPC) to Japanese veterinary practitioners. The JSVAS and JSSAP will continue to play an important role in the pain management education to veterinary practitioners in Japan.

2. Pain management education in curriculum of veterinary schools

Approximately 1,000 graduates from sixteen veterinary schools take a National Examination of Veterinary License every year in Japan. The veterinary education in Japan shifted to six-years system from four-years system in 1978. Historically, pain management education had been provided as a part of veterinary surgery in Japanese veterinary schools for a long time. In the early 2000, some veterinary schools started to teach "veterinary anesthesia and analgesia" as an independent subject in their curriculum. However, this movement in pain management education did not spread through all veterinary schools.

The All-Japan University Convention on Veterinary Medicine has advanced educational reforms since 2009 and drew up the Veterinary Education Model Core Curriculum in 2011. This Core Curriculum consists of 52 offering subjects including "veterinary anesthesia and analgesia" and 19 training subjects including "clinical rotation". In 2010, the Ministry of Agriculture, Forestry and Fisheries approved that veterinary students acquiring proper ability can treat owner-owned animals in the "clinical rotation" at university veterinary medical teaching hospitals although persons without veterinary license have been strictly restricted from treating owner-owned animals by the Veterinary Medical Act in Japan. This decision by the Ministry of Agriculture, Forestry and Fisheries makes the Veterinary Education Model Core Curriculum including "clinical rotation" to be practical. Now, the

Panel discussion

Takeuchi Memorial Panel Discussion
Pain management education in Asian countries

All-Japan University Convention on Veterinary Medicine is preparing the Veterinary Common Achievement Tests (vet-CAT) for evaluating veterinary students' ability before they participate in the "clinical rotation". The vet-CAT will start in 2017. The area covered in the vet-CAT includes "veterinary anesthesia and analgesia". Therefore, pain management education will be a compulsory subject in all Japanese veterinary schools from 2016.

Oral

Session 1 Small animal analgesia

Tuesday 1st September | Room D | 14:50−15:05

O1-1 Pilot evaluation of a novel unilateral declaw model and efficacy of an extended release buprenorphine product

○Masataka Enomoto[1], Patricia D Kigin[2], David Bledsoe[2], Jon Hash[1], Charles E Smith[3], B Duncan X Lascelles[1,4]

[1)]North Carolina State University College of Veterinary Medicine, [2)]Farnam Companies Inc., [3)]North Carolina State University, [4)]UNC school of Dentistry

Introduction:
Extended duration analgesics for cats undergoing surgery would be of benefit. A proof of concept study of an extended release formulation of buprenorphine HCL (BupXR) was conducted using objective kinetic measures collected from cats in a unilateral onychectomy model.
Methods:
Using a blinded, randomized, two period crossover design, four cats were allocated to placebo (saline) or BupXR (0.6 mg/kg, subcutaneously [SC]) treatment groups. All animals underwent a unilateral forelimb onychectomy per period with a washout period in between. Observational pain scores and kinetic data (using a pressure sensitive walkway [PSW]) were collected prior to (baseline) and for 72 hours following surgery. Symmetry indices (SI) were derived for kinetic variables (peak vertical force [PVF]; vertical impulse [VI]) of each forelimb for landing following a jump from an elevated perch and for walking. A rescue analgesic protocol was in place. Effect of surgery and treatment were evaluated using a mixed model statistical approach.
Results: No cats required rescue analgesics based on subjective pain score. BupXR had a positive influence on subjective pain scores during the 72 hours postsurgery ($p=0.0012$). PVF and VI of the operated limb were significantly decreased for both landing ($p<0.0001$ and $p<0.0001$) and walking ($p<0.0001$ and $p<0.0001$) following placebo. BupXR resulted in significantly decreased asymmetry in limb use during landing (PVF, $p<0.0001$; VI, $p<0.0001$) and walking (PVF, $p=0.0002$, VI $p<0.0001$). The novel use of data collected following a jump from an elevated perch (0.7m) appeared to provide all desired information and was easier to collect than walking data.
Conclusion: This study demonstrates that SC administration of BupXR may be an effective analgesic for a 72 hour period postoperatively. Furthermore, landing onto a PSW from an elevated perch may be a useful and efficient way to assess analgesics in cats using a unilateral model of limb pain.

Tuesday 1st September | Room D | 15:05−15:20

O1-2 Thermal antinociception after subcutaneous, buccal or intravenous administration of a high-concentration formulation of buprenorphine in awake cats

○Graeme M. Doodnaught[1], Beatriz Monteiro[1], Javier Benito[1], Elizabeth Cozzi[2], Paulo Steagall[1]

[1)]Faculty of Veterinary Medicine, University of Montreal, [2)]Abbott Animal Health, Abbott Park Road, Abbott Park, IL, U.S.A.

The aim of this study was to evaluate onset, magnitude and duration of thermal antinociception of buprenorphine after subcutaneous (SC), buccal (OTM) or intravenous (IV) administration.

Six healthy adult cats (4.9 ± 0.7 kg) were included. Skin temperature (ST) and thermal threshold (TT) were evaluated using a wireless device at baseline, 0.5, 1, 2, 4, 6, 8, 12, 24, 30, 36, 48, 60 and 72h after treatment. In period 1, TT was evaluated after SC administration of saline 0.9% (SAL). In period 2, a high-concentration formulation of buprenorphine (Simbadol; 1.8 mg/mL) was injected by the SC (0.24 mg/kg), IV (0.12 mg/kg), or OTM (0.12 mg/kg) route of administration in a randomized, prospective, blinded, crossover design with a minimum14-day wash-out period. Temporal changes were analyzed using one-way ANOVA followed by Dunnett's test. Treatment comparisons were performed using two-way ANOVA with Bonferroni's correction ($P<0.05$).

Euphoria and hyper-responsiveness were observed in all opioid-treated groups. Skin temperature (ST) was significantly increased after SC treatment from 1-12h (except 2 and 6h). Hyperthermia was not observed. Thermal thresholds were significantly increased after SC, IV and OTM from 1-24h (except 2h), 0.5-8h (except 6h), and 1-8h (except 6h), respectively, when compared with baseline values. Thermal thresholds were significantly increased after SC (1-30h), IV (1-8h) and OTM (1-12h) when compared with SAL, but not different among buprenorphine-treated cats.

In cats, SC administration of a high-concentration formulation of buprenorphine provides long-lasting antinociception (≥ 24h). These effects were of increased duration when compared with the IV and OTM routes.

Tuesday 1st September | Room D | 15:20−15:35

O1-3 Effects of Bupivacaine and Morphine on the Electroencephalogram and Postoperative Pain in Castrated Dogs

○Robert Sawicki[1,2], Kavitha Kongara[1], Craig Johnson[1], Rao Dukkipati[1], Mike Geiseg[2]
[1)]Massey University, [2)]Veterinary Health Research

The aim of this study was to investigate the effects of bupivacaine and morphine separately or in combination, on the electroencephalogram (EEG) and postoperative pain in dogs undergoing castration. Dogs (n=7 per group) received bupivacaine (2 mg/kg; infiltration at the incision site, IB) or morphine (0.5 mg/kg; subcutaneously, SQ) or a combination of morphine (0.5 mg/kg SQ) and bupivacaine (2 mg/kg IB) preoperatively. Thirty to sixty minutes after premedication with acepromazine (0.5 mg/kg, SQ), anaesthesia was induced with intravenous propofol and maintained with halothane in oxygen via a rebreathing circuit. The EEG was recorded in a three electrode montage. Median frequency (F50), 95% spectral edge frequency (F95) and total power (P_{tot}), derived from EEG power spectra recorded before skin incision (baseline) were compared with those recorded during castration of both testicles (T_1 & T_2). Post-operatively, pain was assessed at 1, 3, 6 and 9 hours using the short form of the Glasgow composite measure pain scale (CMPS-SF). Statistical analysis tested the data for normality and was carried out using a linear mixed model to compare effects between treatment groups. Non-normally distributed data was analysed using Mann-Whitney-U tests and Kruskal-Wallis ANOVA. Dogs in the morphine and bupivacaine groups had a significantly higher F50, F95 and a lower P_{tot} (EEG indices of nociception) compared to those in the combination group. No significant differences in the EEG were found between the baseline period and T_1 & T_2 in the combination group. CMPS-SF pain scores of dogs in the combination and bupivacaine only groups were significantly lower than those of the morphine only group. No significant differences in pain scores were found between dogs of the combination and bupivacaine groups. This suggests that a bupivacaine local anaesthetic / morphine opioid combination provides superior anti-nociception than either drug used alone for the castration of dogs.

Tuesday 1st September | Room D | 15:35−15:50

O1-4 Evaluation of renal safety of carprofen and meloxicam in anaesthetised dogs

○Kavitha Kongara, John P. Chambers, Antony Jacob, Venkata S.R. Dukkipati, Mike Gieseg
Massey University

The aim of this study is to compare the effects of carprofen and meloxicam on glomerular filtration in dogs anaesthetised for 30 minutes. In a randomised crossover design, dogs (n=8) received carprofen (4 mg kg^{-1}) or meloxicam (0.2 mg kg^{-1}) or saline (2 ml), subcutaneously at the time of anaesthetic premedication with acepromazine (0.05 mg kg^{-1}). Thirty to sixty minutes later, anaesthesia was induced with intravenous (IV) propofol to effect and maintained with isoflurane in oxygen for 30 minutes. Systolic arterial blood pressure was maintained above 90 mmHg with IV fluids and by adjusting the inspired isoflurane concentration. A plasma iohexol clearance (ICL) test was used to estimate the GFR. ICL test was conducted twice on each dog, before and 24 hours after induction of anaesthesia. Iohexol was injected as a single IV dose (1500 mg of iodine per dog), over a 30-second period. At 120 and 240 minutes after iohexol injection, 2 ml of blood was collected and iohexol concentration in the plasma measured by reverse phase high-performance liquid chromatography. Iohexol clearance was calculated in a mono-compartment model. The effects of test drugs on ICL as an estimate of GFR were compared using a mixed model analysis in SAS 9.4. Mean ICL rate ranged from 4.47 ml/kg/min (meloxicam group) to 4.78 (saline group) ml/kg/min. There was no significant difference in the ICL rate between treatment groups or between time-points, within each group. Thus, carprofen and meloxicam have non-significant effect on renal perfusion in normotensive dogs subjected to anaesthesia.

Session 2 Small animal analgesia

Tuesday 1st September | Room D | 16:10−16:25

O2-1 Benefit-risk evaluation of pre-emptive administration of meloxicam and robenacoxib for cat spay: analgesia comparison

○Ludovic Pelligand[1], Jonathan N. King[2], Jonathan Elliott[1]

[1)]Royal Veterinary College, [2)]Clinical Development, Elanco Animal Health, c/o Novartis, 4002 Basel Switzerland.

Objective: Evaluate the risk benefit-ratio of pre-operative versus post-operative non-steroidal anti-inflammatory drugs (NSAIDs) in healthy cats.

Study Design: Prospective blinded randomised controlled clinical trial

Animals: Sixty healthy female cats undergoing ovariohysterectomy; median body weight 2.7 kg [1.65-4.1] and age 32 [18-225] weeks.

Methods: Twelve cats were randomly allocated to one of five treatment groups: meloxicam or robenacoxib at admission (MA, RA) meloxicam or robenacoxib at induction (MI, RI) and robenacoxib at extubation (RE). Meloxicam and robenacoxib were administered subcutaneously at 0.2 and 2 mg/kg, respectively. Cats were premedicated (acepromazine 0.02 mg/kg and buprenorphine 0.02 mg/kg intramuscularly); after propofol induction, volatile anaesthesia was maintained with isoflurane in oxygen. Routine clinical monitoring, Doppler systolic blood pressure, capnography and isoflurane concentration were recorded. Rescue (buprenorphine 0.02 mg/kg) was administered if wound palpation elicited a VAS pain response exceeding 50 mm on a scale from 0 to 100. Cats were scored at 3 days postoperatively by owner and investigator. Statistical analysis (RMANOVA and Mann Whitney) was carried out by both treatment and administration time (admission, induction, extubation).

Results: There was no effect of time X treatment interaction on VAS. Eight of 12 cats in both admission groups (MA, RA) received rescue versus 5 (RE, MI) and 4 (RI) cats, but the difference was not significant (P=0.08 admission vs induction). There were no differences in monitoring variables except minimal blood pressure (MA significantly lower than RA, RI and RE groups, $P < 0.009$). Three cats (one from each robenacoxib group) required additional opioids overnight. Of 34 cats seen at 3 days, only owner activity score was significantly higher in induction versus admission ($P = 0.017$) and extubation ($P = 0.032$) groups.

Conclusion: Administration of NSAIDs at extubation was not associated with more frequent rescue or worse pain scores on recovery or at 3 days.

Tuesday 1st September | Room D | 16:25−16:40

O2-2 Benefit-risk evaluation of pre-emptive administration of meloxicam and robenacoxib for cat spay: renal safety comparison

○Ludovic Pelligand[1], Jonathan N. King[2], Jonathan Elliott[1]

[1)]Royal Veterinary College, [2)]Clinical Development, Elanco Animal Health, c/o Novartis, 4002 Basel Switzerland

Objective: To evaluate the risk benefit-ratio of pre-operative non-steroidal anti-inflammatory drugs (NSAIDs) administration in the young healthy cat, using sensitive markers of the renal function.

Study Design: Prospective blinded randomised controlled clinical trial

Animals: Sixty healthy female cats anaesthetised for ovariohysterectomy. Median [range] body weight and age were 2.7 [1.65-4.1] and 32 [18-225] weeks, respectively.

Methods: Twelve cats were randomly allocated to one of five treatment groups: meloxicam or robenacoxib at admission (MA, RA) meloxicam or robenacoxib at induction (MI, RI) and robenacoxib at extubation (RE). Meloxicam and robenacoxib were administered subcutaneously at 0.2 and 2 mg/kg, respectively. Cats were premedicated (acepromazine 0.02 mg/kg and buprenorphine 0.02 mg/kg intramuscularly); after propofol induction, volatile anaesthesia was maintained with isoflurane in oxygen and Ringer Lactate (10 mL/kg/h) was administered. Plasma creatinine and serum Thromboxane(Tx)B_2 were measured before anaesthesia, at extubation ($t_{ext.}$), $t_{ext.}$+2h and 3 days postoperatively. Plasma renin activity (PRA) was measured at extubation and $t_{ext.}$+2h. Prostaglandin(PG)E_2 and Vascular Endothelial Growth Factor (VEGF, kidney hypoxia marker) were measured at $t_{ext.}$+2h. Statistical analysis (ANOVA or RMANOVA) was carried out by both treatment and administration time (admission, induction, extubation).

Results: Plasma creatinine was not different between groups or administration time. The plasma creatinine from one cat (MI group) increased from 1.4 (baseline) to 2.1 mg/dL (3 days). Anaesthesia increased PRA, as extubation values were higher compared to 2h thereafter ($P < 0.0001$). PRA was still higher at $t_{ext.}$+2h in admission groups compared to induction groups ($P = 0.01$). Overall, serum TxB_2 were lower with meloxicam than robenacoxib ($P = 0.001$) with MA TxB_2 significantly lower than each robenacoxib groups ($P < 0.005$). Urinary PGE_2 and VEGF were unaffected by treatment.

Conclusion: The renin angiotensin system was activated during anaesthesia independently of cyclooxygenase inhibition, possibly due to hypotension or surgical stimulation.

Tuesday 1st September | Room D | 16:40−16:55

O2-3 Paravertebral Brachial Plexus Blockade in dogs undergoing shoulder surgery

○Sawako Murakami[1], Shotaro Nagahama[2], Shinya Yamaguchi[1]
[1)]YPC Tokyo Animal Orthopaedic Surgery Hospital, [2)]Veterinary Anesthesia Support

Paravertebral Brachial Plexus Blockade (PBPB) is a regional anaesthetic technique used for analgesia of thoracic limb of small animals. PBPB is not so commonly performed as Axial Brachial Plexus Blockade (ABPB) in veterinary medicine. To our knowledge, there are no published studies on the clinical use of PBPB in dogs.

The objective of this study was to determine the effectiveness of PBPB on dogs undergoing shoulder surgery.

Four Toy Poodles, one Brussels Griffon and one Bernese Mountain Dog were referred to our clinic for shoulder arthrodesis or shoulder stabilization.

Premedication was with atropine intravenously (IV). Anaesthesia was induced with midazolam and propofol IV to effect and maintained with sevoflurane in oxygen under spontaneous ventilation.

PBPB was performed between C4 and T5 using a neurostimulator attached to a 50 mm needle to localize the nerves. 0.14 to 0.2 ml/kg of a solution consisting of bupivacaine, lidocaine, and saline was injected to each location to block the nerve.

The mean ± SD Et-sevo for each patient were 2.84 ± 0.30, 3.21 ± 0.31, 3.05 ± 0.11, 2.45 ± 0.14, 3.68 ± 0.07 and 2.95 ± 0.08. Intra operative heart rate, respiratory rate and mean arterial blood pressure were considered within acceptable limits. No dog required additional analgesics during the surgical procedures.

0.5mg/kg of morphine was given subcutaneously (SC) right before the incision closure. Recovery from anaesthesia was smooth and uneventful. Complete motor and sensory blockade of affected limb was noted with the dogs observed. These patients regained motor function within 24 hours.

According to the staining studies in some literature, there is a high probability of PBPB not blocking all the target nerves. Our result suggests the clinical efficacy of PBPB is sufficient to perform shoulder surgeries though the whole surgical region may not be completely paralyzed.

Tuesday 1st September | Room D | 16:55−17:10

O2-4 Regional analgesia of the pinna, ear canal and soft tissues of dogs undergoing deep ear canal debridement

○Sandra Allweiler[1], Michelle Conetta Tensley[2], Rod Rosychuk[1]
[1)]Colorado State University, [2)]The animal neurology & imaging center

The purpose of this study was to determine whether regional anesthesia of the canine ear reduces perioperative inhaled and injectable anesthetic doses and improves post-operative comfort of animals undergoing deep ear canal debridement.

Twelve client-owned dogs undergoing deep ear canal debridement were randomly assigned to receive either 1 mg/kg each of lidocaine and bupivicaine (group LB) or 0.2 ml/kg saline (group SC) in the form of a regional block encompassing the great auricular, auriculotemporal, and internal auricular nerves. A standardized protocol was used for induction and anesthesia was maintained with isoflurane in oxygen. Either 1 mcg/kg fentanyl or propofol to effect were administered intravenously as rescue anesthetics. Isoflurane level was recorded every 5 minutes. Pain scores were assigned by anesthesia personnel using a pre-determined scale pre-induction, at extubation, 1 hour and 2 hours post-surgery. Clients assigned a pain score 18-24 hours post-operatively using a written scale. Anesthetists, investigators, and clients were blinded to group assignments. Data was evaluated by one-sided Fisher's Exact test, Wilcoxon Rank Sum test, and repeated measures analysis using commercially available software SAS 9.4. A p-value < 0.05 was considered significant.

In the LB group, 33.3% of animals received injectable rescue anesthetic, compared with 100% of dogs in SC group. There was significantly reduced use of rescue (p-value 0.0303) in the LB group. No difference was found for median isoflurane dose between groups. A significantly lower pain score (p-value 0.0048) was noted in the LB group at 18-24 hours. A trend toward lower pain scores in the LB group at other time points was noted but was not statistically significant. Complications secondary to the block were not observed in the post-operative period.

Regional analgesia of the ear results in improved post-operative comfort following deep ear canal debridement and reduces use of injectable anesthetics needed to maintain an effective plane of anesthesia.

Research supported by funds from Colorado State University Center for Companion Animal Studies.

Session 3 Small animal analgesia

Tuesday 1st September | Room D | 17:10−17:25

O3-1 Development of a novel femoral nerve block technique in cats

○Benedict Ong Huai Ern Ong[1], Hui Cheng Chen[2]

[1)]Faculty of Veterinary Medicine, Universiti Putra Malaysia, [2)]Faculty of Veterinary Medicine, Universiti Putra Malaysia

This study was conducted to develop a novel technique of femoral nerve block technique in cats by the use of anatomical landmarks. Feasibility and efficacy of this technique were then evaluated in cats undergoing femoral bone surgery. Anatomical dissections in two cat cadavers revealed that a potential landmark to approach the psoas compartment is via the caudal edge of the transverse process of L7. In this novel approach, a needle is inserted perpendicularly to the skin surface, either at the midpoint between iliac wing and the dorsal spine of L7, or at the medial one-third of the distance from the dorsal spine of L7 to the iliac wing. Once it touches the transverse process of L7, the needle tip is walked off it caudally until it just crosses the edge of the transverse process of L7. Colorant spread was determined using 0.1 ml/kg stamp pad ink on 7 cat cadavers. Seven trials were made using the midpoint landmark and three trials using the medial one-third landmark. All injections using the midpoint landmark successfully entered into the psoas compartment (7/7). None was injected into blood vessels or the peritoneal cavity. There was no evidence of epidural migration or intraneural injections. All injections using the medial one-third landmark showed entry into the iliac vessel (3/3). Hence, the midpoint landmark was chosen for the clinical study. This technique has been tried on ten clinical cases. Results showed that this technique enabled orthopedic manipulation at lower anaesthetic levels. It obtunded sympathetic responses during surgery especially for the surgical area innervated by the femoral nerve only. Combination with the sciatic nerve block is required to increase the utility of this novel technique.

Key words : femoral nerve block, psoas compartment, cats, landmark

Tuesday 1st September | Room D | 17:25−17:40

O3-2 Comparison between the hanging-drop technique and the running-drip method for identification of the epidural space in dogs

○Fernando Martinez Taboada[1], José Ignacio Redondo[2]

[1)]North Downs Specialist Referrals, [2)]Universidad CEU Cardenal Herrera

The aim of this study was to compare the running-drip method (RDi) (Baraka 1972), a simple technique never used in animals, with the hanging drop (HDo) technique in dogs in sternal (S) and lateral (L) recumbency.

Forty-four healthy dogs requiring epidural blocks as part of a standardized balanced anaesthetic plan were randomised into four groups. The same person performed all the blocks using Tuohy needles with a fluid-prefilled hub when advancing through the ligamentum flavum (HDo) or connecting a drip-set elevating 60 cm the drip fluid level from the spinous or the tranverse processes (RDi). The number of attempts, the "pop" sensation, clear drop aspiration or fluid dripping, the time-to-locate-the-epidural-space (TTLES) and the presence of CSF were recorded. When the identification was successful a bupivacaine-morphine combination was injected. The success of the block was assessed by experienced observers, unaware of the method used, based on usage of rescue analgesia (intraoperative fentanyl in response to cardiovascular changes, and postoperative methadone in response to pain scores). Data was checked for normality. Binomial variables were analyzed with the Chi-square or Fisher's exact test when appropriated. The scores of ordinal variables were analyzed using the Kruskal-Wallis and the Mann-Whitney tests ($p<0.05$).

There were no differences between groups except for LHDo which required more attempts (6 of 11 dogs required >1 attempt) than SRDi (0/11) ($p=0.0062$) and the drop-aspiration was more often observed in SHDo (9/11) than in LHDo (2/11) ($p=0.045$). TTLES was lower ($p=0.006$) in SHDo (20 (14-79) sec) than in LHDo (47 (18-82) sec). There were no differences between the other groups. No differences were found in rescue analgesia or pain scores.

In conclusion, RDi is an easy, useful and fast technique to identify the epidural space in dogs. The LHDo was the most difficult technique requiring more time and attempts

References:

Baraka A. (1972). Identification of the peridural space by a running infusion drip. British Journal of Anaesthesia 44, 122 – 122

Tuesday 1st September | Room D | 17:40−17:55

O3-3 Ultrasound-guided placement of brachial plexus catheter in dogs: description of 13 clinical cases.

○Thaleia Stathopoulou, Alejandra Garcia, Diego Castiñeiras, Maja Drozdzynska, Jaime Viscasillas
The Royal Veterinary College

The evidence of perioperative use of brachial plexus catheters (BPC) in veterinary anaesthesia is scarce. The aim of this study is to describe a new technique to place a BPC and show the results we have found with its use.
Thirteen dogs who had ultrasound-guided placement of BPC were included. With the patients positioned in lateral recumbency (with the affected limb uppermost) the ultrasound probe was positioned in a parasagittal plane, parallel to the first rib. The anatomical landmarks used were the main brachial plexus roots together with the axillary artery. Using an in-plane technique, a Tuohy needle was advanced dorso-ventrally until its tip was located adjacent to the brachial plexus where an epidural catheter was inserted. The tuohy needle was removed and used to create a subcutaneous tunnel until the dorsal area of the scapula were the catheter was fixed to the skin.
The data recorded included: breed, age, patient's body weight, type of surgery, pre or postoperative catheter placement using sedation or general anaesthesia, volume, concentration and frequency of ropivacaine administered, lenght of catheter stay, rescue analgesia administration and motor function and complications.
The most common breed was Springel Spaniel (n = 4). Surgeries included humeral fracture (n = 8) and radius/ulnar fracture repair (n = 4). The catheter was placed pre (n = 6) or postoperatively (n =7) and kept a median of 3 days (range 1-7 days). The concentration and volume of ropivacaine was 0.25% and 0.3 ml/kg +- 0.3 respectively. All the patients showed low pain score with motor function while the BPC was in place. The complications were: catheter dislodgement (n = 3) and transitory Horner´s syndrome (n = 4).
This technique seems easy to be perform and the results are promising. Prospective studies are needed in order to further evaluate this technique.

Tuesday 1st September | Room D | 17:55−18:10

O3-4 Evaluation of Epiduroscopy as a viable diagnostic and therapeutic tool in dogs: A cadaver study

○Fernando L Garcia-Pereira[1], Timo Prange[2], Aaron Seller[3], Victoria Obert[1]
[1)]Department of Large Animal Clinical Sciences of the College of Veterinary Medicine, University of Florida, [2)]Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, [3)]Department of Anesthesiology of the College of Medicine, University of Florida

Objectives- To evaluate the use of epiduroscopy as a tool in clinical diagnostic and therapeutics of vertebral canal and spinal cord lesions in canine patients.
Animals- 6 mix breed cadavers
Procedure- Cadavers were place in sternal recumbency and an endoscope was introduced on the lumbosacral epidural space. Three specimens were scoped with a 0.9 mm fiberscope and the reminder with a 2.8 mm videoscope. Visibility and identification of anatomical structures, as well as maneuverability of the endoscopes were evaluated. Macroscopic tissue damage was evaluated by dissection of the vertebral canal at the end of the procedure.
Results- Three attempts were made in dogs using the fiberscope. Only one dog in the videoscope group was scoped 3 times. Intermittent saline boluses, CO2 insufflation and endoscope navigation improved visualization by separating the epidural fat from the anatomical structures of interest. The image of the fiberscope was small and of poor quality, making identification of specific structures difficult. Maneuverability was difficult and target structures could not be reliably reached or identified. Maneuverability and image quality of the videoscope were superior and spinal nerve roots, the spinal dura mater, epidural fat and vessels could be identified. During necropsy, no gross damage was found in the spinal cord, nerve roots or vessels.
Conclusion and Clinical Relevance- The 2.8 mm videoscope was successfully used to perform epiduroscopy through the lumbosacral space in canine cadavers. Epiduroscopy is a potential tool for diagnostic and therapeutic interventions. Further polishing and evaluation of the technique in live animals is necessary prior to its use in clinical cases.

Tuesday 1st September | Room D | 18:10−18:25

O3-5 Ultrasound guided thoracic paravertebral block: cadaveric study in foxes

○Jaime Viscasillas, Paolo Monticelli, Ian Jones
The Royal Veterinary College

Thoracic paravertebral block (TPVB) is a technique used during thoracic surgical procedures in human patients to provide perioperative analgesia. The aim of this study is to describe ultrasound guided TPVB in a population of 12 fox cadavers.

A 10 MHz linear transducer was used to visualise the space between the pleura and the transverse spinous process (paravertebral space) at the level of the fifth thoracic vertebrae (T5). 0.2 ml/kg of iohexol 300 mgI/ml was injected into the right and left paravertebral spaces at T5 under ultrasound guidance using a 20-gauge, 50 mm Touhy needle. The needle was advanced in a lateral to medial direction using in-plane technique. Injections were performed by two operators, each operator performing twelve injections in six cadavers. A thoracic Computer Tomographic (CT) examination was then performed and evaluated by a single operator. The following features of iohexol distribution were recorded: Paravertebral location (Yes/No), Number of intercostal spaces with contrast, Location relative to T5 (Cranial/Caudal/Mixed), Pattern of distribution (Linear/Cloud-like/Intercostal), Epidural contamination (Yes/No), Pleural contamination (Yes/No), Mediastinal contamination (Yes/No).

Every injection (100%) resulted in identification of iohexol within the paravertebral space (5±1.5 intercostal spaces). 54% had a caudal, 29% cranial and 17% mixed location of the spreading relative to injection point in T5. 58% had a linear, 25% cloud-like and 12.5% an intercostal distribution. 50% of injections resulted in pleural contamination and 41.6% resulted in mediastinal contamination. A single injection resulted in epidural contamination. Iohexol was identified in the right atrium of a single cadaver.

The described technique seems easy to be performed and provides good distribution of contrast in the paravertebral space. Possible complications include epidural, pleural, mediastinal and intravascular contamination. Further studies are neeeded to evaluate the technique in clinical settings.

Wednesday 2nd September | Room A | 13:30–13:45

O4-1 Influence of MK-467 on the absorption of medetomidine after intramuscular administration in dogs – Preliminary results

○Flavia Restitutti[1], Marja Raekallio[1], Johanna Kaartinen[1,2], Juhana Honkavaara[1], Otto Wejberg[1], Emmi Mikkola[1], Mika Scheinin[3], Outi Vainio[1]

[1)]Department of Equine and Small Animal Medicine, University of Helsinki, [2)]The Animal Health Trust, Kentford, UK, [3)]Institute of Biomedicine, University of Turku, Finland

We evaluated the effects of MK-467, a peripheral α_2-adrenoceptor antagonist, on the absorption of medetomidine's enantiomers after intramuscular (IM) administration.

Medetomidine (20 μg kg^{-1}; Med) was administered alone or combined with MK-467 (400 μg kg^{-1}; MedMK) IM in the same syringe to eight purpose-bred dogs in a randomized, cross-over design, at least two weeks apart. Central venous samples were collected at 5, 10, 15, 20, 30, 45, 60, 90 and 120 minutes after treatments. Blood was centrifuged and the plasma was separated and frozen until analyzed. The concentrations of dexmedetomidine (Dex), levomedetomidine (Levo) and MK-467 in plasma were determined with HPLC-MS/MS. The maximum plasma concentration (C_{max}) and the time to reach the maximum concentration (T_{max}) were measured and the areas under the concentration-time curves ($AUC_{0\text{-}120}$) were calculated by the trapezoidal method. Data were analysed with paired t-tests. Results are expressed in Table 1 (mean ± SD).

The addition of MK-467 accelerated the absorption of medetomidine, and
lead to higher peak concentrations of both of its enantiomers. This effect was probably mediated by inhibition of medetomidine-induced vasonconstriction at the injection-site. The exposure to Levo was less than to Dex within both treatments. MK-467 was absorbed slower than Dex or Levo after simultaneous IM administration.

Acknowledgements: Vetcare Ltd, Finland, funded the study and provided the drugs.

Table 1: Selected pharmacokinetic parameters of eight dogs receiving medetomidine or medetomidine and MK-467 intramuscularly

Treatment	Analyte	C_{max} (ng mL^{-1})	T_{max} (min)	$AUC_{0\text{-}120}$ (min ng mL^{-1})
Med	Dex	3.95 ± 1.15	43 ± 16	327 ± 93
	Levo	2.58 ± 0.76[§]	44 ± 17	215 ± 61[§]
MedMK	Dex	5.54 ± 1.04[¶]	17 ± 7[¶]	253 ± 48
	Levo	4.04 ± 0.67[§]	18 ± 6	196 ± 34[§]
	MK-467	658 ± 155	38 ± 28	61612 ± 19698

[¶] $p < 0.05$ different from Med; [§] $p < 0.05$ different from Dex within treatment

Wednesday 2nd September | Room A | 13:45–14:00

O4-2 Pharmacokinetics of dexmedetomidine, MK-467, and their combination following intravenous bolus administration in cats

○Bruno H Pypendop[1], Juhana Honkavaara[2]

[1)]University of California, Davis, [2)]University of Helsinki, Finland

This study aimed to characterize the pharmacokinetics of dexmedetomidine and MK-467, alone and in combination.

Seven healthy adult cats were used. Cats were administered dexmedetomidine [12.5 (D12.5) or 25 (D25) μg/kg], MK-467 [300 μg/kg (M300)], or dexmedetomidine (25 μg/kg) with MK-467 [75, 150, 300, or 600 (D25M600) μg/kg]. Treatments were administered intravenously in a medial saphenous vein at least 2 weeks apart, in random order. Blood samples (2 mL) were collected from a jugular catheter prior to drug administration, and at various times between 1 min and 8 hours thereafter. Blood was centrifuged and the plasma was separated and frozen until analyzed for dexmedetomidine (D) and MK-467 (M) concentrations with liquid chromatography/mass spectrometry in the D12.5, D25, M300, and D25M600 groups. The limit of quantitation was 0.1 ng/mL for both analytes. Accuracy and imprecision were 90-111% and 2-13% for D and 89-108% and 2-7% for M, respectively. Compartment models were fitted to time-concentration data using non-linear regression. The best fitting model was selected based on observation of residual plots and Akaike's information criterion. Pharmacokinetic parameters, corrected for dose where appropriate, for dexmedetomidine in the D12.5, D25 and D25M600, and for MK-467 in the M300 and D25M600 groups were compared using the paired Wilcoxon signed rank test.

Two-compartment models best fitted the time-concentration data for both D and M. Median (range) for selected parameters is presented in Table 1; no significant difference was found.

At the doses tested, dexmedetomidine and MK 467 did not significantly affect each other's disposition in cats.

Table 1

	Clearance (mL/min/kg)	Terminal half-life (min)	Area under concentration time curve (ng*mL/min)
D12.5	14.6 (9.6-22.7)	48 (40-69)	858 (552-1304)
D25	18.2 (12.4-22.9)	52 (40-76)	1382 (1090-2023)
D25M600	D 22.7 (18.5-36.4)	D 48 (35-60)	D 1099 (686-1349)
	M 2.8 (2.1-4.8)	M 118 (97-172)	M 214892 (126217-281694)
M300	3.0 (2.0-4.5)	122 (99-139)	100665 (66124-152054)

Wednesday 2nd September | Room A | 14:00－14:15

O4-3 Effect of two doses of the peripheral alpha-2-adrenoceptor antagonist MK-467 on the minimum alveolar concentration (MAC) of sevoflurane in dogs receiving dexmedetomidine

○Khursheed Mama[1], Marlis Rezende[1], Eugene P Steffey[1], Rachel C Hector[1], Nadaphat Bunnag[1], Juhana Honkavaara[2], Marja Raekallio[2], Outi Vainio[2]

[1)]Colorado State University, [2)]University of Helsinki, Finland, [3)]Please note while Dr. Mama is presenting author she is also the second author - Dr. Rezende is first author!

Alpha2-adrenergic receptor agonists have potent MAC sparing effects which may be influenced by the peripheral alpha-2-adrenoceptor antagonist MK-467. We evaluated the effect of 2 doses of MK-467 on dexmedetomidine–sevoflurane MAC.

Six healthy, adult beagles, weighing 11.0-13.8 kg were anesthetized with sevoflurane in oxygen. Fourty minutes was allowed for instrumentation (e.g.,esophageal temperature, arterial blood pressure) and anesthetic equilibration prior to administration of dexmedetomidine (4.5 ug kg-1 over 10 minutes, followed by 4.5 ug kg-1 hour-1, IV). Dexmedetomidine-sevoflurane MAC determination (in duplicate using the tail clamp technique) was initiated 30 minutes later. Ventilation was controlled to maintain PaCO2 at 40 +/- 5 mmHg and temperature was maintained at 38 +/- 5 ℃. After dexmedetomidine-sevoflurane MAC determination, dogs received 2 incremental doses of MK-476 (90 ug kg-1 over 10 minutes followed by 90 ug kg-1 hour-1 and 180 ug kg-1 over 10 minutes followed by 180 ug kg-1 hour-1, IV); the infusion of dexmedetomidine remained unchanged. MAC was re-determined 30 minutes after the initiation of each dose. End-tidal anesthetic values were corrected for analyzer calibration and adjusted to sea level barometric pressure. Statistical significance ($p<0.05$) was determined by one-way ANOVA and pairwise multiple comparisons (Holm-Sidak).

Dexmedetomidine-sevoflurane MAC (Mean +/- SD) increased from 0.63 +/- 0.11 to 0.81 +/- 0.14 and 1.09 +/- 0.12 % with incremental doses of MK-467 (an increase of 28.6 and 73.0 %, respectively). All these changes were significant.

MK-467 dose-dependently attenuates the sevoflurane MAC sparing effect of dexmedetomidine.

Acknowledgments: Financial support provided by Vetcare Ltd. Finland

Wednesday 2nd September | Room A | 14:15－14:30

O4-4 Cardiovascular effects of dexmedetomidine, MK-467, and their combination in cats

○Bruno H Pypendop[1], Juhana Honkavaara[2]

[1)]University of California, Davis, [2)]University of Helsinki, Finland

The aim of this study was to characterize the cardiovascular effects of dexmedetomidine, MK-467, and their combination following intravenous administration to cats.

Six cats were used. Cats were anesthetized with desflurane in oxygen. Catheters were placed in a carotid artery and a medial saphenous vein. A thermodilution catheter was positioned with its tip in the pulmonary artery as verified by fluoroscopy. Cats were allowed to recover for 60 minutes. ECG, and systemic, central venous, and pulmonary artery pressures were continuously recorded. Baseline pulmonary artery occlusion pressure and cardiac output were measured. Cats were administered one of three treatments according to a Latin square design, at least 2 weeks apart: dexmedetomidine (25 μg/kg IV, D25), MK-467 (600 μg/kg IV, M600), or dexmedetomidine (25 μg/kg IV) and MK-467 (600 μg/kg IV, D25M600). One cat in D25M600 did not complete the study, so data from 5 cats is available for that treatment. Cardiovascular variables were recorded at various times from 3 minutes to 8 hours following drug administration. Data were analyzed for treatment and time effects using a two-way repeated measures ANOVA, followed by pairwise comparisons to baseline within treatment groups using Dunnett's test. Significance was set at $p<0.05$. Data is presented as mean ± SD.

In D25, heart rate decreased from 202 ± 20 to 123 ± 15 bpm (mean ± SD at time of largest change); mean arterial pressure (MAP) increased from 122 ± 15 to 177 ± 23 mm Hg; central venous pressure increased from 7 ± 4 to 19 ± 3 mm Hg; pulmonary artery occlusion pressure increased from 14 ± 5 to 22 ± 5 mm Hg; and cardiac output decreased from 654 ± 80 to 277 ± 87 mL/min. In D25M600, MAP decreased from 121 ± 7 to 95 ± 11 mm Hg with no other significant changes from baseline. No significant changes from baseline were seen in M600.

At the doses used in this study, MK-467 effectively prevented dexmedetomidine-induced cardiovascular effects in cats.

Wednesday 2nd September | Room A | 14:30–14:45

O5-1 Cardiovascular and sedative effects of intramuscular co-administration of medetomidine and MK-467, a peripheral alpha-2 adrenoceptor antagonist, in dogs – Preliminary results

○Flavia Restitutti[1], Johanna Kaartinen[1,2], Marja Raekallio[1], Otto Wejberg[1], Emmi Mikkola[1], Juhana Honkavaara[1], Outi Vainio[1]

[1)]Department of Equine and Small Animal Medicine, Faculty of Veterinary Medicine, University of Helsinki, Finland, [2)]The Animal Health Trust, Kentford, UK

Medetomidine is often administered intramuscularly (IM) in dogs. We aimed to evaluate the effect of MK-467 on the cardiovascular and sedative effects of medetomidine after IM administration.

Medetomidine (20 μg kg^{-1}, Med) was administered IM alone or in combination with MK-467 (400 μg kg^{-1}, MedMK) to 8 purpose-bred dogs in a randomized, cross over design (treatments administered at least two weeks apart). Heart rate (HR), cardiac output (CO), mean arterial pressure (MAP) and central venous pressure (CVP) were measured, systemic vascular resistance (SVR) was calculated and sedation assessed with a composite sedation score (CSS) modified from Honkavaara et al (2008) at baseline, then 5, 15, 30 and 60 minutes after drug administration. Data were analysed with 2-way repeated measures ANOVA and post-hoc t-tests corrected with Bonferroni.

Results are summarized in Table 1 (mean ± SD). With both treatments, significant decreases from baseline in HR and CO were observed, while CVP and SVR increased. All cardiovascular parameters were different between treatments at 30 and 60 minutes. There were no significant differences in sedation between treatments.

MK-467 did not prevent the initial medetomidine-induced cardiovascular effects after IM administration. However, MK-467 improved later hemodynamic performance without seemingly affecting sedation. With the doses studied, medetomidine appeared to have a faster onset of action than MK-467 after simultaneous intramuscular administration.

Honkavaara JH, Raekallio MR, Kuusela E *et al* (2008) The effects of L-659,066 a peripheral α2-adrenoceptor antagonist, on dexmedetomidine-induced sedation and bradycardia in dogs. *Vet Anaesth Analg* **35**, 409-413

Acknowledgments: Vetcare Ltd, Finland, funded the study

Table 1: Cardiovascular and sedative effects of IM administration of medetomidine (20 μg kg^{-1}; Med) or Med with MK-467 (400 μg kg^{-1}; MedMK)

Parameter	Treatment	Time (min) -5 (baseline)	5	15	30	60
HR (beats min^{-1})	Med	85±10	49 ± 23†	40 ± 5†	36±7†	37±5†
	MedMK	99±18	44±6†	52±10†	60±13$^{\dagger\sharp}$	62±9$^{\dagger\sharp}$
CO (L min^{-1})	Med	2.82±1.11	1.21±0.48†	0.98±0.17†	0.91±0.13†	0.85±0.09†
	MedMK	3.20±0.77	1.28±0.44†	1.45±0.31†	1.78±0.35$^{\dagger\sharp}$	1.91±0.5$^{\dagger\sharp}$
MAP (mmHg)	Med	102±12	123±35†	121±23†	121±18†	107±10
	MedMK	106±7	122±12	106±11	87±13$^{\sharp}$	74±10$^{\dagger\sharp}$
CVP (mmHg)	Med	2±1	6±2†	6±2†	6±1†	6±1†
	MedMK	0±2	7±3†	5±1†	4±1$^{\dagger\sharp}$	2±1$^{\sharp}$
SVR (dynes sec cm^{-5})	Med	3187±1066	9712±5625†	9809±2722†	10566±2163†	9833±1165†
	MedMK	2778±766	7685±1754†	5813±1325	3917±1122$^{\sharp}$	3190±962$^{\sharp}$
CSS	Med	0±1	6±3†	12±3†	13±2†	14±2†
	MedMK	1±1	8±3†	14±2†	13±3†	11±2†

Within the same treatment, †significantly ($p < 0.05$) different from baseline. Within time point, $^{\sharp}$MedMK significantly different from Med ($p < 0.05$)

Wednesday 2nd September | Room A | 14:45–15:00

O5-2 The effects of MK-467, a peripheral α$_2$-adrenergic receptor antagonist, on the cardiovascular system and sedation in dogs receiving atipamezole to reverse medetomidine-induced sedation

○Heta Turunen[1], Marja Raekallio[1], Magdy Adam[2], Henriikka Helin[1], Katri Nevanperä[1], Ira Kallio-Kujala[1], Juhana Honkavaara[1], Flavia Restitutti[1], Paula Larenza[1], Outi Vainio[1]

[1)]Department of Equine and Small Animal Medicine, University of Helsinki, Finland, [2)]Pharmacology Department, Faculty of Veterinary Medicine, Beni-Suef University, Egypt

MK-467 maintains (dex)medetomidine induced sedation while preventing its cardiovascular effects, whereas atipamezole reverses both the cardiovascular and sedative effects. We aimed to study the influence of MK-467 in dogs treated with medetomidine and atipamezole.

Eight adult healthy beagles received intramuscular (IM) medetomidine [20 μg kg^{-1} (MED)] with or without MK-467 [400 μg kg^{-1} (MEDMK)], and 30 minutes later IM atipamezole [100 μg kg^{-1}] in a prospective, randomized, experimental cross-over study. Heart rate (HR), mean arterial pressure (MAP) and cardiac output (lithium dilution) were recorded until 120 minutes after medetomidine. Sedation scores were determined by a blinded investigator. Cardiac index (CI) and systemic vascular resistance index (SVRI) were calculated. Differences between treatments after atipamezole administration were evaluated with ANOVA for repeated measurements and Bonferroni post hoc test ($p < 0.05$).

After atipamezole, HR remained lower with MED than with MEDMK (e.g. 45.1 ± 8.6 min^{-1} (mean ± SD) and 60.0 ± 18.1 min^{-1} at 10 minutes, respectively); MAP was lower with MEDMK (83.5 ± 12.3 mmHg) than with MED (98.5 ± 10.8 mmHg) five minutes after atipamezole, when its lowest average value was detected. Overall, CI was higher and SVRI lower with MEDMK than with MED. Sedation scores were significantly higher at 90 minutes after atipamezole with MED than with MEDMK.

Atipamezole can be used without adverse cardiovascular effects in dogs sedated with medetomidine and MK-467. Atipamezole failed to increase CI in dogs receiving MED, while MK-467 enhanced hemodynamic function and prevented resedation.

Acknowledgements: Vetcare Ltd, Finland, funded this study.

Wednesday 2nd September | Room A | 15:00－15:15

O5-3 MK-467 for the prevention of dexmedetomidine-induced bradycardia in cats: a dose-finding study

○Bruno H Pypendop[1], Juhana Honkavaara[2], Heta Turunen[2]
[1)]University of California, Davis, [2)]University of Helsinki, Finland

The aim of this study was to determine a dose of MK-467, a peripherally-acting alpha-2 adrenergic receptor antagonist, that attenuates dexmedetomidine-induced bradycardia without altering sedation, in cats.

Seven cats were used in a randomized, crossover study. Heart rate was measured using a telemetric ECG transmitter. Sedation was scored by an investigator (blinded to treatment and heart rate) on a 0-4 scale, with 0 representing no sedation and 4 representing a cat in lateral recumbency, unresponsive to loud clapping of the hands. Following recordings of baseline heart rate and sedation, cats were administered dexmedetomidine [12.5 (D12.5) or 25 (D25) μg/kg], MK-467 [300 μg/kg (M300)], or dexmedetomidine (25 μg/kg) with MK-467 [75 (D25M75), 150 (D25M150), 300 (D25M300), or 600 (D25M600) μg/kg]. Treatments were administered intravenously at least 2 weeks apart. Heart rate and sedation score were recorded at various times between 3 minutes and 8 hours following drug administration. Heart rate data was analyzed for treatment and time effects using a 2-way repeated measures ANOVA, followed by Dunnett's test for pairwise comparisons to baseline values. Sedation scores were analyzed for the time effect using Friedman's test followed by Dunn's test for pairwise comparisons to baseline values, and for the treatment effect using Kruskal-Wallis' test followed by Dunn's test for pairwise comparisons to the D25 group. Significance was set at $P<0.05$.

Heart rate (mean ± SD) was 197 ± 30 at baseline; mean ± SD heart rate at the time of the largest change is shown below.

Group	Heart rate (bpm)
D12.5	113 ± 14
D25	108 ± 16
D25M75	122 ± 5
D25M150	127 ± 14
D25M300	123 ± 11
D25M600	158 ± 11
M300	244 ± 27

Sedation score significantly increased from baseline in all groups except M300. There was no significant difference in sedation score with the D25 group for any treatment except M300.

MK-467 dose-dependently attenuated dexmedetomidine-induced bradycardia in cats with little impact on sedation.

Wednesday 2nd September | Room A | 15:15－15:30

O5-4 Influence of acepromazine and/or a constant rate infusion of MK-467 on cardiovascular parameters of dogs anaesthetized with isoflurane and a step up infusion of dexmedetomidine – Preliminary data

○Flavia Restitutti, Juhana Honkavaara, Robert A Menzies, Tommaso Rosati, Outi Vainio, Marja Raekallio, M. Paula Larenza Menzies
Department of Equine and Small Animal Medicine, University of Helsinki, Finland

The cardiovascular effects of acepromazine and/or MK-467 were evaluated in isoflurane-anesthetized dogs receiving dexmedetomidine infusions.

After ethical committee approval, 6 beagles (13.4 to 18.45 kg) anesthetized with propofol (6 mg kg^{-1}) and isoflurane (end-tidal concentration 1.7%) were stabilized and received 4 treatments in a randomized, crossover fashion (≥ 2-week washout interval). At 0 min, dogs received acepromazine 0.02 mg kg^{-1} (AceMkDex and AceSalDex) or saline (SalMkDex and SalSalDex) IV. At 20 min, all dogs received a loading dose (LD) of dexmedetomidine 1 μg kg^{-1} $5\text{-}min^{-1}$ followed by a 1 μg kg^{-1} $hour^{-1}$ constant rate infusion (CRI) and either MK-467 (LD: 25 μg kg^{-1}; CRI: 30 μg kg^{-1} hour; AceMkDex and SalMkDex) or saline (AceSalDex and SalSalDex). Dexmedetomidine CRI was increased at 45 min (LD: 1.5 μg kg^{-1} $5\text{-}min^{-1}$, CRI: 3 μg kg^{-1} $hour^{-1}$). End-tidal isoflurane concentrations were decreased to 1.4% and 1.05% at 20 and 45 min, respectively. Cardiovascular parameters were obtained at baseline (-5 min) and at 15, 40 and 65 min. Data were analysed with repeated measures ANOVA followed by Bonferroni-corrected t-tests.

Results are summarized in table 1.

Overall, MK-467 and/or acepromazine ameliorated dexmedetomidine-induced cardiovascular changes. MK-467 promoted higher heart rates while MK-467 and/or acepromazine maintained cardiac index over time. Mean arterial pressure decreased initially with acepromazine and increased in all groups over time. Systemic vascular resistance increased with all treatments except AceMkDex. Severe hemodynamic depression was not evident with any treatment.

Acknowledgments: Vetcare Ltd Finland for financial support and providing MK-467

Table 1: Cardiovascular parameters of isoflurane anesthetized dogs receiving dexmedetomidine and acepromazine and/or MK-476 and/or saline.

	Time point	-5 min	15 min	40 min	65 min
	End-tidal isoflurane	1.7%	1.7%	1.4%	1.05%
Parameter	Treatment				
Heart rate (beats min^{-1})	AceMkDex	95±9	98±12	$83±8^{‡a}$	$66±11^{†‡fa}$
	SalSalDex	87±14	98±13	$66±6^{†‡a}$	$50±7^{†‡fab}$
	AceSalDex	99±11	97±6	$74±13^{†‡}$	$54±4^{†‡f}$
	SalMkDex	99±13	97±14	$81±11^{†‡}$	$67±10^{†‡fb}$
Cardiac index (L min^{-1} kg^{-1})	AceMkDex	117±13	108±19	115±17	112±16
	SalSalDex	126±22	136±21	$104±18^{‡}$	$96±24^{†‡}$
	AceSalDex	108±33	119±36	104±35	95±53
	SalMkDex	99±26	108±29	113±21	90±17
Mean arterial pressure (mmHg)	AceMkDex	67±3	63±8	$68±3^{ab}$	$78±5^{†‡fab}$
	SalSalDex	65±2	$68±5^{a}$	$78±11^{†‡ac}$	$90±7^{†‡fac}$
	AceSalDex	67±3	$59±3^{a}$	$78±8^{†‡bd}$	$89±7^{†‡fbd}$
	SalMkDex	65±4	66±6	$67±8^{cd}$	$81±11^{†‡fcd}$
Systemic vascular resistance (dynes sec cm^{-5})	AceMkDex	2721±333	2729±345	2780±368	$3300±643^{ab}$
	SalSalDex	2532±482	2474±660	$3589±869^{‡}$	$4610±1523^{†‡fa}$
	AceSalDex	3099±755	2518±353	$3843±926^{‡}$	$5121±901^{†‡fb}$
	SalMkDex	3217±824	3043±831	2821±571	$4370±734^{†‡f}$

Within the same treatment, †significant difference from baseline, ‡significant difference from 15 minutes, ᶠ65 minutes significant difference from 40 minutes; [abcd]within time point, treatments with same letter are significantly different ($P < 0.05$)

Wednesday 2nd September | Room A | 16:00−16:15

O6-1 Cardiovascular effects of dexmedetomidine alone and in combination with two doses of the peripheral α-2-adrenoceptor antagonist MK-467 in sevoflurane anesthetized dogs

○Khursheed Mama[1], Marlis Rezende[1], Eugene P Steffey[1], Rachel C Hector[1], Nadaphat Bunnag[1], Juhanna Honkavaara[2], Marja Raekallio[2], Outi Vainio[2]

[1)]Colorado State University, [2)]University of Helsinki, Finland, [3)]Please note Dr. Mama is presenting author but should be second author. Dr Marlis Rezende is first author

Alpha-2-adrenergic agonists are potent MAC sparing drugs, but also cause significant cardiovascular depression. We determined the cardiovascular effects of dexmedetomidine alone and in combination with 2 doses of MK-467 in sevoflurane anesthetized dogs.

Six healthy, adult beagles, weighing 11.1-14.4 kg were anesthetized with sevoflurane in oxygen. Cardiac output (CO) was determined by thermodilution for sevoflurane, sevoflurane-dexmedetomidine (4.5 ug kg-1 over 10 minutes, followed by 4.5 ug kg-1 hour-1, IV) and sevoflurane-dexmedetomidine plus 2 incremental doses of MK-476 (90 u kg-1 over 10 minutes followed by 90 ug kg-1 hour-1 and 180 ug kg-1 over 10 minutes followed by 180 ug kg-1 hour-1, IV) for both controlled and spontaneous ventilation at equivalent anesthetic doses (1.2 x individual MAC). Heart rate (HR) and mean arterial pressure (MAP) were also recorded for each treatment. Statistical significance ($p<0.05$) was determined by one-way ANOVA and multiple pair-wise comparisons.

A 61 % reduction ($p<0.001$) in CO (0.56 +/- 0.05 [mean ± SD] from 1.44 +/- 0.34 L min-1) and 53 % reduction ($p<0.001$) in HR (45 +/- 7 from 96 +/- 8 bpm) was observed with dexmedetomidine. MK-467 dose-dependently attenuated these to 21 and 5 % for CO and 30 and 15 % for HR. MAP increased ($p<0.001$) with dexmedetomidine (118 +/- 18 from 70 +/- 14 mmHg) and decreased with the addition of low and high dose MK467 (to 80 +/- 7 and 68 +/- 10 mmHg).

In sevoflurane anesthetized dogs, MK-467 dose-dependently attenuates the cardiovascular changes caused by dexmedetomidine.

Acknowledgments: Financial support provided by Vetcare Ltd, Finland.

Wednesday 2nd September | Room A | 16:15−16:30

O6-2 The cardiovascular effects of dobutamine in isoflurane-anaesthetised dogs treated with dexmedetomidine and MK-467, a peripheral α2-antagonist

○Vilhelmiina Huuskonen[1], Flavia Restitutti[2], Juhana Honkavaara[2], Marja Raekallio[2], Rachel Bennett[1], Maija Hagman[2], Outi Vainio[2]

[1)]School of Veterinary Medicine, University College Dublin, Ireland, [2)]Department of Equine and Small Animal Medicine, University of Helsinki, Finland

Preventing α_2-agonist-induced vasoconstriction with MK-467 may promote hypotension. We investigated the effect of dobutamine in dexmedetomidine/MK-467-treated anaesthetised dogs.

Eight beagles, anaesthetised with 1.3% end-tidal isoflurane, received the following treatments in a randomised crossover study after baseline measurements:
DEX-S: dexmedetomidine (2.5 $\mu g\ kg^{-1}$ IV) and saline infusion
DEXMK-S: dexmedetomidine + MK-467 (100 $\mu g\ kg^{-1}$ IV) and saline infusion
DEXMK-D: dexmedetomidine + MK-467 and dobutamine infusion.

The infusions were adjusted between 20 and 50 min by an investigator blinded to all treatments, targeting a mean arterial pressure (MAP) between 70 and 90 mmHg. Heart rate (HR), MAP and cardiac output (CO) were re-measured at 15 and 50 min. Treatments were compared with ANOVA and Tukey's post hoc method ($p< 0.05$).

Results are summarized in Table 1. With DEXMK-D, the median infusion rate of dobutamine at 50 min was 3.75 $\mu g\ kg^{-1}\ min^{-1}$ (range 1.25-10).

Dobutamine maintained normotension in dogs receiving dexmedetomidine, MK-467 and isoflurane.

Table 1. Mean (SD) cardiovascular variables.

		DEX-S	DEXMK-S	DEXMK-D
HR (min^{-1})	Baseline	78 (11.2)	74 (11.1)	77 (11.8)
	15 min	56 (14.7)†§	74 (13.5)*	71 (7.3)*
	50 min	69 (10.4)§	75 (12.7)§	57 (7.6)*†
MAP (mmHg)	Baseline	61 (9.7)	58 (7.2)	61 (5.8)
	15 min	99 (4.2)†§	73 (2.1)*	74 (10.4)*
	50 min	72 (6.5)†	53 (4.2)*§	73 (9.5)†
CO ($L\ min^{-1}$)	Baseline	1.6 (0.3)	1.3 (0.2)	1.4 (0.2)
	15 min	0.9 (0.1)†§	1.5 (0.3)*	1.4 (0.3)*
	50 min	1.4 (0.3)	1.6 (0.3)	1.5 (0.6)

*significantly different from DEX-S
†significantly different from DEXMK-S
§significantly different from DEXMK-D

Wednesday 2nd September | Room A | 16:30−16:45

O6-3 Anaesthesia quality of alfaxalone IM compared to Ketamine IM when given combined with dexmedetomidine and butorphanol to cats undergoing castration.

○latifa khenissi[1], Segolene Broussaud[2], Olga Topie[2], Gwenola Touzot-Jourde[2]
[1)]University of Bristol, [2)]Oniris National Veterinary School, Nantes

Anaesthesia quality after alfaxalone given Intramuscularly (IM) or intravenously (IV) has previously been investigated with conflicting results. (Gieseg et al., 2014; Grubb et al., 2013).
This study investigates the difference in anaesthesia quality between Alfaxalone or ketamine IM combined with dexmedetomidine and butorphanol.

Thirty two client owned cats, aged between 4 months and 2 years, weighing between 2.8 kg and 5.4 kg were all undergoing a castration procedure.
All cats were randomly assigned to receive either alfaxalone (A) (n=16) (3 mg/kg IM) or ketamine(K) (n=16)) (5mg/kg) IM combined with dexmedetomidine (10 μg/kg) and butorphanol (0.2 mg/kg).
After endotracheal intubation, cats breathe 100 % oxygen for the duration of the procedure. Quality of injection, intubation and recovery were evaluated with simple descriptive scores (Gurney et al., 2009; Grubb et al., 2013; Gieseg et al.2014). Quality of anaesthesia was evaluated by the number of top-ups needed. The cats attitude, ability to walk and presence of ataxia was assessed at T15, T30, T45, T60, T120, T240 after extubation, and the time between IM injection and extubation recorded. Pain was assess at T120 and T240 with the A4vet pain score. Recovery time started at extubation.
A T-test was used to compare the extubation time and number of top-ups needed. Scores were analysed using a Kruskal-Wallis rank sum test at each time point.
Procedure duration was equivalent in both group (group A= 27 min, group K = 27.27 min)
Extubation time was longer in group A (TA= 62 min, TK= 45.13 min, p=0.00046). Cats from group K needed more top-ups, were more ataxic at T120 (p=0.003), had a worse recovery score at T60 (p=0.028) and were less willing to walk at T30.

Cats receiving alfaxalone had a better quality anaesthesia and a longer, but slightly better, quality recovery than cats receiving ketamine.

Wednesday 2nd September | Room A | 16:45−17:00

O6-4 Cardiorespiratory effects of alfaxalone IM compared to Ketamine IM when given combined with dexmedetomidine and butorphanol to cats undergoing castration.

○latifa khenissi[1], Segolene Broussaud[2], Olga Topie[2], Gwenola Touzot-Jourde[2]
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Cardiorespiratory effects of Alfaxalone given Intramuscularly (IM) has previously been investigated with conflicting results (Grubb et al., 2013; Ribas et al., 2014), but never compared to ketamine for cats undergoing a surgical procedure.

This study investigates the difference in cardiorespiratory parameters between Alfaxalone or ketamine IM combined with dexmedetomidine and butorphanol for cats undergoing castration.
Thirty two client owned cats, aged between 4 months and 2 years, weighing between 2.8 kg and 5.4 kg were randomly assigned to receive either alfaxalone (A) (n=16) (3 mg/kg IM) or ketamine (5mg/kg) (K) (n=16)) IM combined with dexmedetomidine (10 mcg/kg) and butorphanol (0,2 mg/kg).
During the procedure, cats received 100 % oxygen via endotracheal tube.
Heart rate (HR), respiratory rate (RR) and rectal temperature (T °) were recorded prior to drug administration. The pulse rate (PR) and RR were recorded 10 (T10) and 15 (T15) min after injection. The oxygen saturation (SpO2) was measured 15 min after injection.
Cardiorespiratory values (PR, RR, SPO2, blood pressure, End Tidal CO2 (ETCO2)) were recorded every 5 min for the duration of procedure. The PR, HR and T ° were measured after extubation.
Statistical analysis was performed using a linear mixed model for repeated measures (treatment and time were fixed effects and the animal the random effect). T-test was used for baseline values, T10, T15 and after extubation values.
The RR was significantly lower in group K at T10 (group A= 43.24 (+/-7.04), group K=28 (+/-13.35) , p=0.00075) and T15 (group A= 43 (+/-12.18), group K= 28 (+/-11.53) , p=0.0018). The PR decreased over time in both groups (p= 0.005). No abnormal values were found in either group.

Cardiorespiratory parameters are stable and clinical acceptable following IM injection of either alfaxalone or ketamine in healthy cats.

Wednesday 2nd September | Room A | 17:00−17:15

O7-2 Incidence and Duration of Apnoea Following Induction of Anaesthesia with Propofol or Alfaxalone in Dogs

○Sarah E. Bigby, Thierry Beths, Sebastien H. Bauquier, Jennifer E. Carter
University of Melbourne

Objective
To compare the incidence and duration of post-induction apnoea in dogs after premedication with methadone and acepromazine (MA) or methadone and dexmedetomidine (MD) followed by induction with propofol (P) or alfaxalone (A).

Study design
Prospective, randomized clinical trial.

Animals
Thirty-two healthy (ASA I or II) client-owned dogs scheduled for elective neutering procedures (15 females, 17 males), aged 4 months-4 years, and weighing 3-40 kg.

Methods
Dogs were randomized to receive either intramuscular MA+P, MA+A, MD+P or MD+A. Thirty minutes after premedication all dogs were preoxygenated for five minutes. The induction agent was administered via a syringe driver with P given at 4 mg/kg/min or A given at 1 mg/kg/min until intubation was achieved. Dogs were intubated and connected to a circle system with oxygen flow at 2 L/min. SpO_2, and RR were monitored continuously from the start of preoxygenation and, once intubated, $EtCO_2$ was monitored. If apnoea (≥ 30 seconds without a breath) occurred the length of time to the first spontaneous breath was measured. If SpO_2 decreased below 90% the experiment was stopped and manual IPPV initiated. Data were analysed with general linear models and significance was set at $p \leq 0.05$.

Results
There was no significant difference in the incidence (between 5-7/8 dogs in each group), or duration of apnoea (67-355 seconds) between any of the groups. One dog in the MD+P group desaturated (SpO_2<90%) during the apnoeic period and received IPPV.

Conclusion
Propofol and alfaxalone both cause post-induction apnoea and the incidence of apnoea is not influenced by the use of acepromazine or dexmedetomidine in premedication.

Wednesday 2nd September | Room A | 17:15−17:30

O7-3 The anesthetic effect of intramuscular combination of alfaxalone and butorphanol in dogs.

○Jun Tamura[1], Naohiro Hatakeyama[1], Tomohito Ishizuka[2], Takaharu Itami[2], Mohammed Ahmed Umar[3], Kenjiro Miyoshi[1], Tadashi Sano[1], Kazuto Yamashita[1]
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This study aimed to assess the anesthetic and cardio-respiratory effect of intramuscular combination of alfaxalone and butorphanol in dogs.
Six adult beagles (3 males, 3 females, 11.0 ± 3.1 kg) received two treatments at least 10 days interval apart. Before each treatment, all dogs were instrumented with arterial and central venous catheters under sevoflurane anesthesia. The dogs were allowed to breathe room air and treated with an intramuscular injection of alfaxalone (2.5 mg/kg) alone (ALFX) or combined with butorphanol (0.25 mg/kg) (ALFX-BTR) at 60 minutes after the recovery from sevoflurane anesthesia. Neuro-depressive effects (behavior changes and subjective scores) and cardio-respiratory parameters [rectal temperature, heart rate (HR), respiratory rate (RR), arterial blood pressure (ABP), central venous pressure, partial pressures of carbon dioxide ($PaCO_2$) and oxygen (PaO_2) were evaluated before and at 2 to 120 minutes after each treatment. Data were analyzed using the paired *t* test, Friedman test followed by Scheffe test and 2-way repeated measured ANOVA followed by Dunnett test ($P< 0.05$).
Each of the treated dogs became lateral recumbency. The duration of lateral recumbency was longer in ALFX-BTR compared with ALFX (92 ± 37 versus 46 ± 13 minutes, $P = 0.007$). Endotracheal intubation was achieved in 5 dogs in ALFX-BTR and one dog in ALFX. The neuro-depression score did not differ between treatments. The cardio-respiratory parameters were maintained within clinically acceptable ranges after each treatment although ALFX-BTR produced lower HR (61-80 versus 79-121 bpm, $P< 0.001$), mean ABP (82-101 versus 96-102 mmHg, $P< 0.001$), RR (16-23 versus 20-33 bpm, $P< 0.001$) and PaO_2 (79-92 versus 88-99 mmHg, $P = 0.003$) and higher $PaCO_2$ (41-44 versus 36-41 mmHg, $P = 0.001$) compared to ALFX.
The intramuscular combination of alfaxalone and butorphanol produced an anesthetic effect that permitted endotracheal intubation without severe cardio-respiratory depression in dogs.

Wednesday 2nd September | Room A | 17:30－17:45

O7-4 Influence of medetomidine and dexmedetomidine for premedication prior to general anesthesia on pupil size and intraocular pressure in healthy dogs

○Petr Rauser, Jana Zapletalova, Marketa Mrazova
Small Animal Clinic, Faculty of Veterinary Medicine, University of Veterinary and Pharmaceutical Sciences Brno

Dexmedetomidine is an enantiomer of medetomidine. The hemodynamic effects of both drugs are similar. Medetomidine or dexmedetomidine influence intraocular pressure (IOP). Effects of comparable doses of both drugs used for premedication prior to general anesthesia in dogs have not yet been reported.

Forty healthy dogs mean (SD) body mass 24.2 ± 13.4 kg and age 3.6 ± 3.0 years, 27 males and 13 females were included. Prospective, "blinded" clinical study was performed. Dogs were allocated randomly to receive IV medetomidine (Domitor; Orion Pharma, Finland) 0.01 mg kg^{-1} (MED A), 0.02 mg kg^{-1} (MED B) or dexmedetomidine (Dexdomitor; Orion Pharma, Finland) 0.005 mg kg^{-1} (DEX A), 0.01 mg kg^{-1} (DEX B). Ten minutes later, anesthesia was induced with propofol and maintained with isoflurane in oxygen-air. Intraocular pressure (using applanation tonometry), pupil size (PS), pulse (PR) and respiratory (f_R) rates and noninvasive blood pressure (NIBP) were measured prior to premedication (T0) and at 10 (T10), 20 (T20), 30 (T30), 40 (T40), 50 (T50) and 60 (T60) minutes after premedication. Oxygen saturation of hemoglobin (SpO_2) and end-tidal CO_2 concentration ($EtCO_2$) was measured at T20, T30, T40, T50 and T60. During measurements dogs were without painful stimulation, positioned in lateral recumbency with the head maintained in relaxed fashioned at the level of the thorax. Data were analyzed by ANOVA followed by Dunnett's test for multiple comparisons. Changes were considered significant at $P < 0.05$.

Following drug administration, PS, PR and f_R decreased significantly within all groups at all-time points, but did not differ significantly between groups. No significant changes in IOP and NIBP within and between groups and SpO_2 or $EtCO_2$ between groups were observed at all-time points.

Comparable doses of medetomidine or dexmedetomidine induced significant reduction in pupil size, respiratory and pulse rate, however without significant influence on intraocular pressure.

Wednesday 2nd September | Room B1 | 13:30–13:45

O8-1 Sedation, cardiovascular function and recovery of medetomidine versus dexmedetomidine isoflurane balanced anaesthesia in horses – preliminary study results

○Muriel Sacks, Simone K. Ringer, Andrea S. Bischofberger, Regula Bettschart-Wolfensberger
Vetsuisse Faculty, University of Zurich

Aim of this prospective blinded clinical study was to compare the effects of two balanced anaesthetic protocols on sedation, cardiopulmonary function and recovery in horses.

Thirty-six elective surgical patients were randomly assigned to either group Dex (dexmedetomidine, 13 horses) or Med (medetomidine, 23 horses). Sedation with Dex 3.5 μg/kg or Med 7 μg/kg IV was scored and topped up if necessary. Anaesthesia was induced with ketamine 2.2 mg/kg and diazepam 0.02 mg/kg IV and maintained with isoflurane in oxygen/air (F_IO<ent value="lt" />SUB<ent value="gt" />2 0.45 - 0.55), and Dex 1.75 μg/kg/h or Med 3.5 μg/kg/h. Ringer's Lactate (7 - 10 mL/kg/h) and dobutamine (0.25 - 1.25 μg/kg/min according to MAP) were administered. The lungs were mechanically ventilated to P_E 'CO2 of 5.3 – 6.7 kPa. HR, invasive blood pressures, in- and expired gas compositions and arterial blood gases were measured. For recovery, horses received Dex 1 μg/kg or Med 2 μg/kg IV. Recovery was timed and scored. Data were analysed using ANOVA, fisher's exact and unpaired t-tests with significance level $p \leq 0.05$.

Groups did not significantly differ in weight, age, duration of anaesthesia, recovery time and score. Significantly more horses in group Dex needed additional sedation (Dex 61.5%, Med 8.7%, $p = 0.001$). There was no significant difference in HR, MAP, required doses of dobutamine and F_E ′iso. In Dex PaCO<ent value="lt" />SUB<ent value="gt" />2 were significantly lower (Mean ± SD in kPa Dex 6.66 ± 0.65, Med 7.04 ± 0.66) and PaO<ent value="lt" />SUB<ent value="gt" />2 (as well as PaO<ent value="lt" />SUB<ent value="gt" />2/F_IO<ent value="lt" />SUB<ent value="gt" />2) were significantly higher (Mean ± SD in kPa Dex 23.22 ± 7.48, Med 19.06 ± 5.92).

These preliminary results suggest that dexmedetomidine at a 50% dose of medetomidine less often induces adequate preoperative sedation and that intraoperative cardiovascular function is not superior. Influence on gas exchange requires further investigation.

This study had ethical approval by the Swiss government (TV – 5455).

Wednesday 2nd September | Room B1 | 13:45–14:00

O8-2 Pharmacokinetic and pharmacodynamic of intravenous romifidine and propranolol alone or in combintation in awake horses

○Alessia Cenani, Robert J Brosnan, Shara Madigan, Heather K Knych, John E Madigan
University of California Davis

Propranolol has been suggested for anxiolysis in horses, but sedation efficacy and side-effects, both alone and in combination with alpha-2 adrenoceptor agonists, remain undetermined. Pharmacokinetics and pharmacodynamics of propranolol, romifidine and their combination were investigated in horses.

Six horses (561 ± 48 kg), enrolled in a randomized, prospective, blinded, crossover study, received IV propranolol 1 mg kg-1 (P), romifidine 0.1 mg kg-1 (R) or their combination (PR) with a minimum 1-week washout period. General alertness, behavioral responsiveness (visual and tactile) and physiologic responses were assessed before and 1, 2, 4, 8, 16, 30, 60, 120, 240, 480, 960 minutes after injection. Venous blood was collected for blood gases and acid-base analysis, and plasma drug concentrations measured by liquid chromatography-mass spectrometry. Data were analyzed using Pearson's correlation, Passing-Bablok, RM-ANOVA, Friedman test, Wilcoxon rank-sum test, Dunn-Sidak test, Paired t-test ($p < 0.05$).

Systemic clearance significantly decreased and the area under the concentration-time curve significantly increased for both drugs in PR compared to P and R. Both PR and R decreased behavioral responsiveness and produced sedation for up to 60 and 480 minutes, respectively. Sedation was deeper in PR for the first 16 minutes. HR significantly decreased with all treatments for 30 minutes. PR significantly increased number of HR measurements less than 20 beats/minute.

Although not associated with reduced behavioral responsiveness or sedation alone, propranolol augments romifidine sedation, probably because of decreased romifidine clearance in horses receiving PR. The potential for severe bradycardia warrants caution for co-administration of these drugs at doses studied.

Wednesday 2nd September | Room B1 | 14:00−14:15

O8-3 Comparison of alfaxalone, ketamine and thiopental for anesthetic induction and recovery in Thoroughbred horses premedicated with midazolam and medetomidine

○Ai Wakuno, Motoki Aoki, Asuka Kushiro, Naomi Mae, Kazumichi Kodaira, Tatsuya Maeda, Yosuke Yamazaki, Minoru Ohta

Japan Racing Association

OBJECTIVE
To compare the characteristics of anesthetic induction, recovery and cardiopulmonary responses between alfaxalone, ketamine and thiopental in Thoroughbred horses premedicated with midazolam and medetomidine.

PROCEDURES
This study was designed as prospective randomized blinded experimental crossover study. Six adult Thoroughbred horses (4 males and 2 females) were randomly anesthetized three times with alfaxalone 1.0 mg/kg, ketamine 2.5 mg/kg or thiopental 4.0 mg/kg after premedication with midazolam 20 μg/kg IV and medetomidine 6.0 μg/kg IV. Qualities of anesthetic induction and recovery were scored on a scale of 1 (poor) to 5 (excellent). Induction time and recovery time were also recorded. Cardiorespiratory values (heart rate, respiratory rate, arterial blood pressures and arterial blood gases) were recorded throughout anesthesia.

RESULTS
The median anesthetic induction and recovery quality scores were 4.0, 5.0, 4.5 and 4.5, 3.5, 4.0 for alfaxalone, ketamine and thiopental, respectively; the differences were not statistically significant. Mean induction time for ketamine (68 ± 12 sec) was significantly longer than that for alfaxalone (47 ± 5 sec) and thiopental (47 ± 3 sec). Mean time to standing for alfaxalone (47 ± 9 min) and thiopental (41 ± 10 min) was significantly longer than that for ketamine (23 ± 3 min). Cardiovascular values were maintained within clinically acceptable level throughout anesthesia. Respiratory rate significantly decreased during anesthesia for all three drugs; however, spontaneous breathing did not disappear, and PaCO2 values were maintained at approximately 50 mmHg.

CONCLUSIONS AND CLINICAL RELEVANCE
All the three drugs showed similar effects in relation to the characteristics of anesthetic induction, recovery and cardiopulmonary responses, with minor differences in induction and recovery times. Alfaxalone is as effective and useful injectable agent for anesthesia induction as ketamine and thiopental in Thoroughbred horses.

Wednesday 2nd September | Room B1 | 14:15−14:30

O8-4 Evaluation of total intravenous anesthesia with propofol-GGE-medetomidine or alfaxalone-GGE-medetomidine in Thoroughbred horses undergoing castration

○Motoki Aoki[1], Ai Wakuno[1], Asuka Kushiro[1], Naomi Mae[1], Tatsuya Maeda[1], Yosuke Yamazaki[1], Shunichi Nagata[2], Minoru Ohta[1]

[1)]Racehorse Clinic, Miho Training Center, Japan Racing Association, [2)]Laboratory of Racing Chemistry

OBJECTIVE
To compare the anesthetic and cardiorespiratory effects of two total intravenous anesthesia (TIVA) techniques with propofol-GGE-medetomidine (PGM) and alfaxalone-GGE-medetomidine (AGM) in Thoroughbred horses undergoing castration.

PROCEDURES
After premedication IV infusion with medetomidine 5.0 μg/kg and butorphanol 0.02 mg/kg, twelve male Thoroughbred horses were randomly anesthetized with either propofol 2.0 mg/kg (Group PGM: n=6) or alfaxalone 1.0 mg/kg (Group AGM: n=6), both in combination with GGE 10 mg/kg. Anesthesia was maintained for 60 min with a constant rate IV infusion of either propofol 3.0 mg/kg/hr (Group PGM) or alfaxalone 1.5 mg/kg/hr (Group AGM), both in combination with GGE 80 mg/kg/hr and medetomidine 3.0 μg/kg/hr. Responses to surgical stimuli and cardiorespiratory values were recorded throughout anesthesia. Qualities of induction and recovery were scored, and recovery times were also recorded.

RESULTS
All the horses received alfaxalone (Group AGM) showed smooth transition to lateral recumbency, whereas one of the horses received propofol (Group PGM) showed severe muscular rigidity and paddling during the induction period. All the horses in Group AGM were maintained at adequate anesthetic depth for castration. In contrast, increased cremaster muscle tension and/or purposeful movement in response to surgical stimuli were observed in 4 of the 6 horses in Group PGM, and additional administrations of propofol were required in one of them to maintain sufficient surgical plane of anesthesia. Cardiorespiratory values were maintained within clinically acceptable level in both groups. Mean plasma alfaxalone concentration in Group AGM was stable throughout anesthesia (1.5 to 2.0 μg/mL). Recovery qualities were good to excellent in both groups. Time to standing was 44 ± 11 min in Group PGM and 58 ± 12 min in Group AGM, respectively.

CONCLUSIONS AND CLINICAL RELEVANCE
Both TIVA techniques were effective in Thoroughbred horses, AGM was more suitable for castration compared with PGM.

Wednesday 2nd September | Room B1 | 14:30−14:45

O9-1 Development of a system for evaluation of horses recovering from anesthesia; Part 1: Inter-horse rater variability and intra-rater consistency of independent raters using a subjective one hundred point composite scale

○Stuart C Clark-Price[1], Kara M Lascola[1], Manuel Martin Flores[2], Andre C Shih[3], Erik H Hofmeister[4], Lydia L Donaldson[5,6], Lysa P Posner[7], Reza Seddighi[8], David J Schaeffer[1]

[1)]University of Illinois College of Veterianry Medicine, [2)]Cornell University College of Veterinary Medicine, [3)]University of Florida College of Veterinary Medicine, [4)]University of Georgia College of Veterinary Medicine, [5)]American College of Veterinary Anesthesia and Analgesia, [6)]AnimalScan, LLC, [7)]North Carolina State University College of Veterinary Medicine, [8)]Universtiy of Tennessee College of Veterinary Medicine

Anesthetic recovery of horses is frequently evaluated using subjective composite scales that may have poor repeatability, leading to conclusions of questionable utility. The inter-horse rater variability (index of the homogeneity of responses for an individual horse among raters) should be minimal for an effective subjective scoring system. The objective of this study was to examine inter-horse rater variability and intra-rater consistency of independent raters using a subjective composite scale to evaluate anesthetic recovery quality of horses.

In a prospective study, 12 horses were anesthetized with xylazine, midazolam, and ketamine in a padded equine recovery stall. Horses recovered unassisted and recoveries were video recorded and independently evaluated by seven Diplomates of the American College of Veterinary Anesthesia and Analgesia using a 100 point subjective composite scale. A Henze-Zirkler test established the multivariate normality of the rater scores. Inter-horse rater variability was determined using repeated measures ANOVA. Intra-rater consistency was determined graphically. Horses were ordered by their total score for the seven raters. Each rater's cumulative score was plotted against the ascending total score of the 12 horses.

Overall, raters' scores of individual horses were significantly different ($P<0.01$). Specifically scores differed for 43% (9/12) of pairs of raters ($P<0.03$). Intra-rater scores were generally consistent: a rater who scored a horse below the mean of the other 6 raters tended to give lower scores for all horses; this resulted in regression lines tending to fan out rather than cross.

These findings suggest that subjective composite scales for evaluation of horses recovering from anesthesia could lead different raters to different conclusions about the recovery status of the horse. Systems that do not rely on subjective data may minimize issues associated with rater subjective factors. Investigation and development of non-subjective methods to evaluate equine recoveries is warranted.

Wednesday 2nd September | Room B1 | 14:45−15:00

O9-2 Development of a system for evaluation of horses recovering from anesthesia; Part 2: An objective assessment system for evaluation of horses recovering from anesthesia using 3-axis accelerometry

○Stuart C Clark-Price[1], Kara M Lascola[1], Manuel Martin Flores[2], Andre C Shih[3], Erik H Hofmeister[4], Lydia L Donaldson[5,6], Lysa P Posner[7], Reza Seddighi[8], David J Schaeffer[1]

[1)]University of Illinois College of Veterinary Medicine, [2)]Cornell University College of Veterinary Medicine, [3)]University of Florida College of Veterinary Medicine, [4)]University of Georgia College of Veterinary Medicine, [5)]American College of Veterinary Anesthesia and Analgesia, [6)]AnimalScan, LLC, [7)]North Carolina State Universtiy College of Veterinary Medicine, [8)]University of Tennessee College of Veterinary Medicine

Anesthetic recovery of horses is frequently evaluated using subjective composite scales that may have poor repeatability, leading to conclusions of questionable utility. Development of other methods may eliminate problems associated with subjective systems. Accelerometry is the quantitative determination of acceleration of the body in performance of a task and is used to evaluate various problems in veterinary medicine. The objective of this study was to develop a system using accelerometry for the evaluation of anesthetic recovery of horses.

In a prospective study, 12 horses were anesthetized and a three axis accelerometer was fixed to a surcingle at the level of the withers. Unassisted recoveries were video recorded. Accelerometry data was used to calculated V_{max} [$V_{max}= \sqrt{(X^2+Y^2+Z^2)}$ where X, Y, and Z are the measured axes in gravities (g)] for each unsuccessful attempt and the successful attempt to stand. Recovery videos were independently viewed by seven diplomates of the American College of Veterinary Anesthesia and Analgesia and scored using a subjective 100 point composite scale. Vmax values and the median visual score for each horse were fitted to a library of nonlinear surface mathematical models by a specific computer program to determine the best fit.

The best fit, via fit statistics and visual verification, was a power model and resulted in derivation of the following equation where a horse's recovery score (RS) = $9.998 \times G^{0.633} \times (\Sigma G)^{0.174}$, where G is the V_{max} of the successful attempt to stand and ΣG is the sum of the V_{max} of unsuccessful attempts to stand. The RS was constrained to a range of 11 to 100 and categorized by score: excellent (11-30), good (30-50), fair (50-70, poor (70-90), and unacceptable (>90).

The developed system may allow objective assessment and facilitate research for improving the recovery of horses from anesthesia.

Wednesday 2nd September | Room B1 | 15:00−15:15

O9-3 Ten years of using the Wilderjans rope recovery system in horses - a retrospective study

○Maria Chie Niimura[1], Florent David[2], David Clifford[3], Hans Wilderjans[4], Lynne JM Hughes[1], Rachel Bennett[1]

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Assisting anaesthetic recovery with the aid of ropes may reduce the risk of injury in horses. This study reports the incidence of complications using the "Wilderjans" rope-recovery system, a simple system handled by a single operator from outside the recovery stall.

A total of 5854 (2003-2013) anaesthetic recovery records from one equine practice were reviewed retrospectively. Information retrieved included: anaesthetic protocol, duration of anaesthesia and recovery, type of surgery, and complications during recovery.

Thirty horses experienced complications during recovery (0.51%). Major complications (death or euthanasia) occurred in twelve horses (0.2%), including three cardiac arrests, two irreparable fractures, one open dislocation of the hock, four myopathies, one metabolic acidosis, and one hyperthermia. Six of the horses that died presented for exploratory laparotomy and five were older mares (15-18 years old). Eighteen horses (0.31%) had minor complications (e.g. facial paralysis, broken tail hair, loose head collar) of which five (0.08%) were related to failure of the rope recovery equipment.

At this practice using the "Wilderjans" rope-recovery system, the mortality rate during recovery from general anaesthesia was 0.2%, with ˜3/5 of the lethal injuries involving the musculoskeletal system. Consistent with Bidwell et al. (2006), older mares and systemically ill horses were more prone to develop serious problems during recovery. The mortality rate using the "Wilderjans" rope-recovery-system compares favorably with other reported recovery techniques. A better identification of the horses at increased risk prior to anaesthesia, and provision of additional support, may further reduce the rate of fatal recovery injuries in the future.

Wednesday 2nd September | Room B1 | 15:15−15:30

O9-4 Evaluation of a device for non-invasive and continuous monitoring of hemoglobin concentration in anesthetized horses

○Claire BL Scicluna

EquInstitut, Clinique du Plessis

The pulse co-oximeter is indicated and has demonstrated good accuracy for non-invasive and continuous monitoring of total hemoglobin concentration (SpHb) in human patients. Pulse oximetry (SpO2) is routinely used in equine anesthesia monitoring, therefore, a clinical study was performed to measure Hb continuously and assess SpHb accuracy in anesthetized horses.

Nineteen (19) healthy adult horses were anesthetized for elective surgical procedures. SpHb was continuously monitored with a Masimo Radical 7 rainbow co-oximeter (1). A total of 53 blood samples were obtained from facial artery and analyzed with a Vet ABC Scil machine (2). The results were then compared by time to the non-invasive values obtained with the Masimo Radical 7 rainbow. Data were statistical analyzed using a student t-test ($p<0.05$ significant).

Mean (SD, med) SpHb and Hb were 10.12 (2.19; 9.95) and 12.11 (1.51; 11.95) respectively. No statistical difference was found in the mean difference [Hb-SpHb] =1.99 (1.64; 2.00). The calculated linear regression coefficient was r2=0.445. Applying correction factors to SpHb (SpHbc = SpHb + C) by category (SpHb>14, C=-1; SpHb 12 to 14, C= 0; SpHb 8 to 12, C= +2; SpHb<8, C= +3), mean SpHb reached 11.84 (1.24; 11.95), [Hb-SpHb] = 0.27 (1.18; 0.30) and r2= 0.4211. Sixty percent of the SpHbc results correlated within +-0.5 g/dl of the Vet ABC Scil blood Hb values, and 80% were within a +-1.5 g/dl range.

The SpHb measured by pulse co-oximetry is a useful and reasonably accurate non-invasive method for continuously monitoring Hb concentration in healthy anesthetized horses. This monitoring device may also be useful for determining the Hb concentration in non-anesthetized horses.

(1) Masimo Radical 7 Rainbow, Masimo France, Ecully
(2) VetABC, Scil Animal Care Company, Altorf, France

Wednesday 2nd September | Room B1 | 16:00−16:15

O10-1 Cardiorespiratory effects of mild reverse Trendelenburg position in horses

○Stijn Schauvliege, Jacoba J van Dijk, Luc Duchateau, Diego Rodrigo Mocholi, Ilaria Cerasoli, Anna Binetti, Daphné Van Hende, Anja Neumeyer, Frank Gasthuys
Ghent University

The cardiovascular and respiratory effects of mild (7°) reverse Trendelenburg position were investigated in 58 anaesthetized horses undergoing elective surgery in dorsal recumbency.

After sedation (romifidine/morphine) and induction of anaesthesia (midazolam/ketamine), the horses were positioned on either a horizontal (H) or tilted (T) surgical table, following a randomized block design according to bodyweight class (<500, 500-600, >600 kg of bodyweight). Anaesthesia was maintained with isoflurane (FiO_2 55%) and a CRI of romifidine. All horses were mechanically ventilated. Ventilator settings were adjusted according to predefined criteria. Monitoring included electrocardiography, pulse oximetry, respiratory gas analysis and arterial pressure measurement. At 15 minute intervals, all monitored values were recorded and arterial blood gas analysis performed. Oxygenation indices (alveolar-arterial oxygen tension gradient ($P(A\text{-}a)O_2$, PaO_2/FiO_2 ratio and F-shunt) were calculated using standard formulae. Statistical analysis was performed on the data of the first 60 minutes of anaesthesia, using a mixed model with horse as random effect and position, time, weight class and their interactions as fixed effects (α =0.05).

Significantly more dobutamine was needed to maintain mean arterial pressure in group T than in group H (0.40 ± 0.07 vs 0.13 ± 0.07 μg kg^{-1} min^{-1}; P = 0.0069). The arterial oxygen content (CaO_2) and packed cell volume gradually increased and $P(A\text{-}a)O_2$ gradually decreased over time in group T, while an evolution in the opposite direction was observed for these variables in group H. As a result, a significant interaction between position and time was found for CaO_2 (P = 0.0403), packed cell volume (P = 0.0299) and $P(A\text{-}a)O_2$ (P = 0.0213). No other significant effects of table position were found.

Although a mild reverse Trendelenburg position might be beneficial for gas exchange in anaesthetized horses, the increased need for dobutamine warrants further investigation.

Wednesday 2nd September | Room B1 | 16:15−16:30

O10-2 Differences in regional ventilation in horses treated with and without continuous positive airway pressure – novel insights by electrical impedance tomography

○Martina Mosing[1], Andreas D Waldmann[3], David Bardell[2], Ulrike Auer[5], Stephan H Bohm[3], Regula Bettschart-Wolfensberger[1], Paul MacFarlane[4]
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The aim of this study was to evaluate the effect of continuous positive airway pressure (CPAP) on electrical impedance tomography (EIT) variables in anaesthetised horses.

Six healthy experimental horses were anaesthetised twice with isoflurane in oxygen 50% and medetomidine as continuous infusion in dorsal recumbency, receiving in random order either CPAP (8 cmH_2O) or no CPAP (NPAP) for 3 hours. EIT measurements were recorded every 30 minutes and an ensemble average of 10 consecutive breaths was calculated from a 2-minute recording and used for analysis at each time point. Lung regions in which impedance changed minimally during ventilation were defined as Dependent (DSS) and Non-dependent Silent Spaces (NSS) (Swisstom 2015); Centre of Ventilation (CoV) and ventral-dorsal distribution of ventilation (Radke et al. 2012) were calculated. Venous admixture (Qs/Qt) was calculated from arterial and mixed venous blood analysis. Statistical analysis was performed using ANOVA and Pearson correlation. Data are presented as mean ± SD.

DSS were significantly lower in the CPAP group (7.3 ± 0.8) compared to 12.7 ± 0.8 NPAP (p< 0.001), while no difference was seen in NSS. The CoV was located more dorsally (52.6 ± 0.4 vs. 55.6 ± 0.4 for CPAP vs. NPAP; (p< 0.001). The dorsal of the 4 ROIs received more ventilation for the first two hours of anaesthesia in the CPAP group. Qs/Qt was significantly correlated with DSS when time was taken as covariate ((p< 0.0001; r=0.65).

When CPAP is applied to the lungs of anaesthetised horses in dorsal recumbency the amount of DSS, most likely corresponding to anaesthesia-induced atelectasis, is reduced and ventilation is distributed towards the dependent dorsal parts of the lungs thereby improving the matching of ventilation and perfusion.

Radke OC, Schneider T, Heller AR et al. (2012) Spontaneous breathing during general anesthesia prevents the ventral redistribution of ventilation as detected by electrical impedance tomography: a randomized trial. Anesthesiology 116, 1227-1234.

Swisstom (2015) White paper on silent spaces, http://www.swisstom.com/wp-content/uploads/BB2-White-Paper_2ST800-104_Rev.000.pdf.

Acknowledgements: We thank the "Stiftung Forschung für das Pferd" for financing this project.

This study had ethical approval by the Swiss government (TV-4985).

Wednesday 2nd September | Room B1 | 16:30−16:45

O10-3 Fatal complications associated with anaesthesia in a private equine referral hospital

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Anesthetizing horses carries a high risk of fatal complications and the frequently quoted 2002 CEPEF study reported an overall mortality rate of 1.9 % (Johnston et al.). The main objective of the present study was to document and report an updated overall rate of fatal complications associated with anaesthesia at a large equine hospital.

Records of all horses undergoing general anaesthesia from 2010 to 2014 at Evidensia Equine Hospital Helsingborg, Sweden, were reviewed. A total of 3519 horses were identified. Of these, 162 were euthanized intra-operatively due to the poor prognosis associated with the primary disease, resulting in 3357 horses included in the study. The majority of the horses (n=3104, 92%) were recovered free in a padded box and 253 (8%) were either recovered using head and tail rope or manually. In total, 22 (0.66%) of the included horses either died or were euthanized due to anaesthesia related complications.
Death/euthanasia were related to fracture during recovery (n=7, 32 %), failure to stand in the recovery due to myopathy or neuropathy (n=7, 32%), cardiac arrest (n=5, 23%) and myelopathy (n=3, 13%).

Of the 3357 horses, 379 underwent acute abdominal surgery. Thirteen (3.43%) of these died or were euthanized due to anaesthesia related complications.
When excluding horses operated for colic the mortality rate was 0.30 %.

When excluding all horses undergoing acute surgery the mortality rate was 0.23 %.

Two of 139 foals under 1 month of age died of cardiac arrest, leading to 1.4 % mortality rate in this age group.

The overall mortality rate of 0.66 % including colic horses and 0.30 % excluding colic horses is lower than reported in the CEPEF study. Colic and age under 1 month carries a higher risk of fatal complications.

References

Johnston et al. (2002). Vet Anaesth Analg 29; 159–170.

Wednesday 2nd September | Room B1 | 16:45−17:00

O10-4 The effects of xylazine, dexmedetomidine and clonidine on normal and interleukin-1 conditioned equine articular cartilage explants

○Khursheed Mama[1], Jeff J Ullmer[1], Melissa King[2], Casey Thompson[2], David D Frisbie[2]
[1)]Colorado State University, [2)]Gail Holmes Orthopaedic Research Center, [3)]Note Jeff Ullmer should be first author even though Khursheed Mama is presenting author

Intra-articular alpha-2-agonists are used for peri-arthroscopic pain control; knowledge of their effects on articular cartilage is limited. In vitro effects of 3 alpha-2-agonists on normal and recombinant equine interleukin-1beta (reIL-1b) conditioned articular cartilage were studied.

Cartilage explants from stifles of 4 horses were cultured for 8 days following a 25-minute exposure to Plasmalyte (control), 0.5%-xylazine, 0.005%-dexmedetomidine, 0.0075%-clonidine and the same + 10ng ml-1 reIL-1b. Glycosaminoglycan content (GAG) released into media over 8 days and retained in explants (day 8) was evaluated (dimethylmethylene blue assay). DNA content in explants was quantified on day 8 (Hoechst 33258 assay). Data (mean +/- SEM) were analyzed using a mixed model ANOVA; individual comparisons with Least Squares Means. $P \leq 0.05$

The model performed as expected decreasing explant GAG for reIL-1b vs.non-reIL-1b (55 +/- 8.5 vs. 102 +/- 8.5). Explant GAG was significantly higher with xylazine (173 +/- 13) compared to control (34 +/- 13), clonidine (47 +/- 12) and dexmedetomidine (61 +/- 12) independent of IL-1b. Xylazine significantly decreased DNA content in explants compared to other treatments independent of IL-1b. Media GAG varied over time and with exposure to IL-1b and xylazine.
Interestingly xylazine effects differed compared to clonidine and dexmedetomidine. Consistent with prior xylazine dose-response data1 it appears that viable chondrocytes are more anabolically active suggesting a stress response given the loss of viable chondrocytes measured via the DNA content. The clinical significance remains to be elucidated but caution is warranted in the IA use of xylazine at concentrations studied.
Acknowledgements Authors thank Christine Battaglia and Nate Jensrud for their technical expertise.
1 Ullmer J, Mama KR, Lee C, Frisbie D. The effects of xylazine on normal and interleukin-1 conditioned equine articular cartilage explants. Proceedings (web based) 38th Annual Meeting American College of Veterinary Anesthesia and Analgesia, San Diego, CA, September 2013

Session 11 Large animal analgesia

Wednesday 2nd September | Room B1 | 17:00−17:15

O11-1 Detomidine prolonged analgesia for colic in horses

○Claire BL Scicluna
Equ'Institut

Potent, long analgesic effects and "ileus risk", make the use of detomidine in colic horses still controversial despite appreciated benefits in practice.

To propose safe prolonged analgesia protocols, gut motility and analgesia duration with detomidine were studied in 20 adult colic horses treated with 0.01 mg/kg IV (t0), prior to a random top up of 0.02 mg/kg detomidine IV (t90, 10 horses, PA1) or 0.04 mg/kg sublingual detomidine gel (t45, 10 horses, PA2). HR, sedation (0-2), muscle relaxation, gut sounds (0-3) were recorded (t0-t310) and analysed ($p<0.05$ significant).

Left colon displacement (40% PA1, 60% PA2) and colon impaction (25% PA1 and PA2) were mostly observed. Good analgesia (score>1) was provided for 220 mins in PA1 and 300 mins in PA2. IV detomidine top up induced faster (5 vs 25 mins), stronger (-50 vs -30%), but no longer (120 mins) bradycardia than gel. Initial IV detomidine bolus induced abdominal silence (6 horses/PA1, 4 horses/PA2), lasted 10 mins (t10-t20) and was repeatable (t45/PA1). Gel top up induced silence in 1 horse (t75) and decreased transit for15 mins (4/10 horses, t75-t90). Gut sounds returned to normal at t200 in both groups. PA1 muscle relaxation ended t80, then prolonged to t200. PA2 horses started recovering t140. All cases showed abdominal relaxation (rectal palpation) but no adverse effects.

Detomidine prolonged analgesia protocols with 0.01 mg/kg IV bolus + 0.02mg/kg IV or 0.04 mg/kg sublingual gel should be considered as safe 220 or 300 mins analgesia protocols in colic horses with LCD or CI when close medical care.

Wednesday 2nd September | Room B1 | 17:15−17:30

O11-2 A novel approach for the internal and lateral auricular branch of the facial nerve and the caudal and great auricular nerve block in horses: an anatomical study

○Ilaria Cerasoli, Pieter Cornillie, Frank Gasthuys, Stijn Schauvliege
Gent University

Local anaesthesia of the auricular region could be useful in equine practice. A ring block at the base of the ear rarely results in satisfactory desensitization of the area. Previously described techniques (McCoy et al. 2007, Sommerauer et al. 2013) required injection close to the parotid gland.

Anatomical dissection of the innervation of both ears was performed on 19 horse cadavers. In 17 cases, methylene blue (1:1 sterile water) had been injected on either the left (7) or right (10) side of the head, in lateral recumbency: a total amount of 10 mL for the internal auricular branch (IAB), lateral auricular branch (LAB) of the facial nerve and the caudal auricular nerve (CAN) (caudal base of ear) and 2 mL for the great auricular nerve (GAN) block (rostral margin of atlas wing, subcutaneously). In two horses, the injections had been performed on both sides of the head. Following dissection, the accuracy of dye deposition was assessed, as well as occurrence of intravascular, intraneural or intraparotid injection.

Inter- and intra-individual (in 6/19 horses) differences were found in the anatomy of the GAN: 30/38 (79%) divided into 2 or more branches rostrally to the rostral margin of the atlas wing, and 8/38 (21%) caudally to this margin. Further distribution of the nerves on the pinna was unpredictable. The anatomy of the IAB, LAB and CAN showed no variation. Staining was successful in 18/21 (85%) cases for the IAB; in 21/21 (100%) cases for the LAB and CAN and in 20/21 (95%) cases for the GAN. Failure was observed in horses with abundant peri-auricular fat or when the needle was oriented too much medially. No intravascular, intra-parotid or intra-neural injections were detected.

This approach seems safe and suitable for blockade of the GAN, IAB, LAB and CAN of horses.

Wednesday 2nd September | Room B1 | 17:30–17:45

O11-3 Validation of the UNESP-Botucatu unidimensional composite pain scale for assessing postoperative pain in pigs

○Stelio P L Luna[1], Ana Lucélia Araújo[2], Pedro Isidro Nóbrega Neto[2], Flávia Augusta Oliveira[3], Juliana Tabarelli Brondani[1], Filipe Garcia Telles[1], Lilianne Marinho do Santos Azerêdo[2]

[1)]UNESP – Univ Estadual Paulista, Botucatu-SP, Brazil, [2)]Federal University of Campina Grande, UFCG, Patos, Paraiba, Brazil, [3)]Federal University of Goiás, UFG, Brazil

The development of species-specific pain scales is important to determine the requirement and effectiveness of analgesic treatment. This study aimed to evaluate pain behaviour and establish the validity and reliability of a scale to measure acute pain in 40 pigs undergoing castration performed under local anaesthesia. Behaviour was recorded by footage prior and after orchiectomy. The scale was constructed based on previous reports and the analysis of the footage. The edited footage was analysed by a gold standard and three blinded observers at the pre and postoperative periods, before and after rescue analgesia and 24 hours after castration. The footage was re-assessed one month after the first analysis. Refinement of the scale was performed by criterion validity (agreement) and item-total correlation using Spearman's coefficient. Based on factor analysis, a unidimensional scale was adopted. Cronbach's α coefficient was 0.82 after refinement, therefore the internal consistency was excellent. The correlation between the studied scale and the numerical rating, simple descriptive and visual analogue scales was high ($p = 0.000$). The increase and decrease in pain scores after castration and intervention analgesia, confirmed the construct validity and responsiveness respectively ($p < 0.001$). The inter- and intra-observer reliability ranged from moderate to good. The optimal cut-off point for rescue analgesia was >4 out of 18 (maximal score). Discriminatory ability was excellent according to the analysis of the area under the curve (0.972). The UNESP-Botucatu unidimensional pain scale to assess acute postoperative pain in pigs is valid, reliable and responsive.

Approved by the Institutional Animal Research Ethical Committee under the protocol number 189/2009.

Acknowledgements: FAPESP process 2010/08967-0; CNPq process 303937/2011-4 and CAPES for financial support

Wednesday 2nd September | Room B1 | 17:45–18:00

O11-4 Electroencephalographic responses of anaesthetised pigs to tail docking using clippers or cautery iron

○Nikki J Kells[1], Ngaio J Beausoleil[1], JP Chambers[1], Mhairi A Sutherland[2], Rebecca S Morrison[3], Craig B Johnson[1]

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Commercially, tail docking of pigs to reduce tail-biting behaviour is routinely performed without analgesia. The objective of this study was to compare the noxious effects of tail docking using clippers or cautery iron in pigs aged 2- and 20-days. Forty commercial white-line male piglets were randomly assigned to four groups (n=10 per group): tail docking using clippers at 2 days old, tail docking using clippers at 20 days old, tail docking using cautery at 2 days old, or tail docking using cautery at 20 days old. Pigs were anaesthetised using halothane in oxygen and maintained at a minimal plane of anaesthesia (PEHal=0.95–1.05%). Electroencephalogram (EEG) was recorded and following a five-minute baseline period, tails were docked and recording continued for a further 10 minutes. The EEG data were subjected to Fast Fourier transformation offline, yielding the summary variables median frequency (F50), 95% spectral edge frequency (F95) and total power (P_{TOT}). Differences in responses to tail docking over consecutive 15-second intervals were compared using a generalised linear model in SAS 9.3 (SAS Institute Inc., Cary, NC, USA). Pigs docked using clippers demonstrated significant increases in both F50 and F95 after docking ($p<0.05$) that were not observed in pigs docked using cautery. Compared to 2 day-olds, pigs docked at 20 days demonstrated significantly greater increases in F50 from 15–135 seconds and in F95 from 30–60 seconds after docking ($p<0.05$), along with a greater decrease in P_{TOT} from 30–60 seconds after docking ($P<0.05$). Furthermore, the elevation in F95 after docking using clippers was specific to 20-day-old pigs. These data suggest that tail docking using clippers is more acutely painful to pigs than tail docking using cautery, and that docking within the first days of birth may be less acutely painful than docking at a later age.

Wednesday 2nd September | Room D | 13:30–13:45

O12-1 Does pulse contour analysis reflect cardiovascular changes during controlled haemorrhage in anaesthetised piglets?

○Henning Andreas Haga, Joanna Raszplewicz, Susanna Solbak, Andreas Lervik, Birgit Ranheim
Norwegian University of Life Sciences

This study evaluates pulse index continuous cardiac output (PiCCO) in anaesthetised pigs during controlled hae morrhage.

Seven pigs (29 ± 2.9 kg) were enrolled. Ketamine 15 mg kg^{-1}, midazolam 1.0 mg kg^{-1} were injected intramuscularly and propofol 2.6 ± 0.9 mg kg^{-1} was given intravenously. Anaesthesia was maintained using propofol 8 mg kg^{-1} h^{-1}, ketamine 5 mg kg^{-1} h^{-1} and dexmedetomdine (n = 4) or fentanyl (n = 3) at 8 µg kg^{-1} h^{-1} or 100 µg kg^{-1} h^{-1} respectively. Ringer's acetate was administered at 10 ml kg^{-1} h^{-1}. Positive pressure ventilation was initiated at 20 breaths min^{-1} and V_T adjusted to maintain normocapnia. The femoral artery and external jugular vein were catheterized. Base line measurements were recorded 351 ± 11 minutes post induction including mean arterial blood pressure (MAP), pulse rate (PR) and cardiac output (Q) determined by transpulmonary thermodilution. Whole blood was aspirated within 10 minutes through the jugular venous catheter (equivalent to 1.95 % of bodyweight) and MAP, PR and Q were subsequently recorded. Systemic vascular resistance (SVR) was calculated from MAP and Q. During haemorrhage, the anaesthesia monitor estimated the cardiac output (Q_{PiCCO}), SVR (SVR_{PiCCO}) and stroke volume variation (SVV), once a minute, based on invasive blood pressure curve.

Linear regression and student t test were performed. During the haemorrhage Q (p = 0,0001), SVR (p=0.05) and SVR_{PiCCO} (p = 0.005) decreased; SVV increased (p = 0.03) and Q_{PiCCO} did not change significantly (p = 0.53). Post-haemorrhage Q_{PiCCO} and SVR_{PiCCO} differed (p = 0.01, p = 0.0033) from Q and SVR at base line.

During haemorrhage in anaesthetized piglets Q_{PiCCO} is not a good predictor for Q, SVR_{PiCCO} overestimates real changes while SVV indicates the presence of hypovolemia.

Acknowledgments: The project was financially supported by the Inspector of Veterinary Services Norwegian Armed Forces

Ethical approval: The study was approved by the Norwegian Laboratory Animal Research Authority, FOTS id7236

Wednesday 2nd September | Room D | 13:45–14:00

O12-2 Effect of two constant rate infusions of lidocaine on the minimum alveolar concentration (MAC) of isoflurane in commercial pigs

○Chiara De Caro Carella, Thomas W Riebold, Deidre Jones, Ronald E Mandsager
Oregon State University

Introduction: Previous studies describe the use of lidocaine as an adjunct to decrease MAC during general anesthesia with inhalant anesthetic agents in several species.

Methods: Six commercial swine, aged 74 ± 5.3 days, and weighting 31.7 ± 5.4 kg, were enrolled in a prospective randomized crossover study. After randomization to receive lidocaine at 50 µg/kg/min (CRI_{50}) or 200 µg/kg/min (CRI_{200}), pigs were anesthetized with isoflurane in oxygen administered by mask, then intubated and maintained with isoflurane on mechanical ventilation. Baseline MAC (MACb) was determined using supramaximal mechanical stimulus on a dewclaw of a hind limb. A loading dose of lidocaine (2 mg/kg) was then administered IV, followed by either CRI_{50} or CRI_{200}, and maintained for 30 minutes to allow achievement of steady state. MAC was then re-determined during lidocaine infusion. The study was repeated with the other infusion rate after a washout period of six days. Heart rate, direct arterial blood pressure, and body temperature were measured during the study. A linear statistical model was used to compare MACb and MAC under the two infusion rates, as well as to compare HR, SAP, DAP, and MAP. Statistical significance was set at a *p-value* of less than 0.05.

Results: Isoflurane MACb was 1.77% ± 0.34%, while MAC in pigs receiving CRI_{50} and CRI_{200} was significantly lower than MACb, 1.53% and 1.60% respectively. Reduction in MAC was 8.0% for CRI_{50} and 12% for CRI_{200}. No significant difference in MAC reduction was found between the two infusion rates. Cardiovascular variables and recovery time did not differ significantly between the two infusion rates at any time points.

Conclusion and clinical relevance: Lidocaine CRI safely decreases isoflurane requirements in a non dose-dependent fashion, indicating a possible ceiling effect in MAC sparing, without producing appreciable changes in cardiovascular variables and recovery time.

Wednesday 2nd September | Room D | 14:00−14:15

O12-3 Inhibition of kaolin-induced hyperalgesia by flunixin in piglets

○Olivier L. Levionnois[1], Torunn Fosse[2], Birgit Ranheim[2]
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Flunixin is used in several animal species and marketed for analgesia in swine at 2.2 mg/kg in several countries. However, little is known about its effective dose in piglets.
Thirty-two piglets (6-8 days old) were recruited and randomized to receive flunixin meglumine intravenously 4.4 (n=10, group HIGH) or 2.2 mg/kg (n=11, group MEDIUM), or saline (n=11, group CONTROL). Venous blood samples were obtained via a jugular catheter before, and at 10, 45 minutes, 2, 5, 8, 12, 16, 24, 34, and 50 hours after flunixin administration. Flunixin was detected and quantified in plasma using LC-MS/MS. A hand-held algometer with a head of 1 cm2 and cut-off value of 24.5 Newton was used to determine each piglets mechanical nociceptive threshold from both front feet. Pressure thresholds were determined before and after subcutaneous injection of kaolin (kao) in the left metacarpal area. Ten hours after kao, the treatment was administered and further pressure thresholds were determined at blood sampling time points between 2 and 50 hours. Pharmacokinetic and pharmacodynamic parameters were obtained using Phoenix (Pharsight inc.). A group effect on the change in pressure threshold after treatment was tested using a two-way ANOVA for repeated measures (Sigmaplot, Systat software inc.) with significance set at p = 0.05. A PKPD model describing the effect of flunixin on the mechanical nociceptive threshold was obtained based on the inhibition of an inhibitory indirect response model.
A two-compartmental PK model was used. A significant effect of flunixin was observed for both doses compared to control group, with 4.4 mg/kg showing the most relevant (6-10 Newton) and long-lasting effect (24 hours). The median IC_{50} was 6.78 and 2.63 mg/mL in groups MEDIUM and HIGH, respectively. The ED_{50} in this model was 6.6 mg/kg.
Flunixine exhibited antinociceptive effect on kaolin-induced inflammatory hyperalgesia in piglets.

Acknowledgements
The Study was partly funded by the Swiss National Science Foundation.

Wednesday 2nd September | Room D | 14:15−14:30

O12-4 Epidural administration of xylazine alone or in combination with tiletamine-zolazepam in pigs undergoing cryptorchidectomy

○Eduardo Gutierrez-Blanco[1], Carolina Peraza[1], Antonio Ortega-Pacheco[1], Jose Antonio Ibancovichi[3], Carlos Acevedo-Arcique[1], Alejandro Alzina-López[2]
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The aim of this study was to evaluate the effects of xylazine alone or in combination with tiletamine-zolazepam administered epidurally in pigs undergoing cryptorchidectomy.
Twenty-four adult healthy pigs (88 ± 9 kg) were included in a randomized, prospective, clinical trial. Animals were premedicated with azaperone IM (1 mg/kg) and anesthesia was induced with tiletamine-zolazepam IV (0.3 mg/kg). A lumbosacral epidural injection was administered with one of the two following treatments: Xylazine (XYL) (1 mg/kg, n=12), or the combination xylazine-tiletamine-zolazepam (XYLTZ) (1 mg/kg of XYL in combination with 1 mg/kg of TZ, n=12). Heart rate (HR), Respiratory rate (RR), saturation of hemoglobin in oxygen (SpO_2), mean arterial blood pressure (MAP) and rectal temperature (RT) were evaluated during cryptochidectomy. Onset and duration of epidural analgesia were evaluated using tail clamping. Data were analyzed using ANOVA ($P < 0.05$).
There were no significant differences among groups on HR, SpO_2, RR, MAP and RT. Onset of epidural analgesia was not different among XYL and XYLTZ (6.6 ± 1 and 6.9 ± 2 minutes, respectively). Duration of analgesia and time to standing were significantly longer in XYLTZ (386 ± 61 and 455 ± 69 minutes, respectively) than XYL (241 ± 16 and 317 ± 29 minutes, respectively).
Tiletamine-zolazepam prolonged the duration of analgesia and time to standing produced by xylazine when administered by the epidural route in pigs undergoing surgery.

Wednesday 2nd September | Room D | 14:30−14:45

O13-1 Determination of the minimum infusion rate of alfaxalone during its co-administration with fentanyl at 3 different doses by constant rate infusion intravenously in goats

○Brighton Tarisai Dzikiti, Patience S Ndawana, Jacques P Ferreira, Gareth Zeiler, Loveness Dzikiti
University of Pretoria

AbstractObjective: To determine the minimum infusion rate (MIR) of alfaxalone required to prevent purposeful movement of extremities in response to standardized noxious stimulation during its co-administration with fentanyl at 3 different doses by constant rate infusion (CRI) intravenously in goats.
Study Design: Blinded, randomized crossover, experimental
Animals: Eight goats; four does and four wethers
Methods: For induction of anaesthesia, a bolus of fentanyl was administered at 0.005 mg/kg (LFent), 0.015 mg/kg (MFent), or 0.03 mg/kg (HFent) followed by alfaxalone at 2.0 mg/kg. For maintenance, the goats received alfaxalone at an initial infusion rate of 9.6 mg/kg/hour and one of three fentanyl treatments: 0.005 mg/kg/hour(LFent), 0.015 mg/kg/hour (MFent) or 0.03 mg/kg/hour (HFent). The MIR of alfaxalone was determined during fentanyl CRI by testing for responses to stimulation (clamping on a digit with Vulsellum forceps) every 30 minutes. Some cardiopulmonary parameters were measured.
Results: The alfaxalone MIR median (range) was 6.7 (6.7 to 8.6), 2.9 (1.0 to 6.7) and 1.0 (1.0 to 4.8) mg/kg/hour during LFent, MFent and HFent respectively. Alfaxalone MIR was significantly lower during MFENT and HFENT compared to LFENT. Oxygen haemoglobin saturation and arterial oxygen partial pressure were significantly low 2 minutes into anaesthesia following all fentanyl treatments. Recovery from anaesthesia was severely affected by high doses of fentanyl with excitatory behavioural signs predominant for up to 2 hours post-administration following MFent and HFent.
Conclusions and Clinical Relevance: Fentanyl reduces alfaxalone MIR in goats in a dose-dependent manner. Immediate oxygen supplementation after induction of general anaesthesia is recommended to prevent hypoxaemia. Doses of fentanyl equal to or greater than 0.015 mg/kg/hour tend to be associated with severe excitatory behaviour and should be avoided when fentanyl is administered to goats.

Wednesday 2nd September | Room D | 14:45−15:00

O13-2 Maternal and fetal effects of an infusion of Dexmedetomidine in anesthetized pregnant ewes.

○Mauricio Alberto Loria Lepiz[1], Rebecca S Sayre[1], Onkar Sawant[1,2], James Barr[1], Pashmakova Medora[1], Kevin Washburn[1], Shannon Washburn[1]
[1)]College of Veterinary Medicine, Texas A&M University, [2)]Cole Eye Institute, Cleveland Clinic

Alpha 2 adrenergic agonist are widely use in anesthesia and intensive care (Chrysostomou & Smith, 2008). They are known by their remarkable cardiovascular effect (Bloor et al. 1992). However, the information regarding maternal and fetal cardiovascular effects of dexmedetomidine is scarce (Souza et al. 2005).
Eleven pregnant ewes aged 2-5 years, with pregnancies between 114 and 118 days and mean body weight of 79.18 ± 4.12 kg were utilized. Ewes were anesthetized with Propofol 3 mg/kg IV and maintained with Sevoflurane in oxygen. Normocapnia and temperature were maintained. Ewes and fetuses were instrumented with arterial and venous catheters to measure cardiovascular variables and blood gases. Additionally, a thermodilution, pulmonary arterial catheter were placed in the ewes to measure cardiac output and take mixed blood samples. Baseline measurements were taken with end tidal sevoflurane stabilized at 3.4%. Then a constant rate infusion of Dexmedetomidine started at 2 $\mu g\ kg^{-1}hr^{-1}$ IV for 90 minutes, without loading dose. Cardiovascular and blood gases values were compared using repeated measure one-way ANOVA (significance level $p< 0.05$) at baseline, 30, 60 and 90 minutes.
With the infusion of Dexmedetomidine, maternal systemic vascular resistance, blood pressure and heart rate decreased to approximately 30% of their baseline values. Cardiac output, normoxia and acid base status remained unchanged. Pulmonary arterial pressure, pulmonary vascular resistance and stroke volume increased about 27%, 65% and 27%, respectively. Uterine blood flow decreased by 38%. Fetal cardiovascular effect were minimal and decreased arterial partial pressure of oxygen by 15% was observed.
In conclusion, maternal systemic cardiovascular stability is preserved during the administration of Dexmedetomdine to pregnant ewes under inhalant anesthesia. While it produces transient fetal blood gas changes, there are minimal to no existent fetal cardiovascular effects.

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Wednesday 2nd September | Room D | 15:00−15:15

O13-3 Pharmacokinetics and pharmacodynamics of a constant rate infusion of ketamine as a part of a balanced anaesthesia protocol in experimental calves

○Diego Rodrigo-Mocholi[1], Mathias Devreese[2], Bonnie Valgaeren[3], Luc Duchateau[4], Siska Croubels[2], Bart Pardon[3], Frank Gasthuys[1], Stijn Schauvliege[1]

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Our aim was to study the pharmacokinetics and pharmacodynamics of a CRI of ketamine during long-term balanced anaesthesia for an intestinal loop experiment in calves (approval ethical commission no. EC2011/024).

Sixteen calves (106.75 ± 25.18 kg of BWT) were premedicated with xylazine (0.2 mg kg^{-1} intramuscularly). Xylazine (0.02 mg kg^{-1}) and morphine (0.1 mg kg^{-1}) were administered epidurally and anaesthesia was induced with ketamine (2 mg kg^{-1} intravenously). In group S (n = 6), anaesthesia was maintained with isoflurane in oxygen only. In group K (n = 10), a CRI of ketamine was additionally administered (1 mg kg^{-1} h^{-1}) from 120 minutes after induction onwards. Monitored values were recorded every 10 minutes [heart rate (electrocardiography), arterial saturation (pulse oximetry), end-tidal CO_2 (capnography), isoflurane concentrations, inspired fraction of oxygen, body temperature, arterial blood pressure, packed cell volume and arterial blood gas values]. Anaesthetic depth was adjusted according to a flow-chart. Blood samples were taken at predetermined times throughout anaesthesia. Ketamine concentrations were quantified using liquid chromatography-tandem mass spectrometry. For statistical analysis, a mixed model was fitted with time, treatment and their interaction as categorical fixed effects and animal as random effect. A mixed model was also used to examine the influence of the ketamine plasma concentration on the isoflurane requirements.

The inspired and end-tidal concentrations of isoflurane were significantly lower in K (0.87 ± 0.08; 0.85 ± 0.07) compared to S (1.18 ± 0.07; 1.12 ± 0.08). An increase in ketamine concentrations significantly decreased the isoflurane requirements (p = 0.0014). No other significant differences were found. The PK values before the CRI were: mean half-life 0.74 ± 0.37 h, volume of distribution 1.64 ± 1.02 L kg^{-1} and clearance 1.56 ± 0.88 L h^{-1} kg^{-1}.

The CRI of ketamine (1 mg kg^{-1} h^{-1}) reduced the isoflurane requirements during long- term balanced anaesthesia in experimental calves.

Wednesday 2nd September | Room D | 15:15−15:30

O13-4 Anesthetic and cardio-respiratory effects of intravenous induction dose of alfaxalone in calves.

○Sayed F. H. El-Hawari[1], Yusuke Endo[2], Jun Tamura[3], Chika Higuchi[4], Kenjiro Miyoshi[5], Tadashi Sano[6], Suzuki Kazuyuki[7], Kazuto Yamashita[8]

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This study aimed to assess the anesthetic and cardio-respiratory effects of intravenous (IV) induction dose of alfaxalone in calves.

Six calves (5 males, one female, 169 ± 36 kg) were anesthetized with an IV administration of alfaxalone and orotracheally intubated. All the calves were allowed to breathe room air. Neuro-depressive effects (behavior changes and subjective scores ranged from 0 to 19) and cardio-respiratory parameters [rectal temperature, heart rate (HR), respiratory rate (RR), direct arterial blood pressure (ABP), partial pressures of carbon dioxide ($PaCO_2$) and oxygen (PaO_2) were evaluated before (baseline) and at 5, 10, 15, 20, 30, 45, and 60 minutes after starting IV alfaxalone. Data were analyzed using the Wilcoxon signed-rank test (P< 0.05).

All calves progressed to lateral recumbency at 65.5 ± 14.4 seconds and were intubated at 5.0 ± 1.4 minutes after starting IV alfaxalone. The IV doses of alfaxalone required to achieve lateral recumbency and intubation were 1.3 ± 0.2 and 2.3 ± 0.7 mg/kg, respectively. The intubation and lateral recumbency were maintained for 7.5 ± 1.5 and 21.4 ± 2.7 minutes, respectively. The calves stood at 34.1 ± 7.3 minutes after starting IV alfaxalone. The neuro-depression scores were significantly increased from 5 to 20 minutes and peaked at 5 minutes after starting IV alfaxalone (median 14.5, range 9-18). Tachycardia (HR 166 ± 47 bpm), hypertension (mean ABP 147 ± 8 mmHg), and hypoxia (PaO_2 42.8 ± 10.2 mmHg) were observed within 5 minutes and recovered to baseline values until 15 to 30 minutes after starting IV alfaxalone injection. During the early period of the recovery from anesthesia, all calves showed muscular tremor and paddling.

The IV induction dose of alfaxalone (2.3 ± 0.7 mg/kg) provided a rapid induction of anesthesia but produced undesirable effects in the early period of recovery in calves.

Wednesday 2nd September | Room D | 16:00−16:15

O14-1 A dose ranging study evaluating the pharmacodynamics of RD0327 as an anaesthetic and sedative in rabbits after intramuscular administration.

○Wendy Goodwin[1], Kirby Pasloske[2]
[1)]University of Queensland, [2)]Jurox Pty Ltd, Rutherford NSW 2320 Australia

The study aim was to characterise the pharmacodynamics of RD0327, alfaxalone in HPCD with preservative, as an anaesthetic and sedative after intramuscular (IM) administration at 3 different doses in NZ White Rabbits.

Six intact, male rabbits received IM saline and IM RD0327 at 6, 8 and 10 mg kg^{-1} with at least a day washout between treatments. Monitored physiological variables included HR, fR, temperature, SpO2%, $ETCO^2$ and NIBP. One researcher was blinded to treatment and described the response to injection and scored the quality of anaesthesia or sedation using a visual analogue scale (VAS). Key anaesthetic and sedation event times were recorded and a VAS used to assess injections sites for pain, swelling and redness 1 and 24 hours post-injection.

Rabbits that were not anaesthetized after RD0327 all became sedated and the quality judged to be 'good'. Physiological variables were within clinically acceptable ranges and no apnea was observed. Results (median and range) are presented in Table 1:

All rabbits reacted to IM saline (6/6) and there were 13 reactions (13/18) to the IM RD0327. VAS injection site scores were unremarkable and similar between the saline and RD0327 groups.

IM RD037 at 6 mg kg^{-1} produced acceptable sedation in all rabbits. A dose of at least 8 mg kg^{-1} is required to produce anaesthesia.

Table 1: Number or rabbits anaesthetized, anaesthetic/sedation times and anaesthesia VAS scores after IM RD037 administration. Data expressed as median (range).

	Dose IM (mg kg^{-1})		
	6	8	10
Anaesthesia^	0/6	1/6	4/6
Anaesthetic duration* (min)	-	21.6	21.3 (18.1-22.8)
Sedation duration#(min)	36.4(31.6-53.9)	46.5(31.4-57.7)	82.8(79.6-85.9)
Lateral (min)	4.3(2.8-6.1)	4.1(1.8-4.8)	3.2(2-4.4)
Sternal (min)	40.7(32.7-56.7)	48.5(35.4-61.8)	59.5(43.1-90.4)
Moving (min)	41.4 (34.2-66.2)	60 (41.4-69)	83.4(51.8-120.1)
VAS induction (mm)	-	82	78(61-85)
VAS anaesthesia (mm)	-	90	87(84-91)
VAS recovery (mm)	-	96	92(88-93)

^yes if intubation successful; * time from intubation to extubation; #time from lateral to sternal recumbency

Wednesday 2nd September | Room D | 16:15−16:30

O14-2 A dose ranging study evaluating the pharmacodynamics of RD0327 as an anaesthetic in rabbits after intravenous administration.

○Wendy Goodwin[1], Kirby Pasloske[2]
[1)]University of Queensland, [2)]Jurox Pty Ltd, Rutherford NSW 2320 Australia

The aim of the study was to characterise the pharmacodynamics of formulation RD0327, alfaxalone in HPCD with preservative, as an anaesthetic after intravenous (IV) administration at 3 different dosages in NZ White Rabbits.

Seven, intact, male rabbits received IV saline as a control (6 doses) and RD0327 administered IV as single dose at 3 (6 doses), 4 (8 doses) and 5 mg kg^{-1}(7 doses). Monitored physiological variables included HR, fR, temperature, SpO_2%, $ETCO_2$ (if intubated) and NIBP. One researcher was blinded to RD0327 treatment and described the response to the injection and scored the quality of anaesthetic induction (if achieved), anaesthetic period and recovery using a visual analogue scale (VAS). The time of key anaesthetic events from the end of RD0327 administration until recovery were recorded.

All rabbits survived the study and no morbidity or major adverse events were observed. Physiological variables were within clinically acceptable ranges. Results (median and range) are presented in Table 1.

There were 7 reactions to 21 doses of IV RD0327 characterised by ear twitching, scratching and head shaking. No pathology at injection sites was observed 1 and 24 hours post-dosing.

IV RD0327 at 5 mg kg^{-1} allowed for endotracheal intubation in all rabbits. The quality and duration of the anaesthetic period was clinically acceptable.

Table 1: Intubation, anaesthetic times and VAS scores in rabbits administered IV RD0327. Data expressed as median (range).

	Dose IV (mg kg^{-1})		
	3	4	5
No. of successful intubations	2/6	3/8	7/7
Time of 1st breath after end of injection (min)	0.5(0.1-1.3)	1(0-1.5)	0.9(0.1-1.2)
Anaesthetic duration* (min)	9(6.9-11.2)	5.6(3.7-6.2)	9.9(6.7-16)
Time to sternal (min)	13.2(11.6-18.7)	14(9.6-25)	23.8(18.3-30.6)
Time to moving (min)	16.9(13.2-24.3)	25(16.7-39)	33.8(30.4-43)
VAS induction (mm)	85(75-94)	92(74-93)	91(58-92)
VAS anaesthesia (mm)	87(81-93)	86(77-89)	88(64-97)
VAS recovery (mm)	94(91-97)	92(91-99)	93(87-96)

* time from intubation to extubation

Wednesday 2nd September | Room D | 16:30–16:45

O14-3 Effect of different doses of atipamezole on reversal of medetomidine-induced decrease in tear flow in rats

○Teppei Kanda, Manami Gotoh, Ayumi Makino, Kayo Furumoto, Noritaka Maeta, Katsutoshi Tamura, Toshinori Furukawa
Kurashiki University of Science and the Arts

We aimed to investigate the effect of different doses of atipamezole in reversing the medetomidine-induced decrease in tear flow in rats.
Thirty-two Wistar/ST rats were divided equally into a control group and three experimental groups. Each rat received intramuscular injection of 200 μg kg^{-1} medetomidine, followed by intramuscular injection of 0.32 mL kg^{-1} physiological saline (control group) or 400, 800, or 1600 μg kg^{-1} atipamezole (experimental groups) after 15 minutes.
The phenol red thread tear test value (PRTTT) was measured sequentially post-administration. Data were analyzed using two-way ANOVA and Bonferroni's multiple comparison tests ($p < 0.05$).
In all groups, PRTTT values were significantly decreased at 5, 10, and 15 minutes after medetomidine administration. 800 or 1600 μg kg^{-1} atipamezole reversed the decrease within 5 minutes of administration (3.3 ± 0.4 to 10.3 ± 1.4 and 2.7 ± 0.3 to 13.5 ± 0.9 mm/15 s; mean ± SEM, respectively). The PRTTT values at 5 to 105 minutes after atipamezole injection were not significantly different from those before medetomidine injection (14.2 ± 0.9 and 14.3 ± 0.9 mm/15 s for 800 and 1600 μg kg^{-1}, respectively). PRTTT values in both groups never exceeded the baseline. While 400 μg kg^{-1} atipamezole also reversed the decrease in PRTTT within 5 minutes of administration, the value was still significantly lower than that at baseline. In the control group, significantly lowered PRTTT values persisted for 105 minutes after saline treatment.
Atipamezole reversed medetomidine-induced decrease in tear flow. A higher dose of atipamezole did not increase PRTTT value above baseline, indicating that atipamezole antagonizes the effect of medetomidine but does not increase tear flow by itself. The dose of atipamezole needed to reverse medetomidine-induced decrease in tear flow was similar to that required for reversal of sedation, which was four times the dose of medetomidine.

Wednesday 2nd September | Room D | 16:45–17:00

O14-4 Impact of an effective recruitment maneuver and positive end-expiratory pressure in lung structure, function and inflammation in healthy rats under anesthesia

○Mariana B. de Abreu[1], Luciana M. Camilo[2], Mariana B Ávila[1], Ricardo G. de Almeida[2,3], Luís Felipe Cruz[1], Ludmilla D. Teixeira[1], Bruno L Diaz[1], Walter A Zin[1], Alysson R. Carvalho[1,3]
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Recruitment maneuver (RM) aims to improve gas exchange through maximum recruitment of alveolar units, providing a homogeneous ventilation of the lung parenchyma. However, RM is not often used during general anesthesia. The objective of the study was to evaluate the effects of two RM protocols on alveolar stability, gas exchange and inflammation.
The study was approved by Animal Ethics Committee. Thirty male Wistar rats (250–350 g) were anesthetized with ketamine 100 mg/kg and midazolam 5 mg/kg and mechanically ventilated in volume-controlled mode (tidal volume: 6 mL/kg, PEEP: 2 cmH2O, respiratory rate: 90 bpm, I:E ratio: 1:2 and FiO2: 0.5). Rats were randomized into: RM8 group (RM performed by sequentially increasing PEEP to 3, 6, 7 and 8 cmH2O, 30 s/step) and RM15 group (RM performed with 15 cmH2O of PEEP during 5 consecutive breaths) followed by two hours of ventilation with PEEP set at 3 (low PEEP) or 7 cmH2O (high PEEP). Respiratory system airflow and arterial blood pressure were continuously monitored. Volume (V) and Elastance of respiratory system (Ers) were calculated. Arterial gases were analyzed at the beginning and after 2 hours of ventilation. IL-1β and IL-6 were evaluated in lung tissue by ELISA technique. Statistics Analysis was performed by two-way ANOVA and Bonferroni tests (mean ± SD).
PaO2/FIO2 ratio was significantly higher in RM15 groups compared to RM8. Ers was significantly lower in RM15 groups (2.8 ± 0.3 vs 4.2 ± 0.8 cmH2O/mL). Progressive increase in Ers was observed in all groups. In RM8 group, higher rate of increase was observed at low PEEP compared to high PEEP (0.010 ± 0.009 vs -0.001 ± 0.008 cmH2O/mL/min, respectively). IL-1β lung tissue concentration was lower in RM15 groups (RM8_low: 6.74 ± 1.2; RM8_high: 6.88 ± 1.4; RM15_low: 1.34 ± 0.5; RM15_high: 1.74 ± 0.46)
RM15 resulted in significate better oxygenation associated with a reduction in Ers and IL-1β expression on lung tissue in healthy rats.

Wednesday 2nd September | Room D | 17:00−17:15

O15-1 MAC determination with electrical stimulus: defining the lower supramaximal current intensity

○Joao Soares[1], Marivaldo R Figueiró[2], Fabio O Ascoli[3], Stephen Werre[1], Ignacio A Goméz de Segura[4]

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Objective: The aim of this study was to establish the lowest current that provides supramaximal stimulation during isoflurane minimum alveolar concentration (MAC) determination in dogs.
Study design: Experimental prospective randomized controlled trial.
Subjects: Six mixed-bred adult female dogs.
Materials and Methods: Isoflurane MAC (MAC_{ISO})was determined in each dog with the tail clamp ($MAC_{TAILCLAMP}$), and 3 different electrical currents (10, 30 and 50 mA) in three different anatomic sites (thoracic limb, pelvic limb and tail). Each MAC_{ISO}achieved with electrical stimulation was compared with $MAC_{TAILCLAMP}$ using a mixed-model ANOVA followed by Dunnett's procedure for multiple comparisons. The effect of current intensity and anatomic site on MAC_{ISO} was tested by a mixed-model ANOVA followed by Tukey's test for multiple comparisons. In addition, Bland-Altman plots were used to assess the agreement between $MAC_{TAILCLAMP}$ and each MAC_{ISO} derived from electrical stimulation. ($P<0.05$)
Results: MAC_{ISO} achieved with 30 mA was not different from 50 mA independently of the anatomic site, and 10 mA provided lower MAC_{ISO} when applied to the tail and thoracic limb when compared with 30 and 50 mA. The currents of 30 and 50 mA provided MAC_{ISO} comparable to $MAC_{TAILCLAMP}$, while 10 mA only achieved the same result when applied to the pelvic limb. MAC_{ISO} determined with 30 mA presented the best agreement with $MAC_{TAILCLAMP}$ independently of the anatomic site.
Conclusions: Currents of 30 and 50 mA provided supramaximal stimulation during MAC_{ISO} determination in the dog. However, 30 mA was considered the most appropriate current to be used in MAC studies in dogs because it was the lowest supramaximal stimuli with consistent results in the tail, thoracic and pelvic limb, as well as, produced comparable results to $MAC_{TAILCLAMP}$.

Wednesday 2nd September | Room D | 17:15−17:30

O15-2 The effect of ketamine on the minimum infusion rate of propofol preventing motor movement in dogs

○Rachel A. Reed, M. Reza Seddighi, Agricola Odoi, Sherry K. Cox, Christine M. Egger, Thomas J. Doherty

University of Tennessee College of Veterinary Medicine

Objective: To determine the minimum infusion rate (MIR_{NM}) of propofol required to prevent movement in response to a noxious stimulus in dogs anesthetized with either propofol alone or propofol in combination with one of two constant rate infusions (CRI) of ketamine.

Animals: 6 male beagles

Procedure: Dogs were anesthetized on three occasions, at weekly intervals, and were given one of three different treatments on each occasion. Treatments were administered as a loading dose (LD) and an initial propofol CRI as follows: Treatment P, propofol 6 mg/kg LD and 0.45 mg/kg/min CRI; Treatment PLDK, propofol 5 mg/kg LD and 0.35 mg/kg/min CRI combined with ketamine 2mg/kg LD and 25 μg/kg/min CRI; Treatment PHDK, propofol 4 mg/kg LD and 0.3 mg/kg/min CRI combined with ketamine 3 mg/kg LD and 50 μg/kg/min CRI. After 60 minutes, MIR_{NM} determination was initiated using a noxious stimulus (50V, 50Hz, 10 msec). Any motor movement in response to stimulation was considered to be a positive response; conversely, absence of motor movement was considered to be a negative response. If the response to stimulation was positive, the propofol CRI was increased by 0.025 mg/kg/min. If the response to stimulation was negative the propofol CRI was decreased by 0.025 mg/kg/min. MIR_{NM} was determined in duplicate. Statistical analysis was performed using a generalized linear mixed model.

Results:
The propofol MIR_{NM} was 0.76 ± 0.1, 0.60 ± 0.1, and 0.41 ± 0.1 mg/kg/min for treatments P, PLDK, and PHDK, respectively. Treatments PLDK and PHDK resulted in significant ($P = 0.045$ and $P = 0.032$, respectively) decreases in propofol MIR_{NM} of 27 ± 10 % and 30 ± 10%, respectively.

Conclusions and Clinical Relevance:
Ketamine, at the doses studied, significantly decreased the MIR_{NM} of propofol in dogs.

Wednesday 2nd September | Room D | 17:30−17:45

O15-3 Electrocardiograph profile in prolong inhalation anaesthesia in Nigerian indigenous dogs.

○Emmanuella A. O Sogebi[1], Adamu Z Hassan[2], Adebayo I Rasaki[3], John O Olukunle[1]

[1)]Federal University of Agriculture, Abeokuta, [2)]Ahmadu Bello University, Zaria, Kaduna, [3)]Federal Medical Center, Abeokuta, Ogun

Twenty Nigerian indigenous dogs,aged between two and three years with average weight of 12.0 kg were grouped into two (A and B) by simple randomization. They were prepared for anaesthesia and connected to a 5-lead multi-parameter patient monitor (GMI®), monitoring oxygen saturation, heart and respiratory rates, rectal temperature and non-invasive blood pressure. Venous access was secured and 0.9% normal saline administered at a maintenance flow rate of 60ml/kg/day. Tracheae were intubated and anaesthesia maintained with 0.5% halothane (group A) and 1.5% isoflurane (group B) in 2liters/minute oxygen respectively with the animals breathing spontaneously. The readings were taken once prior to induction of anaesthesia (control) and every 30 minutes thereafter for six hours during anaesthesia. Physiological monitoring was undertaken throughout anaesthetic period. Data was analyzed using one-way ANOVA for repeated measures. Differences were considered significant at $p \leq 0.05$. All the ECG parameters measured were within normal range for the two drugs considered except for the values of S-T segment (sec) and P-waves (Duration)(sec) that were both low, 0.068 ± 0.013 and 0.064 ± 0.017 and 0.020 ± 0.001 and 0.020 ± 0.001 respectively for isoflurane and halothane respectively. However the values of P-waves (mV) and P-R intervals (sec) were significantly higher in group A, 0.193 ±0.136 and 0.046 ±0.01 compare to group B,0.193 ± 0.98 and 0.039 ± 0.01 respectively while the values of Q-T intervals (sec) and QRS complex (sec) were significantly higher in group B,0.123 ± 0.018 and 0.023 ± 0.008 compare to group A, 0.121 ± 0.023 and 0.021 ± 0.005.

Friday 4th September | Room A | 14:00−14:15

O16-1 Does the timing of propofol administration influence the cardiovascular and respiratory effects and the dose required for induction of anaesthesia in healthy dogs?

○Mathieu Clément Raillard[1], Emma J Love[2], Pamela J Murison[3]
[1)]Universität Bern, [2)]University of Bristol Veterinary School, [3)]Royal (Dick) School of Veterinary Studies, University of Edinburgh

Propofol may cause adverse effects. Pre-dosing has been shown in human anaesthesia to reduce propofol requirement. This randomized, controlled, blinded clinical study compared propofol pre-dosing with two rates of propofol administration on dose requirements and cardiorespiratory variables.

Thirty-two client-owned dogs (18 male, 13 female, one intersex, ASA I-II, age 6-144 months, weight 3.5-47.2 kg) were recruited. Acepromazine (0.025 mg kg^{-1}) and methadone (0.25 mg kg^{-1}) were administered intramuscularly as premedication. After 30 minutes, propofol pre-dosing group (PP) received a propofol bolus (0.5 mg kg^{-1}), control-propofol group (CP) received an equivalent volume of saline intravenously. The slow-induction group (SI) received propofol (1.3 mg kg^{-1} $minute^{-1}$) administered with a syringe driver. Two minutes later, propofol administration using a syringe driver (4 mg kg^{-1} $minute^{-1}$) was initiated in PP and CP groups and the same blinded anaesthetist entered the room. On reaching an adequate depth of anaesthesia, propofol administration was stopped. After endotracheal intubation, anaesthesia was maintained with a standardized protocol. Pulse rate (PR), respiratory rate (RR) and mean arterial pressure (MAP) were recorded before the administration of the first drug, 2 minutes later and 0, 2 and 5 minutes after intubation. Apnoea >30 seconds was recorded and treated. Sedation, quality of induction and endotracheal intubation were scored using simple descriptive scales. Data were compared using ANOVA, repeated measures ANOVA and chi-squared tests as appropriate and are presented as mean (standard deviation).

Propofol dose requirement was significantly lower in SI; 3.50 mg kg^{-1} (1.25) compared to PP [5.05 mg kg^{-1} (0.94)] and CP [4.76 mg kg^{-1} (0.59)] ($p = 0.003$ & 0.02 respectively). No statistically significant difference was found between groups in mean PR, RR, MAP or incidence of apnoea. Sedation score and quality of induction were similar between groups.

Slow administration of propofol reduced dose requirement, propofol pre-dosing did not.

Friday 4th September | Room A | 14:15−14:30

O16-2 Do Heat and Moisture Exchangers in the anaesthesia breathing circuit alter body temperature in dogs undergoing anaesthesia for MRI?

○latifa khenissi, Helen Binge, Gwen Covey-Grump, Joanna Murrell
University of bristol

Peri-operative hypothermia is common in dogs (Redondo et al., 2012) and use of external warming devices during MRI is problematic. This study investigated whether use of a Heat and Moisture Exchanger (HME) (INTERSURGICAL Ltd)altered body temperature in dogs weighing <10kg anaesthetised for MRI.

Thirty one client owned dogs, aged between 8 months and 11 years and weighing between 2.5 kg and 10 kg were randomly assigned to a treatment group (HME (n= 16) or no HME (n=15)). Premedication and induction agents were not standardised but general anaesthesia was maintained with isoflurane vaporised in 100% oxygen delivered using a T piece and a fresh gas flow of 600 ml/kg. Rectal temperature was measured before premedication (T1), after induction (T2), before moving to the MRI unit (T3), at the end of the MRI scan (T4). Ambient temperatures were measured in the induction room, outside the MRI lorry and in the MRI scanning room. Data were analysed using a GLM with T4 as the outcome variable and linear correlations were performed between T1, T2, T3 and T4 and parameters that predicted T4 were investigated.

Gender, age, bodyweight or breed distribution were not significantly different between groups. There were no significant differences in rectal temperature between groups at any time point (Table 1). Rectal temperature varied directly with ambient temperature in MRI scanning room and inversely with anaesthetic duration.

Using a HME did not alter body temperature in dogs weighing less than 10 kg undergoing an MRI.

Time point	HME	No HME
T1	38.29 (0.44)	38.26 (0.52)
T2	37.98 (0.59)	38.15 (0.53)
T3	37.79 (0.56)	37.92 (0.73
T4	36.26 (1.05)	36.24 (1.41)

Table 1: Mean (SD) rectal temperature of dogs undergoing anaesthesia for MRI

Friday 4th September | Room A | 14:30－14:45

O16-3 Investigation of a mini-fluid challenge based on a fractional change in pulse wave transit time to predict fluid responsiveness in mechanically ventilated anaesthetised dogs

○Hiroki Sano[1], Masako Fujiyama[1], Paul Wightman[1], Nick J. Cave[1], Mike A. Gieseg[2], Craig B. Johnson[1], Paul Chambers[1]

[1)]Institute of Veterinary, Animal and Biomedical Sciences, College of Sciences, Massey University, [2)]Veterinary Health Research NZ, Hamilton, New Zealand

Background. Mini-fluid challenge is a strategy to predict fluid responsiveness based on a fractional change in stroke volume (SVfc) after a small dose of fluid. Pulse wave transit time (PWTT), the time from the electrocardiogram R-wave to the rise point of the pulse oximeter wave, is inversely proportional to stroke volume. We investigated whether mini-fluid challenge based on a fractional change in PWTT (PWTTfc) predicts fluid responsiveness in mechanically ventilated anaesthetised dogs.

Methods. Twelve dogs were anaesthetised twice 4 weeks apart. These 24 anaesthetics were considered independent. After premedication with intramuscular acepromazine, anaesthesia was induced with propofol and maintained with isoflurane. The dogs were mechanically ventilated with constant settings. After 1, 2, and 3 mL kg^{-1} of colloid, $SVfc_{1, 2, 3}$ and $PWTTfc_{1, 2, 3}$ were measured. Fluid responsiveness was defined as SVfc ≥ 15% after 10 mL kg^{-1} colloid to separate dogs into responders and non-responders. Receiver operator characteristic (ROC) curves were generated for central venous pressure (CVP), $SVfc_{1, 2, 3}$ and $PWTTfc_{1, 2, 3}$ to determine cutoff values, and areas under the ROC curves were calculated and compared using a z test as previously described by Hanley and McNeil.

Results. Dogs responded on 14/24 occasions. The areas under the ROC curve for $SVfc_3$ [0.93, 95% confidence interval (CI): 0.79 to 1.00, p = 0.007]] and $PWTTfc_3$ (0.91, 95% CI: 0.80 to 1.00, p = 0.007) were significantly greater than CVP (0.69, 95% CI: 0.46 to 0.92). Cutoff values for $SVfc_3$ and $PWTTfc_3$ were 5.8% (sensitivity: 100%, specificity: 90%), and -2.5% (sensitivity: 86%, specificity: 90%) respectively. $SVfc_{1, 2}$ and $PWTTfc_{1, 2}$ were insignificant.

Conclusions. In mechanically ventilated anaesthetised dogs given a mini-fluid challenge of 3 mL kg^{-1} of colloid, PWTTfc could predict fluid responsiveness.

Friday 4th September | Room A | 14:45－15:00

O16-4 Success rate of the pulse pressure variation (PPV) in detecting fluid responsiveness in dogs undergoing high-risk abdominal surgeries.

○DrożdżyńskaMaja Justyna, Giacomo Stanzani, Ruby Chang, Ludovic Pelligand

Royal Veterinary College

Objectives: The aim of the study was to evaluate success rate of pulse pressure variation PPV≥13% in detecting fluid responsiveness (ΔSV ≥10%) in dogs undergoing high risk abdominal surgeries.

Study design: clinical, observational, prospective study.

Animals: 32 client-owned dogs undergoing abdominal surgeries with high risk of cardiovascular instability were included. Inclusion criteria were defined as: invasive arterial blood pressure measurement, mechanical ventilation in volume controlled mode with tidal volume of 10ml/kg in the absence of spontaneous respiration, regular cardiac rhythm, lack of underlying cardiac disease and stroke volume measurement by transoesophageal doppler (CardioQ).

Methods: Pulse pressure variation (PPV) was calculated manually from invasive BP trace displayed on the Datex monitor according to the following equation: (PPmax -PPmin)*100/(PPmax+PPmin)/2. Fluid challenge defined as 10ml/kg CSL bolus given over 10-15 min was performed when PPV≥ 13 and/or MAP<60 mmHg. Cardiovascular parameters like HR, MAP as well as PPV and SV were measured before and after each fluid intervention. The transoesophageal doppler probe was used in order to measure ΔSV after fluid challenge

Results: 32 dogs were included in the study where 225 observations of PPV, MAP, HR and SV were made. There were 50 fluid interventions performed in 20 patients. The success rate of PPV≥13% in detecting ≥10% increase in SV is 79%. It was calculated by taking into account only first fluid intervention of all dogs which received fluid challenge on the basis of PPV>13%.Out of all the interventions where fluid challenge resulted in ≥10% increase in SV 78.38% of cases where normotensive (MAP≥60 mmHg). Linear mixed effects model was employed to assess correlation between PPV and cardiovascular parameters while accounting for repeated measurements from the same dog. There was significant correlation between ΔMAP and ΔSV (p=0.048) and significant negative correlation between logPPV and MAP (p=0.039). In stable cardiovascular conditions (MAP≥ 60mmHg and PPV<13%) PPV was 8.32 ±3.1 (mean±SE) whereas in unstable cardiovascular conditions (PPV≥13% and/or MAP<60mmHg) PPV was 19.39±8.23 (mean ±SE).

Conclusions: PPV is an useful clinical tool to predict cardiovascular response to fluid challenge and to detect hypovolaemia before hypotension occurs or as a potential reason for hypotension.

Friday 4th September | Room A | 15:00−15:15

O17-1 Effect of perfusion index (PI) on agreement between pleth variability index (PVI) and pulse pressure variation (PPV) in ventilated dogs during anesthesia.

○Yusuke Endo[1], Taku Hirokawa[2], Jun Tamura[3], Chika Higuchi[4], Kenjiro Miyoshi[5], Tadashi Sano[6], Kazuto Yamashita[7]

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Perfusion index (PI) is a ratio of pulsatile blood flow to static blood in peripheral tissue. Pleth variability index (PVI) is a measure of PI that occurs during the respiratory cycle and non-invasive substitute for pulse pressure variation (PPV) to predict fluid responsiveness in human. The aim of this study was to evaluate the effect of PI on agreement between PVI and PPV in dogs.

PVI and PPV were measured simultaneously every 5 minutes during anesthesia for surgery in 17 owner-owned dogs (2 to 17-years-old, weighing 2.6 to 28.5kg) ventilated artificially. PPV was measured using a 22 or 24 gauge catheter placed into the dorsal pedal artery and pressure transducer connected to a hemodynamic monitoring device (PiCCO2, Pulsion). PVI and PI were measured using a pulse oximeter probe attached to tail and a pulse CO oximeter (Radical-7, Masimo). Data were analyzed using Pearson correlation and Bland-Altman analysis. $P<0.05$ was considered statistically significant.

Total of 331 sets of PI, PPV and PVI values were obtained from the dogs (8 to 40 sets from each dog). The average values ± standard deviations are 1.39 ± 0.94% (ranged from 0.11 to 3.90%) for PI, 17.3 ± 6.7% (ranged from 6 to 40%) for PPV, and 17.2 ± 7.0% (ranged from 6 to 41%) for PVI. Correlation coefficients and limits of agreement between PPV and PVI were (r)=0.858 and 0.20 ± 6.9% for overall sets, r=0.781 and 0.01 ± 7.5% for 68 sets of PI<0.5, r=0.942 and -1.39 ± 5.4% for 75 sets of 0.5≦PI<1.0, r=0.837 and 1.25 ± 5.9% for 118 sets of 1.0≦PI<2.0, r=0.520 and -0.04 ± 9.3% for 46 sets of 2.0≦PI<3.0, and r=0.826 and 0.51 ± 4.8% for 35 sets of 3.0≦PI, respectively.

This study demonstrated that PPV and PVI showed a significant correlation and moderate agreement in ventilated dogs during anesthesia. Good agreements between PPV and PI were demonstrated in the range of 0.5<PI<2.0 in dog.

Friday 4th September | Room A | 15:15−15:30

O17-2 Distribution of ventilation in conscious and anaesthetized beagle dogs in four recumbencies. An Electrical Impedance Tomography study

○Tamas D. Ambrisko, Johannes P. Schramel, Ulrike Auer, Yves Moens

University of Veterinary Medicine Vienna

The aim was to examine the effect of recumbency on distribution of ventilation in conscious and anaesthetized beagle dogs using Electrical Impedance Tomography (EIT).

Nine healthy beagle dogs aged 3.7 ± 1.7 (mean ± SD) years and weighed 16.3 ± 1.6 kg were used. Conscious dogs were positioned in right lateral recumbency (RLR) and equipped with 32 EIT electrodes around the thorax. Following five minutes of equilibration, two minutes of EIT recordings were made in each recumbency in the following order: RLR, dorsal (DR), left (LLR) and sternal (SR). The dogs were then positioned in RLR, premedicated (medetomidine 0.01, midazolam 0.1, butorphanol 0.1 mg kg^{-1} iv) and pre-oxygenated. Fifteen minutes later anaesthesia was induced with 1-2 mg kg^{-1} propofol iv and maintained with propofol infusion (0.1-0.2 mg kg^{-1} min^{-1} iv). After induction, the animals were intubated and allowed to breathe spontaneously (FiO_2 = 1). Recordings of EIT were performed again in four recumbencies similarly to conscious state. Centre of ventilation (COV) and global inhomogeneity (GI) index were calculated from the functional EIT images. Repeated-measures ANOVA was used for statistics ($p< 0.05$).

None of the variables changed in conscious state. During anaesthesia left-to-right COV was higher in SR (49.8 ± 2.9%) than in DR (46.8 ± 2.8%; right shift) and ventral-to-dorsal COV was higher in LLR (51.8 ± 1.1%) then in DR (49.8 ± 1.7%; dorsal shift).

Anaesthesia opposed the maintenance of distribution of ventilation. This can be related to loss of respiratory muscle tone and changes in thoracic shape. Changing position of thoraco-abdominal organs under the EIT belt should be considered as alternative explanation of these findings.

Session 18 Zoo animal anaesthesia

Friday 4th September | Room B1 | 14:00−14:15

O18-1 Physiologic and biochemical variables in captive tigers (*Panthera tigris*) immobilized with dexmedetomidine and ketamine or dexmedetomidine, midazolam, and ketamine

○Stuart C Clark-Price, Kara M Lascola, David J Schaeffer
University of Illinois College of Veterinary Medicine

Differences in physiologic and biochemical variables in captive tigers (*Panthera tigris*) immobilized with dexmedetomidine and ketamine or dexmedetomidine, midazolam, and ketamine were evaluated.
In a prospective, randomized study, 30 captive tigers were administered dexmedetomidine (25 μg/kg) and ketamine (3 mg/kg) (group DK) or dexmedetomidine (12.5 μg/kg), midazolam (0.1 mg/kg), and ketamine (group DMK) for immobilization. Degree of sedation was subjectively scored. Heart rate, SPO_2, and blood pressure were measured at 5 min intervals. Arterial pH, PO_2, PCO_2, glucose, K^+, and arterial and venous lactate were measured at 15 and 45 min after immobilization. An ANCOVA was used to compare heart rate, SPO_2, systolic, mean, and diastolic blood pressures. A generalized linear mixed model was used to compare PO_2, PCO_2, K^+, and lactate. Sedation scores and arterial and venous lactate specific time points were compared with a Student's T test.
There was no difference within or between groups at any time point for the measured variables. PO_2 was 73.2 ± 17.5 mm Hg and SPO_2 was 88.9 ± 10.8 %. Systolic, mean and diastolic blood pressures were 170.5 ± 48.4, 138.9 ± 41.8, and 121.8 ± 37.2 mm Hg respectively. Glucose was 195.5 ± 75.2 mg/dL. Venous lactate was higher than arterial lactate within groups at each time point. Seizure-like behavior was observed in 25% of tigers in group DK.
The addition of midazolam into a protocol for immobilization of tigers does not result in improvement of any of the measured variables but may prevent the development of seizure-like behavior.

Friday 4th September | Room B1 | 14:15−14:30

O18-2 Etorphine-acepromazine and medetomdine-ketamine anaesthetic protocols in impala (*Aepyceros melampus*)

○Carsten Groendahl[1], Kathryn L. Perrin[1], Peter Nissen[3], Mads F. Bertelsen[1]
[1)]Copenhagen Zoo, [3)]Copenhagen University, Rigshospitalet

Impala *(Aepyceros melampus)* are a notoriously difficult species to manage in captivity and anaesthesia is associated with a high risk of complications including mortality. Historically, opioid-based protocols have been commonly employed (BALL, 2007). More recently due to both safety concerns and the lack of easy availability of potent opioids in Europe, the use of medetomidine-ketamine combinations have been advocated (BUSH et al., 2004). No studies have compared these in-depth, so the aim of this study was to evaluate an opioid-based protocol with medetomidine-ketamine.
Ten female impala *(Aepyceros melampus)* were studied in a random cross-over design. Subjects received either protocol EA; 15 μg/kg etorphine (Captivon 98®, Wildlife Pharmaceuticals Ltd, White River, South Africa) and 0.15 mg/kg acepromazine (Calmivet Soloution injectable®, Vetoquinol, Lure, France), or protocol MK; 110 μg/kg medetomidine (Zalopine®, Orion Pharma Animal Health, Espoo, Finland and 4.3 mg/kg ketamine (Ketaminol Vet®, MSD Animal Health, AN Boxmeer, Holland) on day 1. Anaesthesia was repeated three days later with the alternative protocol. Subjective assessments of the quality of induction, muscle relaxation and recovery were made by a blinded observer. Objective monitoring included blood pressure, end tidal CO_2, regional tissue perfusion and blood gas analysis.
Significant differences were seen between the two protocols. EA had a quicker and more reliable induction and a faster recovery. Lower respiratory rates were observed with correspondingly higher $Paco_2$, however arterial oxygen saturation was the same or better. Blood pressures with EA were lower with higher heart rates, but regional perfusion was significantly higher.
In conclusion, EA provided superior induction, muscle relaxation and recovery. Arterial oxygenation and tissue perfusion were equal or higher than with the MK protocol despite the differences seen in other parameters.

Friday 4th September | Room B1 | 14:30−14:45

O18-3 General anesthesia with sevoflurane in an indo-pacifi bottlenose dolphin (*Tursiops aduncus*) for surgical treatment of subcutaneous abscess on the left flank

○Makio Yanagisawa[1], Jun Tamura[2], Yusuke Endo[2], Haruka Koga[1], Sayuri Kino[1], Yasuharu Izumisawa[3], Kazuto Yamashita[2]

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This is a case report of sevoflurane anesthesia in an indo-pacifi bottlenose dolphin (*Tursiops aduncus*).

The dolphin (female, 14-years-old, 159kg) with good pre-anesthetic physical status was anesthetized twice with 6-months interval for surgical treatment of subcutaneous abscess with ostitis associated with *Staphylococcus aureus* on the 4, 5 caudal vertebral processus transversus. The dolphin was premedicated with intramuscular midazolam (0.05mg/kg) and butorphanol (0.05mg/kg), anesthetized with intravenous propofol, maintained surgical anesthesia with sevoflurane in oxygen, and artificially ventilated at 6-10bpm with 25mmHg of peak inspiratory pressure (PIP). Lidocaine was infiltrated into the surgical area before the skin incision and saline was infused at 3ml/kg/hr during the anesthesia.

On the first occasion, total durations of anesthesia and surgery were 157 and 102min. A total 1.4 mg/kg of propofol was administered to achieve endotracheal intubation. End-tidal concentration of sevoflurane (ETSEV) ranged from 2.2-2.8% during surgery. Clinically relevant hypotension was not detected. End-tidal carbon dioxide ($ETCO_2$) and percutaneous oxygen saturation (SpO_2) ranged from 36-51mmHg and 77-87%. During recovery, the dolphin seemed to be awake but showed consistent respiratory failure. The dolphin gained adequate spontaneous respiration following intravenous administrations of flumazenil (0.015mg/kg) and doxapram (1mg/kg). The dolphin was extubated at 85min, and finally swam in pool at 106min after the cessation of sevoflurane.

On the second occasion, total durations of anesthesia and surgery, total dose of propofol, ETSEV during surgery were 224 and 159min, 3.7mg/kg including a leakage into the subcutaneous tissue, and 1.5-2.3%. Hypotension was observed and treated with dobutamine infusion (10 μg/kg/min). $ETCO_2$ and SpO_2 were ranged from 35-60mmHg and 87-99%. The dolphin gained spontaneous respiration following flumazenil (0.015mg/kg) and doxapram (1mg/kg), was extubated at 53min, and swam in pool at 63min after the cessation of sevoflurane.

We considered that the ventilator weaning during recovery was the most important challenge in the dolphin anesthesia.

Friday 4th September | Room B1 | 14:45−15:00

O18-4 The effect of dexmedetomidine on the duration of immobilization and selected physiological parameters in Telazol-anesthetized alpacas

○Reza Seddighi, Agricola Odoi, Thomas Doherty

College of Veterinary Medicine- University of Tennessee

The objectives of the study were to evaluate the effect of intramuscularly administered tiletamine-zolazepam (Telazol-TZ) with dexmedetomidine or saline, on the duration of immobilization, selected cardiorespiratory variables, and recovery quality in alpacas.

Using a Latin square design, five adult intact male alpacas were given each of five treatments intramuscularly with a 1-week washout: TZ (2 mg/kg) combined with dexmedetomidine at 5 μg/kg (D5), 10 μg/kg (D10), 15 μg/kg (D15), or 20 μg/kg (D20), or saline (control- C). Characteristics of anesthesia, recovery, and selected cardiorespiratory variables were recorded. Immobilization was assessed by clamping a claw at 5-minute intervals. Data were analyzed using a generalized linear mixed-model and are expressed as least squares mean ± SEM.

The duration of immobilization was longest for animals in treatment D15 (30.9 ± 5.9 minutes) and D20 (40.8 ± 5.9 minutes). Duration of lateral recumbency was significantly longer when animals received dexmedetomidine. The longest time (81.3 ± 10.4 minutes) to standing was observed in treatment D20. Four control animals moved in response to claw clamping at the five minute time point. Heart rate decreased in all dexmedetomidine treatment groups in comparison with the baseline values. Systolic arterial pressure for treatment D20 was significantly greater than for the control group. The PaO2 values for treatments D10, D15, and D20 were significantly less than the control treatment during the first 15 minutes ($P<0.05$); but there was no difference among treatments at 20 minutes. Three alpacas in the control treatment and one in D5 demonstrated muscle stiffness during recovery and had multiple efforts to regain the sternal position. All the remaining attempts to stand were considered to be excellent.

The combination of TZ (2 mg/kg) and dexmedetomidine at 15 and 20 μg/kg resulted in the most clinically relevant period of immobilization and were not associated with significant complications.

Friday 4th September | Room B1 | 15:00−15:15

O18-5 Determination of minimum anesthetic concentration loss of righting reflex (MAC_{LRR}) of isoflurane, sevoflurane, and desflurane in cane toads (*Bufo marinus*)

○Stuart C Clark-Price, Danielle E Strahl-Heldreth, Berit L Fischer
University of Illinois College of Veterinary Medicine

Determination of minimum alveolar concentration (MAC) is used for the purpose of reporting the ED_{50} of inhalant anesthetic. MAC describes the potency and is used for clinical application of anesthetics. In species without alveoli, minimum anesthetic concentration (also MAC) is accepted nomenclature. MAC of inhalant anesthetic in amphibians is poorly described. Loss of righting reflex (LRR) is used to determine anesthetic effect in lesser species.

In a prospective study, 8 cane toads (*Bufo marinus*) were used to determine MAC_{LRR} of isoflurane, sevoflurane, and desflurane. Toads were subject to three trials in a custom chamber with a minimum 2 week washout. LRR was evaluated by placing a toad in dorsal recumbency after a desired anesthetic concentration was reached and maintained for 15 min. If a toad was able to return to sternal recumbency (positive righting reflex), chamber anesthetic concentration was increased 0.2 to 0.3% and another 15 minutes was allowed to elapse. A trial ended when a toad was unable to return to sternal recumbency (LRR). Median and range for each anesthetic was calculated. Normality of distribution was evaluated with a Kolmogorov-Smirnov test. Differences between groups were evaluated with a Kruskal-Wallis test. A $P < 0.05$ was considered significant.

Median anesthetic concentration for isoflurane was 1.4% (0.9-1.4), for sevoflurane was 1.75% (1.1-1.9), and for desflurane was 4.4% (4.3-5.5). There was a significant difference between sevoflurane and desflurane ($P<0.05$) and between isoflurane and desflurane ($P<0.001$). There was no difference between isoflurane and sevoflurane ($P>0.05$), however a post-hoc power analysis indicated that 14 toads would be necessary to control for variability.

These results suggest that MAC for cane toads may be less than MAC for mammalian species. MAC for other amphibians may be similar to the values reported here.

Friday 4th September | Room B1 | 15:15−15:30

O19-1 Completeness of preanaesthetic records at a university veterinary teaching hospital

○Alastair Mair
University of Sydney

A recent human study concluded that there are significant deficiencies in the adequacy of preanesthetic and intraoperative records (Elhalawani et al. 2013). We assessed the completeness of small animal preanaesthetic records at a busy teaching hospital.

A retrospective study analyzing preanesthetic documentation was performed. Relevant information was entered by students onto a pre-designed anaesthetic form (handwritten). Anaesthetic records during the months of September and October 2013 were analyzed for completeness. In order to be classified as complete relevant information had to be present, legible and correct (e.g. the use of generic drug names rather than trade names). Categories included: patient details, anaesthetist, clinician, presenting problem, procedure, physical examination, American Society of Anesthesiologists physical status classification (ASA score), premedication, anaesthetic induction and maintenance, endotracheal tube (ET) size, anaesthetic breathing system and monitoring equipment. Descriptive statistics were performed using Microsoft Excel.

Two-hundred and fifty anaesthetic records were reviewed. Six different anaesthetists were included. The preanesthetic record was found to be complete in only 6% (15/250) of records. Percentage of categories deemed to be incomplete included: date (4%), anaesthetist (32%), clinician (41%), presenting problem (37%), PR (8%), fr (5%), capillary refill time (6%), mucous membrane colour (5%), temperature (13%), weight (0.5%), ASA score (1%), premedication dose (16%), effect of premedication (14%), induction drug (4%), induction drug dose (19%), induction comments (20%), ET tube size (9%), anaesthetic breathing system (13%) and monitoring equipment (6%). Emergency and out of hours records were less complete.

Based on our data, we conclude that there are significant deficiencies in the adequacy of our preanesthetic records. This is true for all cases, but it is more pronounced in emergency cases. Increased surveillance of student record keeping is required and new methods of record keeping should be considered, such as use of information technology (Edwards et al. 2013).

Edwards KE, Hagen SM, Hannam J, et al (2013) A randomized comparison between records made with an anesthesia information management system and by hand, and evaluation of the Hawthorne effect. Can J Anesth 60, 990-997.

Elhalawani I, Jenkins S, Newman N (2013) Perioperative anesthetic documentation: Adherence to current Australian guidelines. J Anaesthesiol Clin Pharmacol 29, 211-5.

Friday 4th September | Room B1 | 15:30−15:45

O19-2 Association between preoperative conditions and risk of anesthesia-related death among dogs in small animal referral hospitals in Japan

○Takaharu Itami[1,2], Tomohito Ishizuka[2], Hiroko Aida[2], Makoto Asakawa[2], Yoko Fujii[2], Ayako Imai[2], Toshie Iseri[2], Takako Miyabe-Nisiwaki[2], Shotaro Nagahama[2], Kiyokazu Naganobu[2], Yoshinori Nezu[2], Ryohei Nishimura[2], Shozo Okano[2], Tadashi Sano[2], Kazuto Yamashita[2], Yoshiki Yamaya[2]

[1)]Graduate School of Veterinary Medicine, Hokkaido University, [2)]Working Group on Veterinary Anesthesia and Analgesia, Japanese Society of Veterinary Anesthesia and Surgery

Detailed studies on the association between preoperative conditions and risk of anesthesia-related death in dogs have not been conducted so far. Our aim was to estimate the risk of anesthesia-related mortality among dogs in referral hospitals in Japan.

Between April 2010 and March 2011, 4323 dogs were anesthetized in 18 referral hospitals in Japan. We conducted a survey using questionnaires with questions on their ASA physical status, complete blood cell counts, serum biochemical tests, and surgical procedures. Anesthesia-related death was defined as death within 48 hours after termination of anesthesia, regardless of the pre-existing conditions and surgical complications. Patient outcomes (alive or dead), time of death (induction, during maintenance of anesthesia, or post-operation), cause of death (preoperative condition, anesthesia, or surgery), and intraoperative complications were investigated. Multivariate analysis was used to identify factors associated with anesthesia-related death.

The mortality rate was 0.95% (41 of 4323 dogs). Patients with preoperative conditions were at the greatest risk of anesthesia-related death (25 of 41, 61.0%). Most of the deaths occurred during the postoperative period (30 of 41, 73.2%). The main factors associated with increased odds of anesthesia-related death were disturbance of consciousness, such as somnolence, stupor, or coma (OR: 16.67, 95% CI: 2.36-63.34), ASA physical categories III-V (OR: 6.52, 95% CI: 2.16-19.70), and heart rate > 150 bpm (OR: 3.49, 95% CI: 1.10-11.09). Serum glucose level < 70 mg/dl (OR: 6.18, 95% CI: 1.89-20.20), white blood cell count > 15,200/μl (OR: 2.84, 95% CI: 1.26-6.40), and packed cell volume < 36% (OR: 2.39, 95% CI: 1.03-5.53) also increased the odds of anesthesia-related death.

Our study revealed that preoperative conditions were associated with a high risk of anesthesia-related death. Specific factors were associated with increased odds of death, especially disturbance of consciousness, ASA III-V, and low serum glucose level. Greater care with improvement in pre-operative clinical conditions may reduce the risk of anesthesia-related death.

Friday 4th September | Room B1 | 15:45−16:00

O19-3 Perceptions and opinions of Canadian pet owners about anesthesia, pain management and surgery in dogs and cats

○Genevieve Luca[1], Paulo V Steagall[1], Beatriz P Monteiro[1], Helene Ruel[1], Guy Beauchamp[1], Jim Berry[2], Susan Little[3], Enid Styles[4], Stephanie H Berry[5], Daniel Pang[6]

[1)]University of Montreal, [2)]Douglas Animal Hospital, [3)]Bytown Cat Hospital, [4)]Sherwood Park Animal Hospital, [5)]Atlantic Veterinary College, [6)]University of Calgary

This study aimed to evaluate the perceptions and opinions of Canadian pet owners about anesthesia, pain management and surgery in dogs and cats.

Six veterinary hospitals from five provinces in Canada were enrolled. Each practice received 200 copies of a questionnaire which was distributed to pet owners during a 6-week period. This included sections about perceptions and opinions of pet owners involving a) the use of analgesics for different medical conditions, b) the importance of anesthesia, cost and client-communication, c) pain management and d) demographic data. Answers were transformed into ordinal scores and analysed with the Cochran-Mantel-Haenszel test ($p < 0.05$).

A total of 849 questionnaires were returned. Pet owners felt that analgesics are always/likely to be needed for a fracture (97.8%), ovariohysterectomy (91.2%), teeth extractions (91.2%), castration (89.1%), "declawing" (87.6%), skin mass removal (88.1%), lameness (70.1%) and ear infection (58.8%). Owners rated as very important/important: expectations during illness/injury/surgery (99.3%), analgesic drugs/techniques that are applied (98.6%), information on procedures/risk (98.5%), having a board-certified anesthesiologist (90.5%) and cost (86%). Owners agreed/partly agreed that pain impacts quality of life (94.2%), analgesics hasten recovery (82.7%), "declawing" should be banned (56.7%), pain can be helpful for limiting activity (52.9%) and pain is easy to recognize in animals (30%). A total of 69% of respondents were women, and they were significantly more concerned than men about anesthesia, pain, cost and client-communication.

The study identified important areas of client communication and pet owners' perceptions and opinions about anesthesia, pain management and surgery.

Friday 4th September | Room D | 14:00−14:15

O20-1 The impact of pre-anaesthetic echocardiography on the anaesthetic management plan of cats with suspected heart disease.

○Louise Clark[1], Julie Kananagh[1], Daniel J. Pang[2], Carl Bradbrook[1], Matthew Gurney[3], Pedro Oliveira[1]

[1)]Davies Veterinary Specialists, [2)]University of Calgary, [3)]Northwest Surgeons

Findings which raise suspicions of heart disease may be encountered in cats presenting for non-cardiac disease. This study aimed to determine the impact of pre-anaesthetic echocardiography on anaesthetic management plans for these cases.

Cases were enrolled prospectively from a single centre from January 2013 to December 2014. Cats referred to services other than cardiology, which required general anaesthesia or sedation, where the clinician or anaesthetist suspected heart disease, were included. Echocardiograms were performed without sedation by a single Board Certified Veterinary Cardiologist.

Clinical history, physical examination findings and results of any pre-anaesthetic tests (minus echocardiography) were independently reviewed by 3 Board Certified Veterinary Anaesthetists. Patient specific peri-operative anaesthetic management plans and ASA physical status classification were determined for each case. Reviewers were then provided with echocardiography results and asked to reassess their plans; subsequent modifications to ASA physical status classification or individual anaesthetic management plans were recorded as either a step-up (e.g. invasive BP monitoring) or a step-down (e.g. reduced monitoring in recovery) in intensity.

Forty cases met the inclusion criteria. Descriptive statistics demonstrated changes in case specific management plans following review of echocardiography in a mean of 24/40 (60%, range 18-35) cases, an escalation of care in 13/24 (54.2%) and a reduction in 11/24 (45.8%). Change in ASA physical status classification (± 1 grade) was reported in a mean of 11/40 (27.5%, range 4-22) cases. An increase was recorded in 6/11 (54.5%) and a decrease in 5/11 (45.5%). There was agreement in change of intensity of management by 2 or more reviewers in 77.5% of cases.

Pre-anaesthetic echocardiography in cats with clinical findings suspicious of heart disease provides additional specific and clinically relevant information for anaesthetic planning, with a large and consistent proportion of anaesthetic management plans impacted, consistent with findings from human studies (1.)

(1) Canty DJ, Royse CF, Kilpatrick D et al. (2012) The impact of focused transthoracic echocardiography in the pre-operative clinic. Anaes. 67, 618-625

Friday 4th September | Room D | 14:15−14:30

O-20-2 Evaluation of the antihistaminic effects of diphenhydramine in dogs undergoing excision of mast cell tumors

○Andrea Sanchez, Alexander Valverde, Melissa Sinclair, Conny Mosley, Brad Hanna, Tony Mutsaers, Ameet Singh, Ron Johnson, Yu Gu

Ontario Veterinary College, University of Guelph

Diphenhydramine (DPH) is recommended to prevent hypotension from histamine released during surgical manipulation of mast cell tumors (MCT). Its efficacy has not been tested. This study evaluated DPH use in anesthetized client-owned dogs undergoing excision of MCT.

Sixteen dogs used in a randomized, blinded study, undergoing MCT excision were premedicated with hydromorphone (0.1 mg/kg, IM), induced with IV propofol, intubated, mechanically ventilated, and maintained with isoflurane (ETIso 1.5%). Dogs received DPH (1 mg/kg, IV) or equivalent volume of saline (S), 10 min after induction. Heart rate, direct arterial pressure, pulse oximetry, end-tidal isoflurane, cardiac index, stroke volume index, temperature, arterial blood gases, and anesthetic depth were recorded throughout anesthesia. Blood samples for DPH plasma concentrations were collected prior to premedication, during surgical prepping, during excision, and 2 hours post-extubation. A general linear mixed model was used for multiple comparisons between groups and within groups ($p<0.05$).

There were no differences in weight (DPH- 25.4 ± 12.2 kg; S- 26.9 ± 9.7; kg), gender (DPH- 2 males, 6 females; S- 3 males, 5 females), age (DPH- 8.1 ± 3.5; S- 8.0 ± 2.1; years), and propofol dose (DPH- 3.0 ± 0.8; S- 3.5 ± 0.9; mg/kg). Despite DPH plasma concentrations of 343.3 ± 152 μg/mL (5 minutes post-administration) and 53.4 ± 39.6 μg/mL (83.3 ± 14.7 minutes- during surgery) in the DPH group, there were no differences between groups for measured variables, except for a significantly lower mean (67 ± 12 versus 81 ± 11; $p = 0.014$) and diastolic (53 ± 10 versus 67 ± 9; $p = 0.0072$) pressure (mmHg) in the DPH group during surgery.

Dogs administered DPH pre-emptively to MCT excision during isoflurane anesthesia, had similar cardiovascular responses to dogs receiving a placebo, except for lower mean and diastolic pressures; therefore no clear benefit resulted from DPH administration.

Friday 4th September | Room D | 14:30−14:45

O20-3 Anaesthetic management and complications of hypophysectomy in cats.

○David M. Neilson, Jaime Viscasillas, Hatim Alibhai, Stijn JM Niessen, Patrick J Kenny, Sandra Sanchis-Mora
Royal Veterinary College, University of London

Hypophysectomy presents unique challenges for the veterinary anaesthetist. This study aimed to describe the anaesthetic management of the feline hypophysectomy case and to identify any risk factors associated with anaesthetic protocol or patient status affecting morbidity and mortality in the peri-anaesthetic period.

A retrospective analysis of the anaesthetic records from 20 cats undergoing hypophysectomy was undertaken. Outcomes investigated included morbidity (the presence of one or more of the following; hypotension, hypothermia, bradycardia, and airway complication) and mortality in the 48 hours following anaesthetic recovery. Descriptive statistics and analysis of anaesthetic and patient variables association with morbidity and mortality were performed using chi-square test.

The median age of the cats undergoing the procedure was 121 months (range 61-177). Diabetes mellitus was confirmed in 19 of the cases. Thoracic auscultation revealed a heart murmur in 15 cases, with structural disease confirmed in 10 of those cases. The median anaesthetic duration for the procedure was 345 minutes (range 245-420). The most common anaesthetic protocol chosen was methadone (14 cases) propofol (13 cases) and sevoflurane (17 cases) with remifentanil constant-rate infusion (10). The animals received controlled mandatory ventilation (18 cases). The most common complications were hypothermia (19 cases), bradycardia (15 cases), hypotension (15 cases) and partial airway obstruction (6 cases). Two cats died within 48 hours of anaesthetic termination. Statistical evaluation revealed no significant effect of anaesthetic protocol on the outcomes measured in these cases.

Hypotension, hypothermia and bradycardia were common intraoperative complications in these cases, and the incidence of airway complication appears higher than in other surgical procedures. The small sample size is a limiting factor in this study, which may have prevented the identification of risk factors affecting morbidity and mortality. Larger studies may help to determine if such factors exist.

Friday 4th September | Room D | 14:45−15:00

O20-4 Clinical Use of Atracurium in General Anesthesia of Dogs and Cats: 548 Cases

○Won-gyun Son, Min Jang, Sang-min Jo, Hyunseok Kim, Chi Won Shin, Inhyung Lee
College of Veterinary Medicine, Seoul National University

Purpose: This study was performed to review the use of atracurium in various types of procedures requiring general anesthesia at Seoul National University Veterinary Medical Teaching Hospital (SNU-VMTH).

Materials and Methods: The medical records were reviewed for 535 cases of dogs and 13 cases of cats receiving atracurium during general anesthesia at SNU-VMTH from March 2010 to April 2015. The medical records were analyzed according to various criteria including type of procedure, American association of anesthesiologists (ASA) grade, antagonism with neostigmine, as well as the major complications observed.

Results: The types of procedures included: soft tissue surgery (thoracotomy, n = 21; others, n = 231), ophthalmic surgery (phacoemulsification, n = 69; others, n = 57), diagnostic imaging (magnetic resonance imaging, n = 35; computed tomography, n = 27), neurologic surgery (n = 61), orthopedic surgery (n = 39), theriogenologic surgery (n = 5), and dental surgery (n = 3). The patients were categorized into ASA grade I to II (27%) and ASA grade III to V (73%) according to individual anesthetic risk. Antagonism of atracurium with neostigmine was performed in 206 patients (37%) after clinical and electrical stimulation tests of neuromuscular recovery. Major complications related to atracurium included residual neuromuscular blockade (n = 3, one dog died in the post-operative recovery period), cardiovascular depression secondary to positive pressure ventilation associated with paralysis of the respiratory muscles, and difficulty in determining anesthetic depth through physical signs.

Conclusions: Atracurium was used in various types of procedures for immobilization and as a component of balanced anesthesia, particularly in patients with higher anesthetic risk. However, considering the complications that can occur, care must be taken when using atracurium in dogs and cats.

Friday 4th September | Room D | 15:00–15:15

O21-1 Agreement between maximum Elastic Pressure estimated by three mathematical models of dynamic respiratory mechanics and Plateau pressure: a test lung study.

○Joao Soares[1], Alysson R Carvalho[2], Antonio Giannella-Neto[3]

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This study investigated the agreement between Plateau pressure (Pplat) and maximum elastic pressure (Pelmax) estimated by three different mathematical models of respiratory mechanics. A test lung was mechanically ventilated with the 4 possible combinations of respiratory system elastance (Ers) of 20 and 50 cmH_2O/L and respiratory system resistance (Rrs) of 3 and 35 $cmH_2O/L/s$. In each combination, tidal volume (VT) was 500 mL, respiratory rate 10 breath/min, and I:E 1:2. Three levels of positive end-expiratory pressure (PEEP) were used in each combination of Ers and Rrs. Pplat was recorded as the airway pressure (Paw) at the end of a 5-second inspiratory pause. The three mathematical models tested were: 1) linear single compartment model (LSCM) - Paw(t) = Rrs.F(t)+E.V(t)+EEP ; 2) volume-dependent single compartmental model (VDSCM) – Paw(t) = Rrs.F(t) + (E1+E2.V(t)).V(t)+EEP; 3) Flow-dependent Volume-dependent single compartmental model (FDVDSCM) - Paw(t) = (R1+R2.F(t)) .F(t) + (E1+E2.V(t)).V(t)+EEP. Where t is time, V is volume, EEP is end-expiratory pressure E1 and R1 are the volume- and flow-independent component, and E2 and R2 the volume- and flow-dependent components, respectively, of the models. Elastic pressure (Pel) was computed as Ers.V(t) for LSCM and (E1+E2.V(t)). V(t) for VDSCM and VDFDSCM, and Pelmax the maximum Pel during the inspiratory phase. Bias and limits of agreement between Pplat and Pelmax for each model were calculated and Bland Altman plots were generated for each combination of Ers and Rrs. A two-way ANOVA was used to compare the Bias between the groups followed by Dunn-Sidak post-hoc test ($P<0.05$). The Bias was different in FDVDSCM when compared with VDSCM and LSCM, as well as, closer to 0 than the other models, independently of the combination of Rrs and Ers used in this model. FDVDSCM provided a better estimation of Pplat than LSCM and VDSCM, with probably minimal clinical significance, especially with normal Ers.

Friday 4th September | Room D | 15:15–15:30

O21-2 The effects of inspiratory pause in the accuracy of respiratory system compliance estimated by two clinical monitors.

○Joao H N Soares[1], Alysson R. Carvalho[2], Antonio Giannella-Neto[3]

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This study investigated the effect of inspiratory pause in the accuracy of two clinical monitors to estimate respiratory system compliance (Crs). A test lung was mechanically ventilated for 5 minutes with tidal volume (V_T) of 500 mL, respiratory rate of 10 breath/min, positive end-expiratory pressure of 3 cmH_2O, and I:E of 1:2. Four conditions of respiratory mechanics were simulated using two levels of Crs: 50 (C50) and 20 mL/cmH_2O (C20), and two of respiratory resistance (Rrs): 3 (R3) and 35 $cmH_2O/L/s$ (R35), generating the 4 combinations of Crs and Rrs used in this study: R3C50, R3C20, R35C50 and R35C20. In each combination, the test lung was ventilated with no inspiratory pause (insPause) or with insPause of 10, 30 and 50%. At the end of the ventilation period, an insPause of 5 s was generated to obtain static Crs (Cstat). S/5 (GE Healthcare, Datex Ohmeda, Inc., WI, USA) and NICO (Novametrix Medical Systems, Inc., CT, USA) monitors were simultaneously used and 5 consecutive measurements of Crs, $C_{S/5}$ and C_{NICO}, respectively, were collected during the last minute of each ventilatory protocol. Bias and limits of agreement between $C_{S/5}$ or C_{NICO}, and Cstat were calculated for all ventilatory protocols and Bland-Altman plots were used to assess the accuracy of both monitors. The larger biases of both monitors were observed in R35C50 and were -22.2 and -9.3 cmH_2O/L for $C_{S/5}$ with no insPause and insPause of 10%, respectively, and -3.8 cmH_2O/L for C_{NICO} without insPause. The presence of insPause of 30 and 50% tended to decrease the biases for both monitors in the two ventilatory conditions with higher Rrs. The estimate of Crs by the two clinical monitors used in this study seemed to be highly affected in the absence of insPause and conditions of high Rrs, especially for the S/5 anesthesia monitor.

Friday 4th September | Room D | 15:30−15:45

O21-3 Indirect oscillometric blood pressure measurement incorporating pulse transit time on cuff pressure in anesthetized dogs

○Youngjoo Kim, Austi Stei, Courteny Campbell, Janet H Han, Lyon Lee
Western University of Health Sciences - College of Veterinary Medicine

Noninvasive blood pressure (NIBP) measurement was compared with invasive BP (IBP) measurement in fifteen anesthetized dogs. A multiparameter veterinary patient monitor measured NIBP using oscillometric principle employing a novel algorithm incorporating pulse transit time (PTT) on measured values of cuff pressure (CP). Systolic arterial BP (SABP), diastolic arterial BP (DABP), and mean arterial BP (MABP) data were analyzed using correlation regression analysis and Bland Altman plots to compare the degree of agreement between the two measurement methods. The correlation between the two measurement methods was strong in medium pressure group (n=86, systolic 90-120 mmHg) and in high pressure group (n=71, systolic above 120 mmHg), but weak in low pressure group (n=47, systolic below 90 mmHg). In medium pressure group, the correlation coefficient (r2) ranged from 0.77 for mean pressure and 0.85 for diastolic pressure. A high correlation was also observed for mean pressure (r2=0.73) in high pressure group. Correlation coefficient for all systolic, diastolic and mean pressures in low pressure group was low with r2 ranging from 0.2 to 0.4. This study demonstrated mean pressure measured between 60 and 150 mmHg from indirect BP method using oscillometric principle incorporating a novel algorithm employing pulse transit time on measured values of cuff pressure correlates highly with that from direct BP method in anesthetized dogs. However, mean BP readings measured from the indirect method falling outside these ranges may require additional validation of accuracy for consequential clinical interpretation in anesthetized dogs. The noninvasive blood pressure monitoring method based on oscillometric principle incorporating a novel algorithm in this study can be particularly useful to alert abrupt and sudden changes in BP from undesirable anesthetic depth and associated cardiovascular abnormalities.

Friday 4th September | Room D | 15:45−16:00

O21-4 Investigation of the effects of different computered-controlled inspired fraction of oxygen on variations in isoflurane concentration in Tafonius

○Mathieu C Raillard[1], Paul D Macfarlane[2]
[1)]Vetsuisse Faculty University of Bern, [2)]University of Bristol Veterinary School

The Tafonius large animal anaesthesia machine has an integral computer controlled digital flowmeter (DF) which can replace the mechanical flowmeter (MF). This bench study compares isoflurane output with either MF or DF.

A calibrated TEC 3 vaporiser was used. Gas concentrations and flows were measured using calibrated Datex S/5 monitor and RI PFM 100 flowmeter. Measurements included:
1. Time to reach 90 % of a target end tidal isoflurane (P_E' iso) whilst ventilating a lung simulator with a range of F_iO_2 and MF or DF set on 5 L.min^{-1}.
2. Flow from the common gas outlet with MF and DF.
3. Duration during which oxygen or air were added to the system at F_iO_2 0.21 or 1.0 for a range of flows with the DF.
4. Isoflurane tension at the common gas outlet, and, in a 30 L mixing bag after 4 minutes of 5 L.min^{-1}, over a range of vaporiser and F_iO_2 settings.
No statistical analysis were performed due to the descriptive nature of the study.

Time to reach 90 % of P_E' iso was 35 minutes with MF, 44 to 85 minutes with DF depending on F_iO_2. Gas flowed intermittently at a fixed rate with DF (7.6 L.min^{-1} and 10.6 L.min^{-1} for F_iO_2 of 0.21 and 1.0 respectively). For MF measured flows were as expected. For DF set to 5 L.min^{-1}, calculated mean flow for an F_iO_2 of 0.21 or 1.0 was 1.9 L.min^{-1} or 4.0 L.min^{-1}. Flows higher than 5 L.min^{-1} generated isoflurane output lower than expected. Isoflurane tension in the mixing bag matched vaporiser setting with MF but not with DF, especially at low settings where isoflurane tension exceeded expectations.

The isoflurane output of the Tafonius is lower for DF compared to MF. The bulk of the difference is attributable to flows lower than expected with DF but a novel 'pumping effect' also appears to be present.

Poster Session

Tuesday 1st September | Event Hall

P-1 Influence of PIP and PEEP in mechanically ventilated dogs undergoing capnoperitoneum on selected cardiorespiratory parameters

○Petr Rauser, Michal Crha, Lucie Urbanova

Small Animal Clinic, Faculty of Veterinary Medicine, University of Veterinary and Pharmaceutical Sciences Brno

Capnoperitoneum during laparoscopy affects cardiorespiratory parameters. Influence of different positive inspiratory pressures (PIP) and positive end-expiratory pressures (PEEP) on selected cardiorespiratory parameters in dogs undergoing capnoperitoneum have not been published yet.

Thirty dogs, mean body mass 39.5 ± 16.5 kg and age 4.1 ± 3.5 years, 12 males and 18 females undergoing laparoscopy were enrolled in a prospective clinical trial. Dogs were sedated with medetomidine-butorphanol, anesthesia was induced with propofol and maintained with isoflurane in oxygen-air. Mechanical ventilation was pressure-controlled, volume-limited (f_R 10 breaths min ^{1}, FiO_2 0.6). After stabilization, dogs were ventilated with 0/15, 5/15, 0/20, 5/20, 0/25 and 5/25 cmH_2O (PEEP/PIP), each pattern for 5 minutes. During all ventilatory patterns, tidal volume (V_T), heart rate (HR), non-invasive blood pressure (BP), end-tidal CO_2 ($EtCO_2$) and oxygen saturation of hemoglobin (SpO_2) were recorded. Subsequently, capnoperitoneum was established with intra-abdominal pressure at 10 mmHg. Thereafter, identical ventilatory pattern were used and data collected. During measurements dogs were without painful stimulation, positioned in ventral recumbency. Comparable data with or without capnoperitoneum and with or without PEEP were analyzed by ANOVA followed by Dunnett's tests for multiple comparisons. Changes were considered significant when $P < 0.05$.

Tidal volume decreased and $EtCO_2$ increased significantly in all ventilatory patterns, HR decreased significantly in 5/25 after capnoperitoneum was established. However, HR in other ventilatory patterns and BP and SpO_2 within and between groups remained without significant changes.

Increased PIP or PEEP for mechanical ventilation in dogs undergoing capnoperitoneum significantly decrease V_T and increase $EtCO_2$ only without significant impairment of HR (except 5/25), BP and SpO_2.

The study was supported by the Ministry of Education, Youth and Sports of the Czech Republic (IGA VFU 80/2014/FVL).

Wednesday 2nd September | Event Hall

P-2 Evaluation of a continuous rate infusion of propofol-ketamine for total intravenous anaesthesia in one humped camels (*Camelus dromedarius*) after xylazine premedication: a clinical case series

○Adel I Almubarak[1,4], Jean-Claude Ionita[2], Abdulgader M Homeida[3], Ramdan O Ramadan[1]

[1)]King Faisal University, [2)]Large Animal Clinic for Surgery, University of Leipzig, Leipzig, Germany, [3)]College of Science, University of Dammam, Saudi Arabia

Seven adult dromedary camels anaesthetized to undergo surgical procedures. All patients were premedicated with an intravenous (IV) administration of 0.2 mg kg^{-1} xylazine. Anaesthesia was induced with 1.0 mg kg^{-1} propofol (P) and 0.8 mg kg^{-1} ketamine (K) given IV and was maintained with a a continuous rate infusion (CRI) of 4 mg kg−1 hour−1 P and 3.3 mg kg−1 hour−1 K. Heart rate, respiratory rate, arterial blood pressure and quality of anaesthesia were recorded before and after xylazine administration (XA) as well as at 5 minutes after induction and every 10 minutes until the end of the procedure. Mean anaesthetic duration was 82.9 ± 16.0 minutes. Mean heart rate increased after induction and remained at relative constant levels during maintenance. Respiratory rate dropped after XA, but quickly returned the baseline level. Mean arterial blood pressure significantly decreased below baseline level after XA, but rose within anaesthesia maintenance, without reaching baseline values though. The mean recovery time was 37.6 ± 24.2 minutes. A very good level of surgical anaesthetic depth was achieved and maintained during all procedures and all animals could be discharged safely after a smooth and uneventful recovery. This P-K CRI after XA seems to be clinically safe and effective in dromedary camels and provides very good operating conditions for major surgeries in this species. Still, further studies are necessary to evaluate more cardiorespiratory and haematological parameters in order to confirm the safety of this new technique.

Tuesday 1st September | Event Hall

P-3 The challenges of epidural anaesthesia in cats

○Benedict Ong Huai Ern Ong[1], Hui Cheng Chen[1]

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Injections into the lumbosacral epidural space were attempted in four clinical cases using the dorsal approach, with cats on sternal recumbency. Three of the cases underwent hindlimb orthopaedic procedures. Two of the orthopaedic patients were induced with tramadol-midazolam, and maintained on isoflurane. Another orthopaedic patient was premedicated with tramadol, induced with thiopental and maintained on isoflurane. The fourth case was a dystocia, and was induced with tramadol-diazepam. Hanging-drop method and loss of resistance test were used to identify the epidural space.

Epidural anaesthesia was successful in two of the orthopaedic cases, resulting in significant MAC reduction and obtunded sympathetic response during surgery. A false positive on the loss of resistance test in the third orthopaedic case resulted in significant sympathetic stimulation and higher inhalant requirement during surgery. In the dystocia case, first attempt resulted in cerebrospinal fluid while second attempt had blood flowing from the needle, indicating inadvertent subarachnoid and ventral venous plexus puncture respectively. Epidural anaesthesia was aborted in this case.

These four cases demonstrated the difficulty to correctly place the needle into the lumbosacral epidural space in cats, and the complications that may arise.

Key words : Epidural anaesthesia, cats, intrathecal, anaesthesia complication

Wednesday 2nd September | Event Hall

P-4 The postoperative analgesic effect of bilateral paravertebral nerve block for abdominal surgery in dogs.

○Tomoya Iizuka, Masatoshi Kamata, Dai Nagakubo, Kanako Muta, Ryohei Nishimura

Laboratory of Veterinary Surgery, Graduate School of Agricultural and Life Sciences, The University of Tokyo

The aim of the study was to investigate postoperative analgesic effect of bilateral paravertebral nerve block (BPNB) in dogs undergoing abdominal surgery.

Twenty-four client-owned dogs were randomly assigned to either a control group (n=12) or a BPNB group (n=12). Anesthesia was induced with propofol and maintained with isoflurane, fentanyl, and ketamine. BPNB was performed only in the block group, at the 10th and 12th thoracic paravertebral space with 0.25% bupivacaine (a total volume was 0.4 mL kg^{-1}). During surgery, fentanyl was infused at a rate of 20 μg kg^{-1} $hour^{-1}$ in the control group and 10 μg kg^{-1} $hour^{-1}$ in the BPNB group. After the end of surgery, the dogs were allowed to recover from the anesthesia, and visual analogue scale of pain (VAS), pain score, and sedation score were assessed at 0, 2, 4, 6, 8, 12 hours after the recovery. For postoperative analgesia, fentanyl was infused at a rate of 2.5 μg kg^{-1} $hour^{-1}$, and, if necessary, 2.5 μg kg^{-1} of fentanyl was administered as rescue therapy. All variables were compared between groups using Mann-Whitney test or Fishers exact test. A multiple linear regression model was used to explore the influence of covariates including postoperative analgesia on the VAS and pain score. Significance was $p< 0.05$.

The VAS at 12 hours after the recovery in the BPNB group was significantly lower than that in the control group. In the multiple linear regression model, whether control or block group, surgical time, and time points of postoperative assessments were significantly associated with the VAS, and whether control or BPNB group, intraoperative fentanyl infusion rate, sedation score, and postoperative fentanyl infusion rate were significantly associated with the pain score.

In conclusion, the bilateral paravertebral nerve block could be an effective technique for abdominal surgery to alleviate postoperative pain in dogs.

Tuesday 1st September | Event Hall

P-5 Clinical pharmacokinetics and pharmacodynamics of intravenous alfaxalone in Thoroughbred horses at two different anesthetic induction doses

○Asuka Kushiro[1], Ai Wakuno[1], Shun-ichi Nagata[2], Motoki Aoki[1], Minoru Ohta[1]
[1)]Miho Training Center, Japan Racing Association, [2)]Laboratory of Racing Chemistry

OBJECTIVE
To investigate the clinical pharmacokinetics and pharmacodynamics of intravenous alfaxalone in Thoroughbred horses at two different anesthetic induction doses.

PROCEDURES
Seven healthy Thoroughbred horses (6 males and 1 female), aged 3.0 ± 0.5 years and weighing 460 ± 23 kg, were randomly anesthetized twice with either 1.0 mg/kg (Low) or 2.0 mg/kg (High) of intravenous alfaxalone after premedication with midazolam 20 μg/kg IV and medetomidine 6.0 μg/kg IV. Qualities of anesthetic induction and recovery were scored, and induction time and recovery time were also recorded. Cardiorespiratory values were measured throughout anesthesia. Blood samples were collected at predetermined time points up to 2 hr after administration. Plasma alfaxalone concentrations were quantified by a liquid chromatography tandem-mass spectrometry method and analyzed by two-compartmental pharmacokinetic analysis.

RESULTS
Induction and recovery qualities were good to excellent at both doses. Recovery time was prolonged at high dose (Low: 54 ± 13 min, High: 84 ± 26 min). There were no significant differences in cardiovascular values between the two doses. In contrast, respiratory rate significantly decreased at high dose (Low: 8 ± 5 bpm, High: 3 ± 2 bpm), which resulted in an increase in PaCO2 (Low: 48 ± 2 mmHg, High: 54 ± 1 mmHg).
The mean ± SD of area under curve, total clearance and elimination half-life were 79.1 ± 8.2 μg*min/mL, 12.2 ± 1.5 mL/min/kg and 57.7 ± 8.4 min at low dose and 136.6 ± 15.5 μg*min/mL, 14.1 ± 1.7 mL/min/kg and 57.3 ± 7.5 min at high dose, respectively.

CONCLUSIONS AND CLINICAL RELEVANCE
High dose of alfaxalone induced respiratory depression and prolonged recovery. Alfaxalone is rapidly eliminated from the plasma, which makes it suitable for use as an induction agent in Thoroughbred horses.

Wednesday 2nd September | Event Hall

P-6 Five degrees reverse Trendelenburg in sevoflurane-anesthetized calves: hemodynamic and oxygen content-bases index effects

○Paulo Sergio Patto dos Santos[1], Marcelo Augusto Araújo[2], Mauricio Deschk[3], Beatriz Perez Floriano[1], Juliana Tessália Wagatsuma[1], Cynthia Yumi Oshiro Okamura[1], Bruna de Moraes M. Games[1], Carlos Eduardo de Siqueira[1], Guilherme Lopes da Silva[1]
[1)]Sao Paulo State University - UNESP, [2)]Federal University of Mato Grosso do Sul - UFMS, [3)]Federal University of Acre - UFAC

Objective: The purpose of the study was to compare the hemodynamic and oxygen content-bases index effects of five-degree reverse Trendelenburg ("head-up") and horizontal position in dorsally recumbent sevoflurane-anesthetized calves.
Material and methods: A total of eight, healthy, male Holstein calves weighing 145 ± 27kg were included in the study. Each animal was anesthetized twice composing the two experimental groups: Control group (CG), table without tilt (horizontal position) and treatment group (TG) table positioned with five degrees of inclination (reverse Trendelenburg). The calves were physically restrained and positioned in supine position on the operating table in the slope determined for each group. Anesthesia was induced via face mask with 8% sevoflurane administered diluted in oxygen (5 L minute $^{-1}$) and maintained with 1.3% MAC previously determined for each animal. A period of 40 minutes was awaited in order to obtain anesthetic concentration stability and to allow for all the preparation of the animals. Hemodynamic parameters (heart rate; systolic, diastolic and mean arterial pressure, central venous pressure, cardiac output and core temperature) were recorded immediately after the stabilization period (T0), and after that at intervals of 30, 60, 120 and 180 minutes. Derived cardiovascular variables (cardiac index, stroke volume, pulmonary and systemic vascular resistance index) and oxygen content based index (oxygen supply, oxygen consumption, oxygen extraction rate and venous admixture) were calculated. Repeated measures were evaluated using repeated measure analysis of variance (ANOVA) with Tukey *post-hoc* test or Friedman test with Dunn *post-hoc* test. Statistical significance was set at $p < 0.05$.
Results: There were no significant differences in hemodynamic parameters and oxygen content based index between groups.
Conclusion: The five degree reverse Trendelenburg position in calves sevoflurane-anesthesized did not change significantly the hemodynamic parameters and oxygen content based index evaluated in this study compared with dorsal recumbency.

Tuesday 1st September | Event Hall

P-7 Analgesic effect of a T6-T11 bilateral intercostal nerve block in a dog undergoing surgical excision of an abdominal wall tumor

○Diego F. Echeverry[1,2], Jessica T. Pelaez[1], Diego A. Ospina[1], Edwin F. Buriticá[1], Fabian E. Castañeda[1]

[1)]Department of Animal Health, Faculty of Veterinary Medicine and Zootechny, Universidad del Tolima, Ibagué, Colombia., [2)]Small Animal Medicine and Surgery Research Group, Tolima University, Ibagué, Colombia.

Abdominal surgery elicits considerable nociceptive input, where much of the pain described by humans exposed to this type of surgery seems to originated from the incision of the abdominal wall. Recently, the transverse abdominal plane (TAP) block has been proposed as a suitable alternative to traditional loco-regional techniques such as epidurals or wound infiltration, to improve analgesia in procedures performed on the abdominal wall. Nevertheless, the TAP block can be ineffective in providing analgesia in the most cranial part of the abdominal wall; and complementary intercostal nerves blocks (INB) have been indicated to cover this deficit. The objective of this case report is to describe the intraoperative analgesic effect of an intercostal nerveblock in a dog undergoing a surgical excision of a tumor located in the cranial abdominal wall.

A 8-years-old, female Golden retriever dog weighing 33.7 kg was admitted to surgery to remove a fibrosarcoma located on the abdominal wall, caudal to the xiphoid process. The dog was premedicated with acepromazine 0.01 $mg.kg^{-1}$ IV, tramadol 3 $mg.kg^{-1}$ IV and meloxicam 0.3 $mg.kg^{-1}$ SC. Anaesthesia was induced with propofol 5 $mg.kg^{-1}$ IV, and maintained with isofluorane in oxygen (100%). A T6-T11 INB was performed bilaterally using 0.5 mL of bupivacaine (0.5 %) to infiltrate each nerve (0.9 mg kg^{-1} total dose). The nerves were approached at the chondrocostal junction level using a 22 G spinal needle. Intraoperative nociception was controlled by fentanyl (3 $\mu g.kg^{-1}$ IV) in the event of an increase in HR or MAP > 20%. Physiological parameters were stable during the entire surgical procedure: HR 90 bpm, MAP 73 mm of Hg, ETIso 2%. Fentanyl was not supplemented. The INB technique employed here was effective to provide an adequate analgesia to perform the surgical resection of this fibrosarcoma, located at the craneal abdomen, in this dog.

Wednesday 2nd September | Event Hall

P-8 Clinical usefulness of the bispectral index as an indicator of anesthetic depth in sevoflurane-anesthetized Thoroughbred horses

○Hirotaka Tokushige[1], Masashi Kakizaki[1], Hirotaka Ode[1], Atsushi Okano[1], Jun Okada[2], Taisuke Kuroda[2], Ai Wakuno[2], Minoru Ohta[1]

[1)]Racehorse Clinic, Miho Training Center, Japan Racing Association, [2)]Racehorse Clinic, Ritto Training Center, Japan Racing Association

OBJECTIVE
To investigate the clinical usefulness of the bispectral index (BIS) as an indicator of anesthetic depth in sevoflurane-anesthetized Thoroughbred horses.

EXPERIMENT 1
Procedure: BIS values were measured at multiple stages during sevoflurane anesthesia in five horses (age: 3.2 ± 1.1 years).
Results: The BIS values at the end-tidal sevoflurane concentration of 1.2 MAC (59 ± 8) and 1.5 MAC (66 ± 13) were significantly lower than those in awake (98 ± 0) or under sedation with xylazine (88 ± 5). The BIS values were not significantly different between at ETSEVO of 1.2 MAC and 1.5 MAC. During the recovery phase, the mean BIS values increased gradually over time.

EXPERIMENT 2
Procedure: BIS values were measured in seventeen horses undergoing orthopedic surgery. The first group (n = 11) (age: 2.8 ± 0.4 years) received sevoflurane and a local nerve block, mepivacaine, in the injured leg (Group M). The second group (n = 6) (age: 2.2 ± 0.4 years) received sevoflurane and an injection of saline (Group C).
Results: Although there were no significant differences in BIS values between the two groups during surgery, BIS values in Group C were somewhat higher than those in Group M, and BIS values slightly increased in Group C following the presentation of surgical stimuli. In response to surgical stimuli, nystagmus was observed in 33% of the horses in Group C, but not in Group M. On the other hand, there were no significant differences in cardiovascular values between the two groups.

CONCLUSIONS
BIS values were considered to be a better indicator of anesthetic depth rather than cardiovascular parameters. Because BIS values varied for individual horses, it was considered that the absolute BIS values did not represent the exact depth of anesthesia. However, the overall changes in BIS values reflected the overall changes in anesthetic depth.

Tuesday 1st September | Event Hall

P-9 Effects of nitrous oxide at 50% on intracranial parameters in pigs anesthetized with propofol.

○Newton Nunes, Patricia Cristina Ferro Lopes, Paloma do Espirito Santo Silva, Cleber Kazuo Ido, Helen Roberta Amaral Silva, Eliselle Goveia de Faria Biteli, Ana Paula Gering, Rodrigo Lima Carneiro
Sao Paulo State University - UNESP

It is known that nitrous oxide may increase intracranial pressure (ICP), though it is endowed with good analgesic potential. On the other hand, propofol reduces the ICP, but does not create analgesia. Therefore, we sought to evaluate the association of both anesthetics and their effect on ICP, the cerebral perfusion pressure (CPP) and intracranial temperature (ICT) in pigs, since the use of this species has increased as an experimental model. For this, we used 16 pigs of Large White breed, with weights between 18 and 20 kg, divided into two groups of 8 animals each named GN50 and GA50. The animals received azaperone (2 mg/kg intramuscularly) followed, 20 minutes after, by propofol intravenously administered in doses sufficient to allow tracheal intubation. They were, then, intubated and we started the continuous infusion of propofol at a dose of 0.5 mg/kg/minute. From this moment, the animals GN50 received nitrous oxide diluted in 50% oxygen and the animals of the GA50 received oxygen diluted with air at 50%. In each animal a parenchymal catheter (Integra NeuroCare 110-4BT) was inserted to measure the ICP and ICT, displayed in a monitor (Integra NeuroCare MMP-1), and measured mean arterial pressure (MAP) to calculate the CPP (CPP = MAP - ICP). The measurements were made 40 minutes post-induction of anesthesia and every 15 minutes thereafter for one hour. Numerical data were statistically analyzed by ANOVA followed by Bonferroni test and no difference was found between the groups, but in both groups, the ICT decreased throughout the experiment while the other values remained constant. It was concluded that nitrous oxide in the tested concentration did not interfere with intracranial parameters studied in pigs anesthetized with propofol

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P-10 Metabolic and hemodynamic evaluation for two long term sedation protocols in dogs

○Nilson Oleskovicz, Doughlas Regalin, Martielo Ivan Gehrcke, Bruna Ditzel Da Costa Regalin, Felipe Comassetto, Vanessa Sasso Padilha, Aury Nunes De Moraes
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The aim of this study was evaluate the hemodynamic and metabolic effects of two sedation protocols for long term ventilation in dogs. Were 12 healthy dogs used, allocated in two groups: GMF who received constant rate infusion (CRI) of midazolam (0.5mg/Kg/h), fentanyl (10μg/Kg/h) and propofol (0.3mg/Kg/min) or GKM who received CRI of ketamine (10μg/Kg/min), morphine (4.4μg/Kg/min) and propofol (0.3mg/Kg/min). The CRI were maintained for 24 hours duration and the dogs were mechanically ventilated to normocapnia. Nurse care was applied in all patients and central temperature was maintained in 37.6 ± 0.5 °C. HR decreased in both groups (32% in GMF and 34% in GCM), reducing CI (24% in GMF and 29% in GCM), but MAP, systemic vascular resistance index, pulmonary arterial pressure and left ventricle work index remained within reference ranges. Pulmonary resistance index and right ventricle work index increased in GMF (58% and 27%). $ETCO_2$, pH, PaO_2, and $PaCO_2$ were maintained in reference values in both groups, but CaO_2, $CmvO_2$, oxygen delivery and oxygen consumption decreased in GCM and GMF. Mixed venous oxygen partial pressure, and mixed venous oxygen saturation decreased in both groups. Sedation scores were higher in GMF than GCM, requiring less propofol for adequate sedation. The number of rescues with dopamine (SAP or MAP decreased 90 or 60 mm/Hg respectively) was higher in GMF (2.8 ± 2.6) than GCM (0.2 ± 0.4). Urine output remained above minimal acceptable values for dogs in both groups. No differences between groups for time (minutes) to extubation (38 ± 17 and 29 ± 14), sternal recumbency (147 ± 73 and 122 ± 49) and total recovery (225 ± 88 and 190 ± 68) in the GMF and GCM respectively. We concluded that both protocols were effective for mechanical ventilation. Bradycardia was responsible for CI reduction in both groups, but metabolic rate decrease minimizes CI reduction. GMF promoted more hemodynamic depression, and should be used with caution.

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P-11 Indirect calorimetry in hemodynamic and metabolic monitoring in dogs under different hemodynamics states

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The aim of this study was evaluate the use of indirect calorimetry (IC) compared to thermodilution (TD) in dogs under different hemodynamics states. There were 9 healthy dogs (3±1 years old and 19.6±1.3 kg) used, anesthetized with isoflurane 1.4V% (Baseline), undergoing mechanical ventilation (MV) (Vt 12 ml/kg, inspiratory pressure 10 cmH_2O), hypodynamic state (Hypo) with isoflurane and the hyperdynamic state (Hyper) with dobutamine. We used a Swan-Ganz for measurement of cardiac index (CI) by TD, calculation of oxygen consumption by the Fick method (VO_2^{Fick}) and to collect samples of central and mixed venous blood. With the IC, oxygen consumption (VO_2), production (VCO_2) and end tidal CO_2 ($EtCO_2$) were obtained. For the determination of CI by IC we used the Fick principle with VO_2 values, and arterial and mixed (Fickmix) or central (Fickvc) venous blood; or the ratio of the values of VCO_2 and $EtCO_2$ ($FickCO_2$). Statistical analysis was by Dunnet tests for difference between the phases and Tukey for differences between the methods ($p \leq 0.05$), Pearson correlation and Bland-Altman analysis. IC provided VO_2 values 30 to 40% higher than the VO_2Fick. The VCO_2 values decreased in VM and Hypo. CI values decreased in Hypo with all methods and increased in Hyper with TD and Fickvc. The CI values for Fickmix and Fickvc were greater than TD at all times and $FickCO_2$ was lower than TD in the Hyper. None of the methods presented agreement and correlation with TD (% error at Baseline (80, 87, 49), MV (61, 63, 74), Hypo (58, 71, 79) and Hyper (37, 71, 62) in Fickmix, Fickvc and $FickCO_2$ respectively. It is concluded that IC can be used to measure the VO_2 and VCO_2 in dogs, but the CI values obtained by this method cannot be compared to thermodilution, can only identify the different hemodynamics states.

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P-12 Pharmacodynamics and pharmacokinetics of rocuronium in sevoflurane-anesthetized Thoroughbred horses

○Kazumichi Kodaira[1], Masashi Kakizaki[1], Shun-ichi Nagata[2], Hirotaka Ode[1], Atsushi Okano[1], Norihisa Tamura[1], Fumiaki Mizobe[1], Yoshikazu Matsuda[1], Shinjiro Kurimoto[3], Hiroko Aida[4]
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OBJECTIVE
To investigate the pharmacodynamics and pharmacokinetics of rocuronium administered by bolus injections in sevoflurane-anesthetized Thoroughbred horses.

PROCEDURES
Five healthy horses were anesthetized twice with an interval of at least 2 weeks. The horses were pre-medicated with 0.75mg•kg $^{-1}$ xylazine. Anesthesia was induced with 2.5 mg•kg^{-1} ketamine and maintained with sevoflurane in 100% O_2 (ETsevo 3.0%). The peroneal nerve was stimulated using acceleromyography in train-of-four mode at 2 Hz every 15 s. Each horse was randomly selected to receive an intravenous bolus of either 0.2 mg•kg $^{-1}$ (D02) or 0.4 mg•kg $^{-1}$ (D04) rocuronium bromide. Onset time (OT), clinical duration (DUR $T1_{25}$), and recovery time ($T1_{25\text{-}75}$) were measured, and these pharmacodynamic parameters between D02 and D04 were statistically compared (paired Student's *t*-test). Blood samples were collected at predetermined time points up to 240 min after the administration of rocuronium bromide, and plasma rocuronium concentrations were measured using chromatography–tandem mass spectrometry.

RESULTS
Complete neuromuscular block was observed in all horses. OT for D04 (96.2 ± 10.1 s) was significantly lesser than that for D02 (118.4 ± 12.8 s), and DUR $T1_{25}$ for D04 (67.0 ± 17.8 min) was greater than that for D02 (42.5 ± 11.2 min) ($P<0.05$). $T1_{25\text{-}75}$ did not significantly differ between D02 and D04 (13.2 ± 1.4 min vs. 18.5 ± 6.7 min). Plasma concentrations of rocuronium showed a biphasic elimination pattern. The rocuronium concentration at 3, 5, 10, and 15 min after injection and the distribution half-life values for both doses showed positive correlation with the DUR $T1_{25}$ values; the correlation for D02 was very strong ($r > 0.7$).

CONCLUSIONS
Rocuronium showed dose-dependent onset and clinical duration in sevoflurane-anesthetized horses. Clinical duration of rocuronium may be affected by plasma rocuronium concentrations at the initial stages and by the rate of drug elimination from the blood.

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P-13 Validation of the French version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats

○Beatriz P Monteiro[1], Paulo V Steagall[1], Anne-Marie Lavoie[1], Diane Frank[1], Eric Troncy[1], Stelio P Luna[1], Juliana Brondani[2]

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The purpose of this study was to validate the French version of the UNESP-Botucatu multidimensional composite pain scale (MCPS) to assess postoperative pain in cats.

The English scale was translated to French with subsequent back-translation. Videos of 27 cats in the preoperative and postoperative period (before and after rescue analgesia and 24 hours post-surgery) were randomized. Three French-speaking individuals (a DVM student, a PhD candidate and a board-certified veterinary behaviourist) with training on scale use completed the video analysis. Validity and reliability tests were performed. The cut-off point to discriminate the need for rescue analgesia was determined by the Receiver operating characteristic curve.

Three domains were identified by factor analysis. The Cronbach's alpha coefficient was excellent for 'psychomotor change' and 'protection of the painful area' (0.94 and 0.90, respectively) and moderate for 'physiological variables' (0.61). Relevant changes in pain scores at clinically distinct time points (e.g., post-surgery, post-analgesic therapy), confirmed the construct validity and responsiveness (Wilcoxon test, $p < 0.001$). Good to very good agreement between blinded observers and 'gold standard' evaluation supported criterion validity. Inter- and intra-rater reliability for each scale item were good to very good. The optimal cut-off point identified was > 7 (scale range 0 – 30 points), with a sensitivity of 97.8% (95% CI: 92.2 – 99.7%), and specificity of 99.1% (95% CI: 96.9 – 99.9%).

The French version of the UNESP-Botucatu-MCPS is a valid, reliable and responsive instrument for assessing acute pain in cats undergoing ovariohysterectomy when used by individuals with different experience. The instrument has high discriminatory ability with a cut-off similar to the English version.

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P-14 Evaluation of the bispectral index in pigs anesthetized with propofol, in spontaneous ventilation using 0.5 of FiO_2 associated with 0.5 of N_2O

○Paloma do Espírito Santo Silva, Newton Nunes, Patricia F. Lopes, Eliselle G. F. Biteli, Cleber K. Ido, Ana Paula Gering, Isadora M. Rodrigues

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Background and objectives: In spite of propofol being a widely used anesthetic, it does not promote analgesia. Therefore, its association with nitrous oxide (N_2O), which has good analgesic effect, seems to be complementary and beneficial. The researches have been insufficient to determine if this association employing FiO_2=0.5 interferes on bispectral index in pigs. Methods: For this research 16 pigs in nursery phase were used, divided into two groups: GN50 (0.5 N_2O with 0.5 O_2) and GA50 (0.5 compressed air with 0.5 O_2). Animals were pre-medicated with intramuscular azaperone (2mg kg-1). After 20 minutes, the induction with propofol was made and thereafter maintenance was performed with propofol infusion at a dose of 0.5mg / kg / min. Following intubation, the corresponding mixture of gases was provided to each group. After shaving and cleaning of the head area, the electrodes were positioned. Forty minutes after the induction the values of the bispectral index (BIS) were colected, as well as the EMG (electromyography) and SQI (signal quality index), which were repeated at 15 minutes intervals (M0 to M60). Results: The results are shown in Table 1. Conclusion: The use of FiO_2 0.5 associated with N_2O did not alter the bispectral index in pigs, under these experimental conditions.

Table 1. Mean values of BIS, SQI and EMG in pigs (n = 16) anesthetized with propofol using FiO_2=0.5 associated with compressed air (GA50) or N_20 (GN50).

Variable	Group	Moments				
		M0	M15	M30	M45	M60
BIS Average	GA50	61.88	58	60.63^{A}	60.38	54.13
	GN50	53.75	56.13	50^{B}	54	54.88
EMG	GA50	33.63	33.38	34.63	31.38	33.13
	GN50	31.25	32.25	30.25	32.75	32.13
QS	GA50	93.63	90.88^{a}	94.63	97.88^{b}	96.38
	GN50	88.63	91.75	92.88	90.38	92.38

Different capital letters in the same column of a variable show statistical difference ($p<0.05$)
Different lower case in the same column of a variable show statistical difference ($p<0.05$)

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P-15 Evaluation of bupivacaine administered epidurally at the first lumbar vertebra on sensory and anesthetic block in bitches submitted to an elective ovariohysterectomy

○Paloma do Espírito Santo Silva, Newton Nunes, Ana Paula Gering, Tiago C. Prada, Ana Paula R. Simões, Thiago F. V. Bompadre, Raquel V. G. Castro

Sao Paulo State University

The epidural catheter is a safe alternative for debilitated animals who require abdominal surgery. In veterinary medicine, there is no definition of a safe dose for using bupivacaine 7.5% cranial to the seventh lumbar vertebra. For this research 16 bitches were used, divided equal into two groups which differed in the dose of epidural bupivacaine, 1 mgkg-1(G1) or 2 mgkg-1(G2), diluted to the same final volume (1ml4kg-1). The animals were pre-medicated with butorphanol intravenously and induced to anesthesia with etomidate. The epidural catheter was inserted in the seventh lumbar vertebral space until the first lumbar vertebral space. After 30 minutes, bupivacaine was administered and 30 minutes later the sensory block was evaluated by clamping the tail, anus, vulva, right hindlimb and left hindlimb with a Kocher clamp. Scores were assigned according to the patient' s response, as follows: 0 absent, 1 decreased and 2 normal. The results were analyzed by Wilcoxon Two-Sample test. Completed this evaluation, the ovariohisterectomy surgery was initiated. The anesthetic block was evaluated using the table 1, at 5 points: M1: incision of the umbilical scar; M2: ligature of left ovarian pedicle; M3: ligature of right ovarian pedicle; M4: uterine stump transfixation; M5: skin suture. After the sum of scores the values between 0-4 were considered as good anesthetic block, values between 5 and 7 were considered discreet anesthetic block, and above 7 anesthetic block was considered insufficient or absent. The results of sensory block are shown in table 2, there were statistical differences between groups for all variables. For de anesthetic block, only one bitch of G1 and seven bitches of G2 had pain scores below 4 at all evaluation points. It was possible to conclude that the epidural dose of 2 mgkg-1of bupivacaine promotes better sensory and anesthetic block than the dose of 1mgkg-1.

Table 1. Qualitative analysis of the effectiveness of anesthetic block during the surgical period through score given by an observer, acoording to the possible changes that could be found.

Parameters	Criterion	Scores
Heart rate Respiratory rate Systolic blood pressure	≤10% greater than the preoperative value	0
	11 a 30% greater than the preoperative value	1
	31 a 49% greater than the preoperative value	2
	50% greater than the preoperative value	3
Salivation	Normal	0
	Above normal	1
Pupillary diameter	Normal	0
	Mydriasis	1
Vocalization	No vocalization	0
	Vocalization present and controlled without medication	1
	Uncontrolled vocalization	2
Agitation	Asleep or calm	0
	Little agitation	1
	Moderate agitation	2
	Severe agitation	3

Table 2. Percentage of dogs (n=16) that underwent epidural bupivacaine administered at the first lumbar vertebra at 1 $mgkg^{-1}$ (G1) or 2 $mgkg^{-1}$ (G2), and framed the scores 0 (absent), 1 (decreased) and 2 (normal), answering the stimulus given for assessment of sensory block.

Scores	Variables									
	Tail		Anus		Vulva		Right hindlimb		Left hindlimb	
	G1	G2	G1	G2	G1	G2	G1	G2	G1	G2
0	75%	100%	50%	87.5%	50%	87.5%	50%	100%	50%	100%
1	12.5%	0	25%	12.5%	25%	12.5%	12.5%	0	25%	0
2	12.5%	0	25%	0	25%	0	37.5%	0	25%	0

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P-16 Treatment of pruritus induced by epidural administration of morphine using xylazine and naloxone in bitch- case report

○Paloma do Espírito Santo Silva, Newton Nunes, André Escobar, Lilian W. Campos, Ana Paula R. Simões, Marina B. S. Brito

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Pruritus after epidural administration of morphine is a common complication in humans, although the incidence in dogs is low. The mechanism involved in epidural morphine-induced pruritus is not completely understood, but it is known that treatment with antihistamines is not effective. A healthy pregnant mixed-breed bitch, approximately four years old was referred for cesarean section. Anesthesia was induced with propofol, followed by endotracheal intubation for oxygen supply. Subsequently, lidocaine 2% (1 mL 4kg-1) associated with morphine (0.1 mg kg-1) were epidurally administered, animal was extubated and placed in dorso-lateral recumbency, remaining conscious in an oxygen mask during the procedure. Buscopam, meloxicam and tramadol were administered after removal of the puppies. After surgery and 45 minutes after epidural administration, the dog began to severely bite the pelvic limbs and tail, and did not allow manipulation of that area. Animal allowed the puppies to suckle and felt no pain on palpation of the surgical wound, suggesting pruritus induced by morphine. Treatment was performed administering 0.01 mg kg-1 IV of naloxone. After 20 minutes, the animal showed a small improvement and a supplementary administration of 0.007 mg kg-1 IV of naloxone was performed due to maintenance of hypersensitivity to touch. After another 20 minutes, she still showed sensitivity to touch, but at lower intensity and an administration of 0.1 mg kg-1 IV of xylazine was done. After one hour the animal had no more hypersensitivity in the pelvic region. The administration of naloxone and xylazine was effective in the treatment of pruritus induced by epidural administration of morphine. Our report suggests that xylazine has not an anti-pruritic action, but relieves symptoms by promoting sedation in the patient.

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P-17 Cardiac output in pigs anesthetized with propofol associated or not to nitrous oxide and submitted to pressure controlled ventilation.

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The aim of this work was to evaluate the effects of nitrous oxide at 50% on the cardiac output (CO) in pigs For this, we used 16 pigs of Large White breed, with weights between 18 and 20 kg, divided into two groups of 8 animals each named GN50 and GA50. The animals received azaperone (2 mg/kg intramuscular) followed, 20 minutes after, by propofol intravenously adminstered in doses sufficient to allow tracheal intubation. They were then intubated and we started the continuos infusion of propofol at dose of 0.5 mg/kg/minute. From this moment the animals GN50 received nitrous oxide diluted in 50% oxygen and the animals of the GA50 received oxygen diluted with air at 50%. Rocuronium was then administered by continuous intravenous infusion at 0.6 mg/Kg/h. The Pressure-controlled ventilation (PCV) was started and adjusted to 15 cm H2O and the frequency was set to achieve capnometry between 35-45 mmHg. The measurement of CO (L/min) was performed using the thermodilution method. The Swan-Ganz catheter was inserted into the left jugular vein and started after administration of rocuronium, repeating every 15 minutes intervals, over 60 minutes. The data were submitted to statistical analisys by the ANOVA followed by Bonferroni test. The results showed that despite the N2O slightly raising the CO for compensatory sympathetic activation and propofol reducing it by decreased peripheral vascular resistance, in this study there were no significant differences between the groups and times corroborating evidence, which demonstrated significant hemodynamic stability associating N2O and propofol. Also some authors found cardiovascular stability using propofol at a dose of 0.4 mg/kg/min, associated to N2O at 30%. There was no effect on CO with the PCV, although it often does reduce it by an increase in pulmonary vascular resistance. It was concluded that the addition of nitrous oxide at 50% to the pigs anesthetized with propofol and kept on PCV did not significantly affect the cardiac output.

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P-18 Evaluation of an indirect oscillometric blood pressure monitor in anaesthetized dogs at three different anatomical locations

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This study evaluated the agreement between invasive blood pressure (IBP) and non-invasive blood pressure (NIBP) using an oscillometric blood pressure device on three locations in anaesthetized dogs.

Eight greyhounds weighing 23.5 to 36.5 kg were anaesthetised and positioned in dorsal recumbency. IBP was measured via a dorsal pedal artery and NIBP was measured using cuffs placed above the carpus, above the tarsus and around the tail base. Haemodynamic changes were induced by the administration of phenylephrine, high concentrations of isoflurane and dobutamine. Measurements were analysed by linear regression and Bland-Altman method.

Seventy two simultaneous measurements were obtained from each location. Most bias (precision) were within 10 (15) mmHg except for SAP on the hind leg. Correlation coefficients for SAP, DAP and MAP were more than 0.9 except for SAP on the hind leg and DAP on the tail. More than 50% of measurements were within 10 mmHg of the IBP except for SAP on the hind leg and more than 80% of measurements were within 20 mmHg of the IBP. SAP tended to be overestimated during low blood pressure and underestimated during high blood pressure, whereas DAP tended to be underestimated on the tail.

This device yielded reliable blood pressure measurements on the front leg and met the ACVIM criteria. MAP measured at all sites met the standards of the Association for the Advancement of Medical Instrumentation (bias ± precision, ≤ 5 ± 8 mmHg).

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P-19 Pharmacokinetics and sedative effects of detomidine administered by intravenous and intramuscular routes in donkeys

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Pharmacokinetics (PK) of detomidine has been described in horses. However, there is lack of information about these data in donkeys. The aim of this study was to determine the PK profile of two doses of detomidine in this species, correlating plasma drug concentrations with sedative effects.

Eight healthy female Nordestino type donkeys, mean weight 139.2 ± 22 kg, aging from three to eight years, were used in this study. All animals received two detomidine treatments (10 µg.kg i.v. and 20 µg.kg i.m), randomly administered at a seven days-interval. Blood samples were collected before and at time points during 12 hours after detomidine administration. Plasma concentrations of detomidine were measured by liquid chromatography-mass spectrometry (LC-MS) and PK parameters were calculated using standard formulas. Sedative effects were evaluated by measuring head height (HH), degree of ataxia and response to auditory stimulus scores. Statistical analysis was performed by Wilcoxon sum rank and paired t tests ($P < 0.05$).

Decreases of plasma detomidine concentration over the time were best described as a two-compartment model. Bioavailability of detomidine administered to donkeys by intramuscular route was 86%. Volume of distribution (Vd), elimination half-life ($t_{1/2\beta}$) and clearence (Cl) calculated for i.v. and i.m. routes were respectively: 629.3 and 1641.5 mL.kg; 30 and 77.8 minutes; 15.4 and 14.5 mL.min.kg. Effective sedation was observed from 5 to 30 (i.v.), and from 20 to 60 (i.m.) minutes after detomidine administration, with drug plasma concentration mean values at these time points decreasing from 23.9 ± 3.5 to 7.1 ± 3.1 (i.v.) ng.mL and from 9.3 ± 4.2 to 6.7 ± 2.4 (i.m.) ng.mL.

Intensity and time of sedation with detomidine in donkeys were closely correlated with plasma concentrations measured and routes of administration. Data reported can be used to properly calculate dosage regimens of detomidine for the asinine species.

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P-20 Pharmacokinetics of oral, intramuscular and intravenous methadone hydrochloride and oral nanostructured lipid carriers of methadone in horses

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It is a challenge to find a balance between a sufficient dose to produce analgesia without excitement in horses. Nanoparticles might increase therapeutic efficacy and avoid these adverse effects. This study investigated the pharmacokinetics of methadone administered orally, intravenously, intramuscularly and oral nanostructured lipid carriers of methadone in horses. Six adult healthy mares (354 ± 34 kg; 2-4 years) received 0.5 mg/kg of oral, intramuscular and intravenous methadone hydrochloride (injectable formulation) or methadone lipid nanocarrier formulation prepared in-house orally (ON), at one week interval. Blood samples were collected from jugular vein for up to six hours after methadone administrations for measurement of plasma methadone concentration, quantified by Liquid Chromatography-Mass Spectrometry. The pharmacokinetic parameters were calculated by non-compartmental and compartmental methods using Scientist 2.0 (MicroMath). After intravenous methadone, elimination was rapid (1 ± 0.3 L/h/kg), elimination half life was short (0.7 ± 0.1 h) and mean retention time (MRT) was 1.1 ± 0.2 h. The area under the curve (AUC) (ng*h/ml) for intravenous, intramuscular, oral, and ON were 547 ± 162, 601 ± 293, 618 ± 189 and 502 ± 155 ng/mL respectively. MRT was higher in intramuscular than intravenous route (1.1 ± 0.2 and 1.6 ± 0.4 h respectively). Elimination half life was longer in oral and intramuscular when compared to intravenous route. It was concluded that intramuscular route appears to be a good option compared to intravenous administration, as MRT was longer. One open compartmental model with first order elimination best described the plasma pharmacokinetics in all groups. Both oral and NO methadone showed a similar pharmacokinetic profile; therefore nanoparticles did not improve the pharmacokinetic profile of oral methadone.

Approved by the Institutional Animal Research Ethical Committee under the protocol number 55/2011.

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P-21 Survey of current equine sedation protocols used in standing equine MRI units to establish current practice to help consider future approaches.

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BELL EQUINE VETERINARY CLINIC

It is important to establish an effective sedation protocol for standing MRI procedures in horses, which are now performed in many centres worldwide. Although this is a non-painful procedure, it does require the horse to stand completely still to obtain the best diagnostic images. Standing sedation for MRI must provide a motionless patient, unresponsive to stimuli, while avoiding ataxia, twitching or other movement. The sedation requires monitoring and adjustment during any individual 30-60minute procedure. A number of different sedation protocols have been developed globally, but to date these have not been compared or standardised. This survey is to investigate current practice and to consider future options.
A questionnaire was sent to centres that had performed the largest numbers of standing fetlock MRI scans. These were selected, as they are more technically challenging to acquire, with greater potential difficulties associated with patient movement, yet still relatively commonly performed by different centres.
For those centres performing a sufficient number of scans consistently, the efficacy of sedation and the efficiency of the scanning procedure were assessed from measurements of the overall time taken to acquire the scan, the number of pilot scans required and also movement issues. The overall length of time is one measure of the efficiency of the procedure and the number of pilot surveys undertaken is another as it indicates any interruptions and adjustments during the procedure. Movement has to be avoided for good image acquisition and more movement is linked to inadequate sedation.
An allowance was made for the type/breed of horse scanned and the sedation used and the mode of administration. The maintenance of sedation for prolonged procedures, complications and additional management measures were also documented.

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P-22 Hypnotic effects and pharmacokinetics of a single bolus dose of alfaxalone in Japanese macaques (*Macaca fuscata*)

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The aim of this study was to describe the hypnotic effects and to develop a pharmacokinetic model of a single bolus dose of alfaxalone in Japanese macaques.
Six male macaques (5-10 years, 8.5-12.1 kg) were used. The macaque was restrained in a squeezing cage and 2 mg kg^{-1} of alfaxalone was administrated intravenously at 2 mg kg^{-1} $minute^{-1}$ on two separate occasions with more than 2 weeks intervals. For the behavioural study, posture and responses to external stimuli were assessed every 2 minutes for 20-40 minutes. For the pharmacokinetic study, the macaques were maintained under sevoflurane anaesthesia for 180 minutes and venous blood samples were collected at 2, 5, 15, 30, 60, 120 and 180 minutes after alfaxalone administration. The plasma concentrations of alfaxalone were measured by LC/MS and pharmacokinetic modelling was performed using NONMEM VII.
Three macaques showed excessive response to stimuli during recovery, resulting in minor injury, and behavioural study was terminated. The three macaques were recumbent for a mean 9.3 ± 5.1 SD minutes and recovered to behave as pre-administration by mean 29.9 ±9.2 SD minutes after the administration. Respiratory and heart rates were stable throughout the experiments (35-52 breaths $minute^{-1}$ and 123-170 beats $minute^{-1}$, respectively). All six macaques were used in the pharmacokinetic study. Our final pharmacokinetic model included 2 compartments and the population pharmacokinetic parameters were: V1 = 3.23 L, V2 = 9.11 L, CL1 =0.47 L $minute^{-1}$, CL2=0.71 L $minute^{-1}$ (the volumes of distribution and
the clearances for the central and peripheral compartments, respectively). Alfaxalone is not recommended to be used *solely* in Japanese macaques due to the excessive response during recovery. The excessive response was not seen when followed by sevoflurane inhalation. The developed pharmacokinetic parameters may enable simulations of administration protocols to maintain adequate plasma concentration of alfaxalone.

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P-23 Efficacy of epidural analgesia with medetomidine on isoflurane requirement and mean systemic arterial blood pressure in dogs.

○Ryota Watanabe, Yukihiro Fujita, Shigeyoshi Kojima, Go Togawa, Akikazu Ishihara, Miyoko Saito
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This study evaluates the Isoflurane reduction effects of epidural medetomidine administered in anesthetized dogs. Five healthy beagles were anesthetized and received medetomidine epidurally (10mcg/kg (M10) or 20mcg/kg (M20), 0.2mL/kg in volume) or saline (S group, 0.2mL/kg in volume) as control. After an interval, each dog was reanesthetized and treated with the alternate epidural infusion. Dogs were anesthesia was induced and maintained with isoflurane. Dogs were intubated and instrumented for measurement of mean systemic arterial blood pressure (MAP) by an oscillometric method and for airway concentration of isoflurane (ISO). The depth of anesthesia was determined by applying mechanical stimulation involved clamping the third metatarsal bone using bone forceps at 1, 2.5 and 4 hours post-administration. The Positive response to stimulus was defined as an increase of either heart rate or MAP over 15% above the value recorded before applying the stimulation. ISO was increased or decreased by 0.1 to 0.2% whether there was exhibiting positive response and the dogs were retested 15 minutes later. Data was analyzed using a one-way ANOVA and post-hoc Tukey' s test. A $p < 0.05$ value was considered statistically significant. ISO for S, M10 and M20 groups were 2.92, 2.08 and 0.88 at 1h, 2.74, 1.94 and 1.08 at 2.5h and 2.64, 1.94 and 1.62 at 4h respectively. Significant differences in ISO were observed between S and M20 at 1h, S and M20, M10 and M20 at 2.5h, and S and M10, M20 at 4h respectively. Additionally, MAP of M20 at 1h was significantly higher compared with S and M10. Furthermore at 2.5h administered M20, kept MAP significantly higher than the S. We conclude that epidural administration of medetomidine had an effect on reduction of isoflurane requirement and maintaining MAP higher than in the control group. Therefore it may be a viable procedure to maintain systemic hemodynamics.

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P-24 Evaluation of an oscillometric blood pressure monitor in anaesthetised dogs using ACVIM guidelines

○Alastair Mair, Oriana Marchetti, Sanaa Zaki, Chris Burrows
University of Sydney

The ACVIM provides instruction for the validation of oscillometric blood pressure devices (Brown et al. 2007). We assessed a new veterinary monitor (Anitek).

Dogs requiring placement of an arterial catheter as part of their anaesthetic management were recruited. Blood pressure cuff width approximately 40% the circumference of the limb was chosen. Paired blood pressure measurements were taken. Bland-Altman plots were drawn (GraphPad). The bias, precision (SD of differences) and 95% limits of agreement (LOA) were calculated. The percentages of measurements within 10 and 20 mmHg of the direct measures were also calculated. Simple linear regression analysis was used to evaluate the relationships between direct and indirect values.

A total of 760 paired measurements were obtained from 35 dogs (21.3 ± 15.3 kg, 7.9 ± 4.2 years). Arterial catheter placement included the auricular artery (3 dogs) and the dorsal pedal artery (32 dogs). Cuff placement included the antebrachium (24 dogs) and the tarsus (9 dogs above; 2 dogs below). Cuff sizes included size 1 (1 dog), 2 (4 dogs), 3 (14 dogs), 4 (10 dogs) and 5 (6 dogs). The bias (mean ± SD) and 95% LOA for SAP, MAP and DAP were 1.5 ± 20.6 (95% CI: -38.9 to 41.8), -1.8 ± 13.4 (-28.0 to 24.5) and 1.8 ± 12.5 (-22.6 to 26.3) mmHg respectively. Correlation for SAP, MAP and DAP were 0.711, 0.753 and 0.733 respectively. Forty percent of SAP, 57% of MAP and 60% of DAP measurements were within 10 mmHg of direct values; 69% of SAP, 88% of MAP and 91% of DAP measurements were within 20 mmHg of direct values.

This monitor satisfied ACVIM guidelines for bias, precision and percent of measurements within 10 or 20 mmHg of direct values for MAP and DAP but only satisfied bias for SAP. It did not meet correlation requirements.

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P-25 The effects of dexmedetomidine, a peripherally acting α2-antagonist (MK-467) and glibenclamide on blood glucose and lactate concentrations in dogs – Preliminary results

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MK-467 increases the secretion of insulin by blocking pancreatic α2A-adrenoceptors. The objective of this study was to investigate the effects of dexmedetomidine and MK-467 on blood glucose and lactate concentrations in a canine model of glibenclamide-induced hypoglycemia.

In this prospective, randomized, cross-over study eight healthy, adult laboratory beagles were treated five times:

1. saline; 30 min later dexmedetomidine (5 μg kg^{-1}) (DEX)
2. saline; 30 min later dexmedetomidine + MK-467 (250 μg kg^{-1}) (DEX-MK)
3. glibenclamide (1 mg kg^{-1}); 30 min later saline (G)
4. glibenclamide; 30 min later dexmedetomidine (G-DEX)
5. glibenclamide; 30 min later dexmedetomidine + MK-467 (G-DEX-MK)

Drugs were administered intravenously. Bloodsamples were collected from central jugular cathether. Plasma glucose and lactate concentrations were assessed with a blood gas analyzer (ABL800 Flex, Radiometer) at intervals until 360 minutes. The maximum treatment effects (lowest for glucose, highest for lactate) were compared between treatments with repeated ANOVA, $p < 0.05$.

Plasma glucose and lactate concentrations are shown in Table 1. The results suggest that the combination of reduced tissue oxygen delivery by dexmedetomidine (Honkavaara et al. 2010) and low plasma glucose concentration may increase anaerobic tissue metabolism.

Reference
Honkavaara J, Restitutti F, Raekallio M et. al. (2011) The effects of increasing doses of MK-467, a peripheral alpha(2)-adrenergic receptor antagonist, on the cardiopulmonary effects of intravenous dexmedetomidine in conscious dogs. J Vet Pharmacol Ther, 34, 332-337.

Acknowledgements: Vetcare Oy provided financial support.

Table 1. Means (SD) of plasma glucose and lactate concentrations (mmol/L); baselines and maximum treatment effects.

	baseline	DEX	DEX-MK	G	G-DEX	G-DEX-MK
Glucose	5.7 (0.9)	4.8 (0.6)*#	4.3 (0.8)*#	2.3 (0.3)*	2.8 (0.8)*#	2.2 (0.3)*#
Lactate	0.6 (0.2)	1.1 (0.5)*#	0.7 (0.3)+	0.7 (0.3)	1.4 (0.5)*#	0.9 (0.4)*

*significantly different from baseline (*t*-test)
#significant difference between the same treatments with and without glibenclamide
+significant difference between the same treatments with and without MK-467

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P-26 The influence of different FiO_2 on leukocyte and platelet count in isoflurane-anesthetized rabbits submitted to hypovolemia followed by reperfusion

○Newton Nunes[1], Patricia Cristina Ferro Lopes[2], Juliana Vitti Moro[1], Eliselle Gouveia Faria Biteli[1], Rodrigo Lima Carneiro[3], Ana Paula Gering[1], Danielli Parrilha de Paula[1], Paulo Sergio Patto Santos[1], Monica Horr[1]

[1)]Sao Paulo State University - UNESP, [2)]Faculdade de Jaguariuna - Department of Veterinary Medicine, [3)]Unime

The use of high-inspired oxygen fractions (FiO2) has been indicated during hypovolemia to prevent tissue hypoxia, but it promotes an increase in tissue injury and in oxygen free radicals, which with inflammatory products attract and activate leukocytes. Thus, the aim was to evaluate the influence of different FiO2 (1.0, 0.6 or 0.40) on leukocyte and platelet count in isoflurane-anesthetized rabbits induced to hypovolemia and submitted to autotransfusion. Thirty animals were randomly assigned to three groups: G100 (FiO2=1.0), G60 (FiO2=0.6) and G40 (FiO2=0.4). Isoflurane was used for induction (2.5MAC) and maintained general anesthesia (1.0 MAC) diluted in total flow of 1 L.minute-1 O2 at 100%, 60% and 40% was determined for each group. After 1 hour of induction, hypovolemia was induced by removing arterial blood (12 ml.kg-1) from femoral artery. The blood was stored in siconized blood bags. After 80 minutes of hypovolemia induction, the autotransfusion was started. The total leukocyte count (Le) and platelets (Plq) were measured before anesthesia (TB), 60 minutes after induction of anesthesia (T0), 10 minutes after hypovolemia induction (T10), 70 minutes after T10 (T80) and, then, at 15-minute intervals (T95 to T140) during 1 hour. Numeric data were submitted to analysis of variance (ANOVA) for repeated measurements followed by Bonferroni test ($P<0.05$). In G100, the highest values of Le were registered. No differences were recorded between G60 and G40 for Le, which decreased in all groups during the procedure. Until T110, in G60, the lowest values of Plq were registered and, only in G100, this variable decreased during the whole procedure. In conclusion, when FiO2 = 1.0 was used, there were oxygen free radicals and leukocyte count increased, while probably there was a reduction in platelet aggregation response.

THE INFLUENCE OF DIFFERENT FIO_2 ON LEUKOCYTE AND PLATELET COUNT IN ISOFLURANE-ANESTHETIZED RABBITS SUBMITTED TO HYPOVOLEMIA FOLLOWED BY REPERFUSION

Nunes N.[1], Lopes Ferro P.C.[2], Moro J.V.[1] et al.

Table 1. Total leukocyte count (Le) and platelets (Plq) in isoflurane-anesthetized rabbits submitted to acute hypovolemia followed by autotransfusion, maintained in spontaneous breathing with FiO_2 of 1.0 (G100) 0.6 (G.60) or 0.4 (G.40).

Variables	Groups	Times							
		TB	T0	T10	T80	T95	T110	T125	T140
Le $10^3/mm^3$	G100	7032±1038^{Aa}	6206±1159^{Aa}	4741±578^{Ab}	4432±704^{Ab}	4911±1191^{Ab}	4697±713^{Ab}	4316±1219^{Ab}	4867±1211^{Ab}
	G60	5367±1257^{Ba}	3411±863^{Bb}	2004±615^{Bc}	1544±579^{Bc}	1511±567^{Bc}	1609±384^{Bc}	1562±362^{Bc}	1509±381^{Bc}
	G40	5878±1790^{Ba}	3700±1072^{Bbd}	2056±851^{Bc}	2544±2001^{Bcd}	1667±942^{Bc}	1589±615^{Bc}	1444±317^{Bc}	1533±702^{Bc}
Plq $10^3/mm^3$	G100	879±39^{Aa}	812±94^{Aab}	682±205^{Abc}	662±212^{Abc}	632±215^{Acd}	602±191^{Ac}	547±217^{Ad}	383±204^{Ae}
	G60	374±160^{B}	380±105^{B}	355±107^{B}	406±88^{B}	350±49^{B}	369±34^{B}	381±98	417±108
	G40	589±208^{C}	630±178^{A}	646±175^{A}	674±174^{Aa}	475±85^{b}	522±113	537±121	591±137^{A}

Data are expressed as means ± SD. Difference among groups: means with different capital letters within each column differed significantly. Difference among times in each group: means with different non-capital letters within each row differed significantly ($p<0.05$).

Acknowledgements

The authors would like to thank the Pró–Reitoria de Pesquisa (PROPE) da Universidade Estadual Paulista "Júlio de Mesquita Filho" – UNESP, for the scholarships.

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P-27 Case Report Anesthetic Management for Patent Ductus Arteriosus Ligation in a Pomeranian Dog: Role of Multimodal Pain Management and Sevoflurane

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An 11-week-old, female Pomeranian dog, weighing 1.7 kilograms was anesthesized for surgical correction of a patent ductus arteriosus (PDA). The dog was premedicated with midazolam and morphine, induced with etomidate, and maintained with sevoflurane. Multimodal pain management including intramuscular and epidural administration of morphine, constant rate infusion (CRI) of fentanyl, intercostal nerve block and intraplerual analgesia with bupivacaine and lidocaine were performed to provide good pain control for the intra-operative and post-operative period. Sevoflurane is a less potent respiratory depressant and provides a more rapid recovery than isoflurane. Moreover, this volatile agent has been used extensively in human pediatric anesthesia. However, sevoflurane produces dose-dependent cardiovascular effects. Multimodal analgesia has been suggested to reduce sevoflurane MAC, thereby reducing its depressant effects on the cardiovascular system and improving the quality of anesthesia. In this report, the dog received low end-tidal sevoflurane concentration (0.25-2%). Heart rate (HR), systolic blood pressure (SBP), end tidal carbon dioxide ($EtCO_2$), body temperature remained stable within normal ranges and electrocardiography (ECG) showed normal sinus rhythm during anesthesia monitoring. The dog was subsequently breathing spontaneously after being weaned off of intermittent positive pressure ventilation (IPPV). The dog was extubated after recovery of consciousness within a short time (4 minutes after turn off vaporizer). No post-operative complications were noted. After 7 hours, the puppy was playful and energetic. This paper report on an excellent outcome obtained using multimodal pain management and sevoflurane in a tiny pediatric dog with PDA undergoing thoracotomy.

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P-28 Evaluation of efficacy of intravenous regional anesthesia and nerve blocks on pain in the distal hind limb of dairy cows

○Samaneh Yavari[1], Nimer Khraim[2], George Szoura[1], Alexander Starke[3], Elisabeth Engelke[4], Christiane Pfarrer[4], Klaus Hopster[5], Sabine Kästner[6], Jürgen Rehage[1]

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Background: The treatment of lameness is important as the third most common health disorder in dairy cows with the frequent cause of deep inflammatory lesions at the pododerma. For surgical treatment adequate pain management is an essential precondition. Although hind limb anaesthesia techniques including intravenous regional anaesthesia (IVRA) and nerve block anesthesia (NBA) are described in textbooks for distal limb local anesthesia in cattle, no evidence has been found of the investigation of efficacy of these two anaesthesia methods. Therefore, the objective of this study is to examine the impact of IVRA and NBA to desensitize the distal hind limb of cattle.
Methods: Initially, CT scan of hind limb and dissections of bovine distal hind limbs were performed to identify the appropriate injection sites for the intended four points NBA. Subsequently, eight non-lactating, non-pregnant HF dairy cows were treated in a cross-over study design. All cows were equipped with indwelling jugular vein catheters for blood sampling (to measure serum Glucose, NEFA, Lactate and Cortisol) as well as ear artery catheters to measure the arterial blood pressure. Heart and Respiratory rates were recorded throughout the study. Pain responses were tested by needle pricks, mechanical pressure, heat and electrical stimuli. Procasel 2% (Procaine) was used in a dosage of 20 ml and 60 ml for IVRA and NBA, respectively.
Results and conclusions: Both anaesthesia techniques provided full anesthesia at the hind limb. However, after NBA compared to IVRA treated cows onset of anaesthesia was in average faster. Furthermore, at the distal hind limb of cows responses on electrical pain stimulation were in contrast to responses on pain stimulated by heat, needle pricks and mechanical pressure clear, easy to detect and repeatable.

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P-29 Agreement between pleth variability index and pulse pressure variation in ventilated dogs under anesthesia.

○Taku Hirokawa, Yusuke Endo, Jun Tamura, Chika Higuchi, Kenjiro Miyoshi, Tadashi Sano, Kazuto Yamashita

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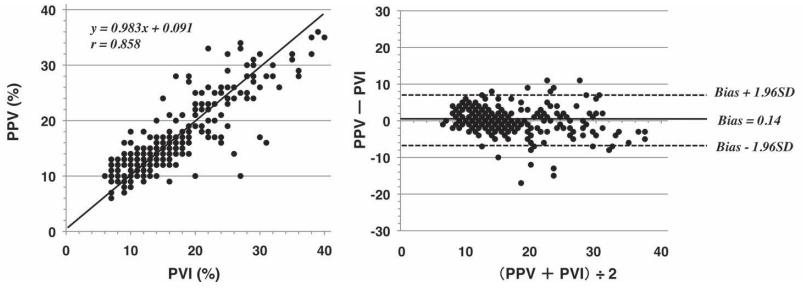
Fluid responsiveness can be predicted by pulse pressure variation (PPV). Pleth variability index (PVI) uses as a non-invasive substitute for PPV in human. The aim of this study was to evaluate agreement between PVI and PPV in dogs.

PVI and PPV were measured simultaneously at every 5 minutes during anesthesia for surgery in 17 owner-owned dogs (2 to 17 years old, weighing 2.6 to 28.5 kg). All dogs were artificially ventilated during anesthesia. PPV was measured using a 22 or 24 gauge catheter placed into the dorsal pedal artery and pressure transducer connected to a hemodynamic monitoring device (PiCCO2, Pulsion). PVI was measured using a pulse oximeter probe attached to their tail and a pulse CO oximeter (Radical-7, Masimo). Data were analyzed using Pearson correlation and Bland-Altman analysis. $P < 0.05$ was considered statistically significant.

A total 331 sets of PPV and PVI values were obtained from the dogs (8 to 40 sets from each dog). The average values ± standard deviations are 16.7 ± 6.0 % (ranged from 6 to 36%) for PPV and 16.4 ± 6.8 % (ranged from 6 to 40%) for PVI. There was a significant correlation ($r = 0.858$, $P < 0.001$) but a moderate agreement (Limits of agreement: 0.20 ± 6.9%) between PPV and PVI.

This study demonstrated that PPV and PVI showed a significant correlation but moderate agreement in ventilated dogs during anesthesia. Further investigations are necessary to determine factors that interfere with the agreement between PVI and PPV in dog.



Wednesday 2nd September | Event Hall

P-30 Post-operative pain levels related to surgical procedures in dogs.

○Yuuki Namiki, Jun Tamura, Yusuke Endo, Chika Higuchi, Kenjiro Miyoshi, Tadashi Sano, Kazuto Yamashita

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Anticipating post-operative pain level is an important factor for planning anesthetic and analgesic protocol and varies by surgical procedures. This study aimed to list various surgical procedures in order of post-operative pain levels in dogs.

We retrospectively investigated the results of peri-operative pain management in owner-owned 2,643 dogs (American Society of Anesthesiologists Class I or II) undergoing one of the 48 surgical procedures. In each dog, the anesthetic protocol including post-operative pain management was graded according to type and number of analgesics incorporated (peri-operative pain management score, POPMS). Additional pain management during the first 24 hours of post-operative period was also graded according to the type and number of analgesics administered to dogs (additional post-operative pain management score, APOPMS). Additional pain management index (APMI) was calculated by dividing the sum of APOPMS by the total number of dogs in each surgical procedure. Post-operative pain score (POPS) was calculated using a formula: POPS = (POPMS + APOPMS) x APMI. The POPS was compared among the surgical procedures using Mann-Whitney U test ($P < 0.05$).

The POPMS, APOPMS, and APMI ranged 2-30, 0-16 and 0-3.50, respectively. The maximum POPS was 45.5 ± 2.1 (mean ± standard deviation) for total ear canal ablation. The minimum POPS was 0.8 ± 1.2 for phacoemulsification and aspiration. The POPS was 0 for craniotomy and surgical excision of perianal tumors because no dog required additional post-operative pain management. The post-operative pain levels were classified in most severe (A-B), severe (C-E), moderate (F-J) and mild (K-N).

Post-operative pain levels in various surgical procedures in dogs.

Level		Surgical procedures (number of dogs/mean of post-operative pain score)
Most severe	A	Total ear canal ablations (6 dogs/45.5), Amputation (26 dogs/39.9), Nephrectomy (7 dogs/36.4)
	B	Pelvic fracture reduction (15 dogs/35.78), Liver lobectomy (23 dogs/34.75), Partial maxillectomy (35 dogs/32.52), Median sternotomy (9 dogs/32.4)
Severe	C	Arthrodesis (13 dogs/25.4), Intercostal thoracotomy (30 dogs/22.6), Intraocular silicone prosthesis-both eyes (10 dogs/20.2)
	D	Splenectomy (32 dogs/17.4), Radical cyctectomy (12 dogs/17.1), Lateral ear canal resection (16 dogs/14.6), Cholecystectomy (21 dogs/14.4)
	E	Tibial plateau leveling osteotomy (73 dogs/13.9), Tibial fracture reduction (10 dogs /13.3), Ventral slot (50 dogs/13.3)
Moderate	F	Ovariohysterectomy (25 dogs/11.7), Mastectomy (19 dogs/11.3), Humeral fracture reduction (15 dogs/10.9), Excision of anal sac adenocarcinoma (9 dogs/10.4), Cystotomy (5 dogs/10.3)
	G	Partial mandibulectomy (68 dogs/10.0), Thyroidectomy (12 dogs/9.9), Lumber lymph node dissection (9 dogs/9.5)
	H	Opthalmectomy (36 dogs/9.2), Femoral fracture reduction (21 dogs/8.9), Femoral head and neck osteotomy (28 dogs/8.8), Extracapsular reconstraction for ranial cruciate ligament rupture (17 dogs/8.1)
	I	Intraocular silicone prosthesis-one eye (138 dogs/7.6), Excision of mast cell tumor (45 dogs/7.1), Reduction of medial patellar luxation (57 dogs/7.0), Herniorrhaphy for perinieal hernia reduction (41 dogs/6.7)
	J	Stabilozation of hip luxation (24 dogs/5.5), Reduction of lateral patellar luxation (11 dogs/5.5), Hemilaminectomy (288 dogs/5.2)
Mild	K	Conjunctival flap plasty (36 dogs/3.6), Rectal pull-through approach for excision of rectal tumor (11 dogs/3.1), Exision of oral tumor (7 dogs/3.0)
	L	Occulusion of portal-systemic shunt using ameroid ring (20 dogs/2.8), Radial and ulnar fracture reduction (63 dogs/2.7), Permanent tracheostomy (7 dogs/2.5)
	M	Catration (4 dogs/1.6), Transarterial embolization for canine patent ductus arteriosus occlusion (7 dogs/1.4), Placement of tube shunt glaucoma surgery (25 dogs/1.2)
	N	Phacoemulsification and aspiration (118 dogs/0.8), Craniotomy (5 dogs/0), excision of perianal tumors (4 dogs/0)

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P-31 The anesthetic effect of intramuscular alfaxalone in dogs premedicated with a low-dose of medetomidine.

○Ken Nomoto[1], Jun Tamura[1], Yusuke Endo[1], Chika Higuchi[1], Mohammed Ahmed Umar[2], Kenjiro Miyoshi[1], Tadashi Sano[1], Kazuto Yamashita[1]

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An Intramuscular (IM) administration of alfaxalone at 7.5mg/kg produced anesthetic effect permitting endotracheal intubation in dogs (Tamura et al. JVMS 77: 289-296, 2015). This study aimed to assess the anesthetic effect of IM alfaxalone in dogs premedicated with a low-dose of medetomidine.

Six adult beagles (3 males, 3 females, 8.5 ± 1.0 kg) received three IM alfaxalone treatments following premedication with medetomidine (5 μg/kg, IM) at 7-days interval. The dogs were anesthetized with an IM injection of alfaxalone at a dosage of 1.0 (ALFX-1), 2.5 (ALFX-2.5), or 5.0 mg/kg (ALFX-5) at 15 minutes after the premedication and allowed to breathe room air. Neuro-depressive effects (behavior changes and subjective scores ranged from 0 to 19) and non-invasive cardio-respiratory parameters were evaluated before and at 2 to 120 minutes after each treatment. Data were analyzed using the paired *t* test, Friedman test and 2-way repeated measure ANOVA ($P< 0.05$).

All dogs progressed to lateral recumbency after the IM alfaxalone. The duration of lateral recumbency was longer in ALFX-5 than ALFX-1 (81 ± 28 versus 38 ± 15 minutes, $P = 0.013$). Endotracheal intubation was achieved in 4 dogs in ALFX-2.5 and 6 dogs in ALFX-5. The maximum neuro-depression scores were recorded at 15 minutes (median 16.5, range 15-17), from 15 to 20 minutes (18, 17-18), and from 5 to 20 minutes (18, 17-19) after the IM alfaxalone in ALFX-1, ALFX-2.5, and ALFX-5, respectively. The neuro-depression score in ALFX-5 was significantly higher than those in ALFX-1 ($P = 0.010$). Heart and respiratory rates ranged from 41-72 and 12-36 bpm in ALFX-1, 43-60 and 14-20 bpm in ALFX-2.5, and 53-68 and 9-27 bpm in ALFX-5, respectively. Hypotension and hypoxia were not observed after each treatment.

Premedication with low-dose medetomidine reduced the anesthetic dose of IM alfaxalone for endotracheal intubation but produced bradycardia in dogs.

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P-32 The anesthetic effect of intramuscular alfaxalone in cats premedicated with low-dose medetomidine.

○Haruka Shinozaki[1], Jun Tamura[1], Yusuke Endo[1], Chika Higuchi[1], Mohammed Ahmed Umar[2], Kenjiro Miyoshi[1], Tadashi Sano[1], Kazuto Yamashita[1]

[1)]School of Veterinary Medicine, Rakuno Gakuen University, [2)]Faculty of Veterinary Medicine, University of Maiduguri

An intramuscular (IM) injection of alfaxalone produced a dose-dependent sedative effect in cats (Tamura et al. JVMS 77: in press, 2015). This study aimed to assess the anesthetic effect of IM alfaxalone in cats premedicated with a low-dose medetomidine.

Five adult cats (3 males, 2 females, 3.9 ± 0.6 kg) received three IM alfaxalone treatments following premedication with medetomidine (5 μg/kg, IM) at 7-days interval. The cats were anesthetized with an IM injection of alfaxalone at 1.0 (ALFX-1), 2.5 (ALFX-2.5), or 5.0 mg/kg (ALFX-5) at 15 minutes after the premedication and allowed to breathe room air. Neuro-depressive effects (behavior changes and subjective scores ranged from 0 to 19) and non-invasive cardio-respiratory parameters were evaluated before and at 2 to 120 minutes after each treatment. Data were analyzed using the paired *t* test, Friedman test and 2-way repeated measured ANOVA ($P< 0.05$).

All cats progressed to lateral recumbency after the IM alfaxalone. The durations of lateral recumbency were 22 ± 15, 48 ± 6, and 69 ± 13 minutes in ALFX-1, ALFX-2.5, and ALFX-5, respectively. Endotracheal intubation was achieved in 2 cats in ALFX-2.5 and 3 cats in ALFX-5. The maximum neuro-depression scores were recorded at 20 minutes (median 15, range 11-17), from 10 to 15 minutes (18, 13-19), and from 10 to 30 minutes (19, 17-19) after the IM alfaxalone for ALFX-1, ALFX-2.5, and ALFX-5, respectively. The neuro-depression score with ALFX-5 was significantly higher than those with ALFX-1 ($P = 0.005$). Heart and respiratory rates ranged from105-172 and 25-54 bpm in ALFX-1, 97-175 and 18-56 bpm in ALFX-2.5, and 112-202 and 17-53 bpm in ALFX-5, respectively. Hypotension and hypoxia were not observed after each treatment.

IM alfaxalone produced a dose-dependent anesthetic effect and severe cardio-respiratory depression was not detected in this study.

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P-33 The effects of age and sex on anesthetic induction dose with alfaxalone or propofol in dogs.

○Mei Sugawara[1], Jun Tamura[1], Yusuke Endo[1], Chika Higuchi[1], Mohammed Ahmed Umar[2], Kenjiro Miyoshi[1], Tadashi Sano[1], Kazuto Yamashita[1]

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This study aimed to clarify the influence of aging and sex on anesthetic induction with alfaxalone or propofol in dogs.

Four hundred and eighty three owner-owned dogs (American Society of Anesthesiologists Class I or II) anesthetized for imaging diagnosis or radiation therapy were used. Anesthesia was induced with an intravenous injection of alfaxalone (n=211, ALFX) or propofol (n=272, PROP) and maintained with oxygen-sevoflurane. Total dose of alfaxalone and propofol required for endotracheal intubation (induction dose) and time from the cessation of sevofulrane to extubation (extubation time) were statistically compared using Student's *t* test, Welch's *t* test, one-way ANOVA with Bonferroni test ($P< 0.05$).

Total anesthetic durations were 29.2 ± 13.9 minutes in ALFX and 30.4 ± 11.6 minutes in PROP. There was no significant difference in induction doses between males (ALFX 2.3 ± 0.6 mg/kg in 138 dogs, PROP 5.4 ± 1.3 mg/kg in 141 dogs) and females (ALFX 2.2 ± 0.5 mg/kg in 73 dogs, PROP 5.5 ± 1.5 mg/kg in 131 dogs). The induction dose of alfaxalone was significantly reduced with aging (2.9 ± 1.2 mg/kg in 6 dogs aged 1-5 years, 2.3 ± 0.5 mg/kg in 59 dogs aged 6-9 years, 2.3 ± 0.6 mg/kg in 109 dogs aged 10-13 years, 1.9 ± 0.6 mg/kg in 37 dogs aged 14-17 years old, $P = 0.0003$). In ALFX, extubation time was significantly shorter in females (5.9 ± 3.4 versus 7.1 ± 3.4 minutes, $P = 0.015$) and prolonged with aging (4.3 ± 2.0 minutes in 1-5 years, 5.4 ± 2.8 minutes in 6-9 years, 7.2 ± 3.6 minutes in 10-13 years, 7.7 ± 3.6 minutes in 14-17 years old, $P = 0.0007$).

Practitioners should note the influences of aging and sex on the induction dose of alfaxalone and recovery from anesthesia in dogs. However, these effects were not severe.

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P-34 Pharmacokinetics and sedative effects of xylazine administered by intravenous and intramuscular routes in donkeys

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Pharmacokinetics (PK) of xylazine has not been described in donkeys. The aim of this study was to determine the PK profile of two doses of xylazine in this species, correlating plasma drug concentrations with sedative effects.

Eight healthy female Nordestino type donkeys, mean weight 139.2 ± 22 kg, aging from 3 to 8 years, were used in this study. All animals received two xylazine treatments (0.5 mg.kg i.v. and 1.0 mg.kg i.m), randomly administered at a seven days-interval. Blood samples were collected before and at points during 12 hours after administration. Plasma concentrations of xylazine were measured by liquid chromatography-mass spectrometry (LC-MS) and PK parameters were calculated using standard formulas. Sedative effects were evaluated by measuring head height (HH), degree of ataxia and response to auditory stimulus scores. Statistical analysis was performed by Wilcoxon sum rank and paired t tests ($P < 0.05$).

Decreases of plasma xylazine concentration over the time were best described as an one-compartment model. Bioavailability of xylazine administered to donkeys by intramuscular route was 77%. Volume of distribution (Vd), elimination half-life ($t_{1/2\beta}$) and clearence (Cl) calculated for i.v. and i.m. routes were respectively: 324.0 and 749.2 mL.kg; 23.2 and 53.3 minutes; 9.88 and 9.74 mL.min.kg. Effective sedation was observed with intravenous treatment, from 5 to 20 minutes after drug administration. Only mild sedative effects were recorded after intramuscular injection, at 20 and 30 minutes. Xylazine plasma concentrations mean values measured were 1.22 ± 0.25 and 0.97 ± 0.18 μg.mL (i.v.) at 6 and 30 minutes, and 0.89 ± 0.28 and 0.95 ± 0.23 μg.mL (i.m.) at 15 and 30 minutes, after administration.

Sedation with xylazine in donkeys was correlated with plasma concentrations measured and routes of administration. PK data reported can be used to properly calculate dosage regimens of this drug in the asinine species.

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P-35 Anesthetic efficacy of 1% ropivacaine administered in two different volumes, with or without sodium bicarbonate 0.33%, after peribulbar blockade guided by ultrasound in dogs.

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Large volumes of anesthetics can elevate the intraocular pressure and increase the occurrence of ophthalmic complications. The use of the adjuvants increase the effects of this drugs using lower volumes, when compared with the drug used alone, reducing the possibility of complications during the procedure. These study aimed to compare the anesthetic efficacy of 1% ropivacaine used in two volumes, the reduction of the anesthetic volume when the peribulbar blockade was performed by ultrasound, and the increase of the anesthetic action with the use of 0.33% sodium bicarbonate as an adjuvant. Five dogs were anesthetized four times, with an interval of one week, with isoflurane to perform the peribulbar blockade guided by ultrasound with 1% ropivacaine (0.1 and 0.2 mL.Kg-1) with 0.33% sodium bicarbonate (0.02 mL) and without the adjuvant using the same volumes. Thirty minutes after the blockade, with the animal awake, the durations of the motor blockade (fotomotor reflex, conjugate movement of eyes and ptosis), sensitive blockade (corneal esthesiometry) and lacrimal production were evaluated every 15 minutes during the first hour and every 30 minutes until the return of the basal parameters. No statistical difference of the tear production (p=0.09), the sensorial blockade (p=0.23), eyes conjugate movement (p=0.41) and palpebral ptosis (p = 0.82) were found. Statistical difference was found with the fotomotor reflex (p=0.03) however the difference between the groups were not possible, once the test had no sensibility to identify this difference. It is concluded that the use of the lower anesthetic volume is enough to provide anesthesia and the addition of the bicarbonate didn' t provide the increase of the blockade, however the high mean and median values indicate that the volume of 0.2 mL.kg-1 and the addition of bicarbonate, in both volumes, should be indicated for prolonged procedures.

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P-36 Prolonged surgical anaesthesia using tricaine methanesulfonate (MS-222) in fire salamander (*Salamandra salamandra*) - a case series

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Objective: To report a case series of prolonged recovery anaesthesia in fire salamanders (Salamandra salamandra)
Study Design: Case series
Animals: Fifteen healthy salamanders were anaesthetised for electromyography wires implantation for research purposes. Mean body weight was (mean ± SD) 24 ± 3.24 g.
Methods: Sodium bicarbonate buffered solutions (0.5 to 4 g L^{-1}) of Tricaine Methanesulfonate (MS-222) were prepared in dechlorinated water and adjusted to pH 7.0. Anaesthesia was induced by partial immersion in pre-oxygenated 3g L^{-1} solution for 20 minutes. Buprenorphine 0.5 mg $kg^{-1}$was administered subcutaneously midway through induction. During microsurgery, heart rate (HR), pH and water temperature were recorded. Reflectance SpO_2) (Masimo Rad57) was recorded in two salamanders. Anaesthesia depth and pH stability (< 7.6) were maintained by constantly renewing administration of oxygenated MS-222 solution (0.5 to 3 g L^{-1}) onto swabs that partially covered the body. Recovery stated at the end of the surgery (MS-222 0 g L^{-1}) and time to first sign of recovery was recorded. Postoperatively all salamanders received orally meloxicam (0.2 mg kg^{-1}). Significance was set to P <0.05 (SPSS 22).
Results: Duration of anaesthesia and time to recovery were 111 ± 12.1 and 31 ± 10.3 minutes, respectively. The time-averaged MS-222 concentration 1.75 g L^{-1}. Two salamanders did not recover (one experienced substantial haemorrhage). Baseline HR was 67.4 ± 34.5 beats min^{-1} and decreased significantly 15 minute intervals until recovery (Mixed effect model, P <0.0005). There was no correlation between the length of anaesthesia and time to recovery (Linear regression P = 0.7198). In 2 salamanders, baseline SpO_2 was 85.5% ± 14.5, dropped to 61% ± 6.4 during surgery and improved to 80.5 % ± 2.1 on recovery.
Conclusion and clinical relevance: Prolonged recovery anaesthesia can be achieved with MS222 dilutions and multimodal analgesia. Reflectance SpO_2 could prove valuable during immersion anaesthesia

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P-37 Epidural catheter long-term implantation in cows

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After being restrained in a stock eight adult cows were sedated (0.04 mg/kg acepromazine + 0.01 mg/kg xylazine IM). The upper coccygeal and right gluteus regions were clipped and surgically prepared. Lidocaine 2% (10mL) was infiltrated in the subcutaneous tissues (SC) around these regions. A semicircular 8 cm incision over the sacrococcygeal area was advanced to expose the SC space. A 16G Tuohy needle was inserted into the epidural space. A 17G Port-a-cath® epidural catheter was introduced and advanced 10 cm cranially. The Tuohy needle was removed and the catheter was maintained in tthe epidural space. Subsequently, a skin incision (4 cm) was performed right gluteus region. The external catheter's extremity was tunneled and transposed through the gluteal skin incision using a pin guide. The end point of the catheter was adjusted to fit the port access external connection and screwed into place. Then, the port was buried in the SC space. Catheter patency and leakage were tested by injection of 1 mL of sterile distilled water through the access port. Skin incisions were closed with 1-nylon simple pattern. The cows were examined daily and sutures removed after 15 days. The epidural catheter patency was evaluated by tail relaxation and perineal sensitivity loss, every 15 days after the injection of 3 mL of 2% lidocaine and flushing with 1 mL of sterile distilled water. The surgical implantation process of the Port-a-cath® epidural catheter is of medium complexity. Tail relaxation and low sensitivity perineal were observed after lidocaine injection. The Port-a-cath® system function remained over 162, 141, 127, 113 and 52 days, respectively for the first two cows implanted on 02/02 until the last one operated on 05/18. There were no signs of obstruction or lack local anesthesia efficacy. In conclusion, the implantation has shown to be feasible to provide repetitive epidural anesthesia.
Acknowledgements: FAPESP #2014/25036-0 *Animal Care Committee #024902/14.

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P-38 Cardiorespiratory effects of morphine in chickens anesthetized with isoflurane

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Morphine (6 mg kg-1) decreases isoflurane minimum anesthetic concentration (MAC) in chickens by 22% after 15 minutes of administration (Escobar et al., 2014). The cardiorespiratory effects of morphine-isoflurane association were evaluated in seven chickens. After anesthesia induction with isoflurane, via face mask, animals were intubated, connected to a Bain circuit and maintained with isoflurane in 100% oxygen under spontaneous ventilation. End-tidal isoflurane was adjusted to 1.0 individual MAC, which was previously determined. For blood gas and electrolytes sampling, and for mean arterial pressure (MAP) monitoring, the ulnar artery was catheterized. Cloacae temperature (T), partial pressure of end-tidal carbon dioxide (PETCO2), heart rate (HR) and rhythm and respiratory rate (f) were recorded. Baseline values were recorded 30 minutes after induction (T1MAC), and subsequently, end-tidal isoflurane was regulated to 0.8 bird's individual MAC. After 15 minutes, physiologic data was recorded (T0.8MAC) and 6 mg kg-1 of morphine was administered IM. Cardiorespiratory responses were evaluated after 1, 5, 10, 15, 30 and 45 minutes (T1 to T45) of administration. To compare data RM ANOVA was used. Morphine induced ventricular premature contractions in four animals. Mean baseline values (T1MAC) were: HR (220 beats minute-1), f (15 breaths minute-1), MAP (95 mmHg), PETCO2 (45 mmHg), T (40.6 ° C), pH (7.43), PaCO2 (36 mmHg), HCO3- (23 mmol L-1), BE (-0.44 mmol/L), sodium (157 mmol L-1), chloride (117 mmol L-1) and calcium (1,07 mmol L-1), and there were no statistical difference from values after morphine administration. PaO2 increased from T1MAC (291 mmHg) at T45 (343 mmHg) and potassium (2.8 mmol/L) increase from T1MAC at T15 (3.2 mmol L-1), T30 (3.2 mmol L-1) and T45 (3.1 mmol L-1). Morphine dosage that produces isoflurane MAC reduction in chickens did not induce hemodynamic and respiratory changes, however electrocardiogram monitoring is recommended due to development of arrhythmias.

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P-39 Comparison of the localization and expression level of μ- and κ-opioid receptors in CNS and DRG between dogs and cats

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Opioid receptor agonists such as morphine or fentanyl have been widely used in various animal species to control moderate to severe pain, but wide interspecies variability in the effects of opioids has been reported. We previously showed that the inhibitory effect of μ-opioid agonist to the sympathetic reflex induced by noxious stimuli was much weaker in cats than in dogs. However, the factors contributing to this variability remain unclear.

This study was approved by the Animal Care Committee of the Graduate School of Agricultural and Life Sciences at the University of Tokyo. In the present study, we compared the localization and expression level of μ-opioid receptor (MOR) and κ-opioid receptor (KOR) in brain, spinal cord and dorsal root ganglia (DRG) between dogs and cats. The localization and expression level of MOR and KOR were evaluated by immunohistochemistry (IHC) and quantitive PCR (qPCR), respectively.

Localization pattern of MOR and KOR shown in IHC were similar in dogs and cats, while the expression levels of MOR and KOR by qPCR were different in some regions and the most significant differences were found in DRG. The expression level of MOR in DRG was much higher in dogs than in cats, and that of KOR was higher in cats than in dogs.

The dorsal root fibers are known to transmit the signal induced by noxious stimuli to the central nervous system. Opioids are known to inhibit this neurotransmission by stimulation of the opioid receptor in DRG. The difference of MOR expression level in DRG, shown in this study, may be associated with the difference of anti-sympathetic reflex potency in dogs and cats.

Further functional and electrophysiological investigation is necessary to identify the mechanism of interspecies variability of opioids.

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P-40 Effects of dexmedetomidine as an adjuvant to ropivacaine on femoral and sciatic nerve blocks in dogs.

○Valeria Nobre Leal de Souza Oliva, Thomas Alexander Trein, Beatriz Perez Floriano, Juliana Tessalia Wagatsuma, Guilherme Lopes da Silva, Paulo Sergio Patto dos Santos

Sao Paulo State University (UNESP)

This study aimed to evaluate the motor and sensory effects of adding dexmedetomidine to ropivacaine, administered perineurally or systemically, for unilateral femoral and sciatic nerve blocks in dogs. Seven healthy beagle dogs, aged 3.3±0.08 years and weighing 11.0±2.35 kg were submitted to three experimental groups which received perineural (0,1 mL/kg/nerve) and intramuscular injections (0,2 mL/kg) as follows: Gcon, perineural ropivacaine 0,743% and intramuscular saline; Gdpn, perineural dexmedetomidine (1 μg/mL) diluted in ropivacaine 0,75% (0,743% solution) and intramuscular saline; and Gdin, perineural ropivacaine 0,743% and intramuscular dexmedetomidine (1 μg/mL) diluted in saline. Blocks were performed under general inhalation anesthesia and guided by ultrasound and electrolocation. Degree and duration of motor blockade were assessed by evaluating ability to walk and proprioception, while degree and duration of sensory blockade were assessed through the response to a Kelly clamp pressure on the skin innervated by the saphenous/femoral, tibial and common fibular nerves. Following Shapiro-Wilk normality test, differences between groups were analyzed using Friedman's Test and Student-Newman-Keuls post-hoc test. Differences were considered statistically significant when $p<0.05$. Data regarding saphenous/femoral nerve sensory blockade in one dog and common fibular and tibial nerves sensory blockade in another dog were disregarded due to block failure. Motor blockade onset time and duration were not significantly different between groups. Sensory onset time of the blocks were not significantly different between groups, however, duration of tibial nerve sensory blockade was increased in Gdpn compared to Gdin [median (min-max), 322.5 (240-360) vs 255 (105-345) minutes, $p=0.0302$], but similar to Gcon [232.5 (120-570) minutes]. At the doses used in this study, addition of perineural or systemic dexmedetomidine to ropivacaine did not affect motor blockade onset or duration, or sensory blockade onset, of femoral and sciatic nerve blocks. However, a prolongation of the tibial nerve sensory blockade was observed when dexmedetomidine was administered perineurally.

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P-41 Arterial blood gas analysis in pigs anesthetized with propofol, associated or not with nitrous oxide at 50% and kept in spontaneous ventilation or controlled pressure with or without PEEP.

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The aim of this study was to evaluate the effects of anesthesia with propofol associated to nitrous oxide or air in FIO_2 of 50%. Sixteen pigs (Large White; 15-20 Kg) were divided into two groups (GN50 and GA50). Azaperone (2 mg/Kg) followed by propofol was administrated to allow tracheal intubation, then continuos infusion of propofol (0.5 mg/kg/minute) was started. Animals received nitrous oxide diluted in 50% oxygen in GN50 and oxygen diluted with air at 50% in GA50. The first blood sample (femoral artery) was taken 125 minutes after induction, during the phase of spontaneous breathing. Pressure controlled ventilation (PCV) was instituted and after 60 minutes there was the second sample, followed by PEEP (5 cm H_2O) and 3 new measurements with 15 minute of intervals each. Data were analyzed by ANOVA followed by Bonferroni test ($p < 0.05$). In this study, the offer 0.5 of nitrous oxide or air did not interfere on the oxyhemoglobin saturation and partial pressure of oxygen, proving to be safe. $PaCO_2$ and pH seems to be similarly influenciated, with improvement in ventilatory support phase compared to spontaneous breathing, getting worse when PEEP was setted. Adverse hemodynamic effects may occur even with lower values of PEEP than recommended (5 cm H_2O). In conclusion, the offer of 50% nitrous oxide or air with spontaneous ventilation or PCV with or without PEEP is sufficient to maintain the PaO_2 and SaO_2 at physiological levels, but do not permit proper maintenance of the pH and $PaCO_2$, during spontaneous or mechanical ventilation, with PEEP offer.

Table 1. Mean and standard deviation values ($\bar{x} \pm s$) of arterial blood gas parameters in pigs (n = 16) anesthetized with propofol associated or not with nitrous oxide at 50% and mantained in spontaneous or pressure controlled ventilation with or without PEEP - Jaboticabal, SP, Brazil - 2015.

		Moments				
Parameter	Group	M_0	M_060	M_375	M_390	M_3105
PaO_2 (mmHg)	GN50	184,8±54,1	201,5±28,3	186,2±32,7	177,9±44,3	196,0±52,4
	GA50	184,5±46,2	212,3±33,1	192,1±25,0	197,5±23,4	207,1±25,4
SaO_2 (%)	GN50	98,0±3,3	99,6±0,2	99,3±0,5	98,7±1,7	98,3±2,9
	GA50	98,4±2,2	99,3±1,3	99,4±0,3	99,4±0,4	99,5±0,3
$PaCO_2$ (mmHg)	GN50	80,4±21,8a	41,4±9,0b	63,5±15,8	68,9±23,4a	73,3±33,3a
	GA50	68,3±26,0a	43,6±8,7b	56,0±10,7	55,8±5,6	61,6±16,2a
pH	GN50	7,201±0,09a	7,357±0,07b	7,281±0,07c	7,255±0,10ac	7,257±0,13ac
	GA50	7,259±0,15a	7,422±0,06b	7,345±0,07	7,343±0,08	7,315±0,08a

Means followed by different lowercase letters, lines differ ($p<0.05$).

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P-42 Bradycardia suspected to be induced by trigeminocardiac reflex during total ear canal ablation in a dog

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Signalment: A 14 kg, 9-year-old, spayed female, Cocker Spaniel was presented to the Veterinary Teaching Hospital of Seoul National University (VMTH-SNU) with a history of head tilt and circling. Otitis media had been diagnosed by computerized tomography imaging, and total ear canal ablation was performed. In preanesthetic evaluation, systemic hypertension and second degree atrioventricular block was observed, but there was no regurgitation through the valve. Systemic hypertension was managed with amlodipine (0.1 mg/kg, PO, BID) for the anesthesia.
Results: The dog was premedicated with cefazolin (22 mg/kg, IV) and midazolam (0.2 mg/kg, IV). Anesthesia was induced with alfaxalone (2 mg/kg, IV) and maintained with isoflurane following intubation. During the surgery, most vital signs (respiratory rate, blood pressure, end tidal CO2 and body temperature) were maintained in normal values, but bradycardia was corrected by glycopyrrolate (5 μg/kg, IV) two times. During skin closure, electrohemostasis was performed at the incision line anterior to the ear canal which was thought to be close to the trigeminal nerve. In no time at all, heart rate dramatically decreased from 110 to 60 beats per minute. No additional treatment was done because mean blood pressure was maintained above 70 mmHg. The heart rate recovered according to the decrease of end tidal isoflurane concentration and there were no complications associated with the anesthesia and surgery.
Clinical relevance: Sudden bradycardia after electrical stimulation around the trigeminal nerve was believed to be trigeminocardiac reflex (TCR). It is recommended to be careful of bradycardia from TCR when electrocautery is used in the craniofacial area during surgery.

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P-43 Do oxygen content or oxygen tension based indices reflect intrapulmonary shunting in anaesthetised horses with varying mixed venous oxygen content?

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Venous admixture (Q_S/Q_T) is calculated by the shunt equation. For oxygen content- or tension based indices mixed venous blood is not needed, but they may still be used to estimate venous admixture.
Nine Standardbred horses (481 ± 62 Kg) were anaesthetised in a randomised cross over study. After premedication with 8 μg/kg dexmedetomidine IV, anaesthesia was induced with 2.5 mg/kg ketamine and 0.05 mg/kg midazolam IV followed by endotracheal intubation. Anaesthesia was maintained with isoflurane in a mixture of oxygen and air and an intravenous infusion of either dexmedetomidine or placebo. IPPV was instituted with a respiratory rate of 6 breaths/min, I:E ratio 1:2 and PEEP 3 cm H_2O. Tidal volume was adjusted to maintain E_TCO_2 between 5.0-6.5 kPa. Fractioned inspired oxygen concentration was adjusted from a minimum of 30 % to maintain PaO_2> 12 kPa. The facial and pulmonary arteries were catheterised and arterial and mixed venous blood were sampled simultaneously into heparinised blood gas syringes and immediately analysed at regular intervals from 75 minutes after induction until end of anaesthesia.
The following calculations were made: CaO_2, CvO_2 and CcO_2: CxO_2 = (1.34 x Hb x SxO_2) + (0.0225 x PxO_2), Venous admixture Q_S/Q_T = [(CcO_2-CaO_2) / (CcO_2-CvO_2)] x 100, FShunt = [(CcO_2-CaO_2) / (CcO_2-CaO_2-3.5)] x 100, PA-aO_2 = F_IO_2 (Pb-PH_2O) – $PaCO_2$/R and PaO_2/ F_IO_2. Q_S/Q_T was compared to FShunt, PA-aO_2 and PaO_2/F_IO_2 respectively using a linear regression model at three different levels of CvO_2 (7.46-10.79(1), 10.87-14.17(2), 14.43-17.67(3) ml O_2/100 ml blood)

At all levels of CvO_2 FShunt (R^2adj = 0.82(1), 0.90(2), 0.96(3)) explained more of the variability in QS/QT than either PA-aO_2 (R^2adj = 0.81(1), 0.87(2), 0.63(3)) and PaO_2/ F_IO_2 (R^2adj = 0.78(1), 0.88(2), 0.50(3)).

All indices explained Q_S/Q_T, but FShunt performed better than the tension based indices examined.

Ethical approval: The study was approved by the Norwegian Laboratory Animal Research Authority, ID no 2012/265642

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P-44 Effects of Tiletamine and Zolazepam on Intraocular Pressure in Dogs

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Purpose: This study was performed to determine the effect of tiletamine-zolazepam (TZ) on canine intraocular pressure (IOP).
Materials and Methods: Six clinically healthy beagle dogs (six male, with a mean age ± standard deviation [SD] of 2.0 ±1.0 years old and a mean body weight of 9.2±1.4 kg) without ocular abnormalities were used. The study was carried out as a cross-over experimental trial with a 7-day interval between treatments. TZ combination was administered intravenously (IV) at a dose of 5, 10, and 20 mg/kg (TZ5, TZ10, and TZ20, respectively). Following initial readings of IOP, each dog received IV TZ and then the IOP values were measured every 10 min for 40 min in all treatments. A one-way ANOVA with repeated measures was used to evaluate within-group changes in IOP over time and compare the IOP of each group at each measurement using Bonferroni' s post hoc method.
Results: The baseline IOP values (mean ± SD) for TZ5, TZ10, and TZ20 were 12.7±0.8, 14.4±1.2, and 15.3±1.7 mmHg, and each IOP changed to 11.1±1.1, 13.1±1.4 and 13.5±1.7 mmHg after IV administration of each TZ treatment, respectively. However, there were no statistical differences between baseline and post-treatment values.
Conclusion: The TZ combination had no clinically significant effect on IOP of the dog. This could be an option for induction or surgical procedures in dogs with ophthalmic problems when an increase in IOP is undesirable.

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P-45 The vasopressor and microcirculatory effects of vasopressin in dogs with severe sepsis that underwent surgery.

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Objectives: The aim of this project is to evaluate the use of vasopressin in the treatment of septic hypotension due to pyometra in dogs who underwent surgery, using spectral image obtained by orthogonal polarization(OPS) .
Methods: Six dogs in severe sepsis were used, each presenting at least two variables of systemic inflammatory response and at least one organ dysfunction variable at baseline. Anesthesia was established by the administration of meperidine (3mg / kg) intramuscularly as premedication , induction with propofol at a dose of 3-5 mg / kg , maintenance with isoflurane in the fraction of inspired oxygen (FiO 2) of 90 % and a fraction expired isoflurane (ETIso) maintained at 1.4% (1 MAC) , and when necessary adjustment was carried out to keep the anesthesia the animal during surgery . All animals received a bolus of 3mcg / kg fentanyl, 5 minutes before being sectioned ovarian pedicle. In all animals initial volume resuscitation was performed with 15ml / kg in 15 minutes of Ringer's lactate solution. If, during anesthesia, mean arterial pressure did not assume values greater than 65 mmHg and central venous pressure did not vary 2 mmHg or present values greater than 8 mmHg (time point T0), these animals initially received an infusion at a dose of 0,0002UI / kg / min of vasopressin. The initial dose may have increased incrementally by 0,0002U / kg / min in order to achieve MAP above of 65 mmHg (time point TG), with maximal dose of the 0,001 U/kg/ min. Real-time images were collected with the probe positioned in sublingual mucosa, 4 cm below the tip of the tongue.The images collected using OPS, were processed and analyzed by specific software. The variables were analyzed by ANOVA (analysis of variance) for repeated measures followed by Tukey's test , allowing the comparison of different times of observation. The level of significance for analysis was $p < 0.05$.
Results: In all animals only the dosage of the 0,001 U/kg/ min was effective to rescue the MAP to above 65mmHg. There was no difference in T0 (MAP <65mmHg) in the Microvascular Flow Index (MFI) 1,63 ± 0,30, De Backer score (DBS) 12,27 ± 2,49 and Total Vessel Density (TVD) 18,02 ± 1,92 in comparison with the values of TG (MAP < 65 mmHg) MFI 1,30 ± 0,32, DBS 11,51 ± 3,37 and TVD 17,13 ± 2,43 ($p>0,05$). The heart rate was lower in the TG 63 ± 15,38 in comparison to the time T0 13O ± 38,4.
Conclusions: Doses of vasopressin below 0.001U/ kg/ min are not effective to restore the blood pressure. Vasopressin infusion at a dose of 0.001U/kg/min does not affect the microcirculation in these study circumstances.

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P-46 Acute Peripheral Gangrene of Newborn Puppies after Cesarean Section

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Signalment: A pregnant Maltese (2-years-old, intact female, 2.1 kg), which had five fetus confirmed by radiography and ultrasonography, underwent cesarean section because of delayed delivery.
Results: Preoperative vital signs of the bitch were stable except for mild depression. Cefazolin (30 mg/kg) and tramadol (2.5 mg/kg) were administrated intravenously (IV) as premedication. Anesthesia was induced with mixed anesthetic of ketamine (2 mg/kg) and medetomidine (0.02 mg/kg) IV. During 15-minute surgery, fluid (lactated Ringer's solution with vitamin B, C and 2.5% dextrose) were administered at a rate of 10 ml/kg/hr. After surgery, the bitch recovered from the anesthesia in 2 hours, and five puppies (M1/F4) were stabilized in an incubator for 30 minutes. All puppies had no congenital malformation in appearance, but they were under sedation with bradycardia constantly. A drop of atipamezole diluted one to ten with distilled water was dripped at sublingual region to antagonize the effect of medetomidine, and then they began active movement and increase of heart rate. After two hours, there were bluish discoloration on the distal part of the ears, limbs and tail in three infants. Over several days, the lesions resulted in dry gangrene and separation, but no treatment was performed. One puppy died after a week. The affected lesions underwent autoamputation and reconstruction in a month, and no other disorders were observed.
Clinical relevance: Peripheral vascular constriction by medetomidine may cause acute peripheral ischemia and gangrene after cesarean section. It is recommended to avoid use of medetomidine for cesarean section in dogs.

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P-47 Total intravenous anesthesia using drug combination of medetomidine, lidocaine, butorphanol, and propofol (MLBP-TIVA) in horses.

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This study is aimed at assessing the clinical usefulness of total intravenous anesthesia using a drug combination of medetomidine, lidocaine, butorphanol, and propofol (MLBP-TIVA) in horses.

Fifteen horses [6.7±6.0 years-old (mean ± standard deviation), 443±87kg] underwent various soft tissue surgeries in an operating room (OPR group) and 19 horses (5.9±5.6 years-old, 466±90kg) were castrated on the field (FLD group) under MLBP-TIVA. All the horses were premedicated with intravenous medetomidine (5 μg/kg) and butorphanol (20 μg/kg), anesthetized with intravenous lidocaine (1mg/kg) and propofol (3mg/kg), and surgical depth of anesthesia was maintained by controlling the infusion rate of propofol combined with constant rate infusions of medetomidine (3.5 μg/kg/hr), lidocaine (3mg/kg/hr), and butorphanol (24 μg/kg/hr). Following endotracheal intubation, the horses breathed 100% oxygen in OPR group or air in FLD group.

Following anesthetic induction, transient paddling was observed in 8 and 12 horses of OPR and FLD groups, respectively. Total anesthetic duration was 95 ± 45min (range 57-195min) in OPR group and 36 ± 8min (range 20-63min) in FLD group. The propofol infusion rates required for maintaining surgical anesthesia were 0.12±0.03mg/kg/min in OPR group and 0.09±0.03mg/kg/min in FLD group. During anesthesia, cardio-respiratory parameters were maintained within clinically acceptable range in all horses, although artificial ventilation was required to support respiratory function in 13 horses of OPR group. The horses recovered uneventfully and stood at 61±34 and 33±6min after the cessation of MLBP-TIVA in OPR and FLD groups, respectively. In OPR group, one horse had prolonged recovery after 59 min of anesthetic duration and stood at 138min after the cessation of MLBP-TIVA.

In conclusion, MLBP-TIVA is a multipurpose anesthetic procedure for both prolonged anesthesia and short-term field anesthesia in horses. Attention should be given during anesthetic induction with propofol and resulting respiratory depression during prolonged anesthesia in horses anesthetized with MLBP-TIVA.

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P-48 Agreement between observers on postoperative pain and sedation assessment in cats

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The aim of this study was to evaluate the agreement between two observers on postoperative pain and sedation scores in cats using similar instruments in two different languages.

Forty-five cats were included in a randomized, controlled, prospective, blinded study after owners' written consent. An ovariohysterectomy was performed using the same anesthetic protocol. Three different analgesic protocols were studied including a testing group (TG), positive control (PG) and negative control (NG) (Benito et al. 2015). Postoperative pain and sedation was evaluated using a dynamic interactive visual analog scale (DIVAS). Pain was also evaluated using the UNESP-Botucatu multidimensional composite pain scale (MCPS). Assessments were made by one observer using the English, and the other using the French version of the MCPS. Rescue analgesia was given if MCPS > 6 using the English version. The intra-class correlation coefficient (ICC) was used to evaluate agreement between observers. The percentage of disagreement between observers for rescue analgesia (DBORA, pairwise comparison that one observer would have given rescue analgesia, but not the other) was calculated.

The ICC was 69.8% and 70% for DIVAS pain scores and MCPS, respectively, indicating a good agreement between observers. The ICC was 20.4% for DIVAS sedation scores indicating a poor agreement between observers. The DBORA was 6.1% but only in 2.2% of the cases, the outcome for rescue analgesia would have changed. In Benito's study, rescue analgesia was significantly lower in TG and PG than NG (TG = PG > NG). Results would have been different if data from the second observer were considered. Rescue analgesia in TG would not have been significantly different than PG and NG, but PG > NG.

The poor agreement between observers on sedation scores did not affect pain scoring assessment. However, the main outcome (rescue analgesia) would have changed.

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P-49 Respiratory effects of one-lung ventilation in dogs anesthetized with propofol or isoflurane

○Valéria Nobre Leal Souza Oliva, Thomas Alexander Trein, Juliana Tessalia Wagatsuma, Joana Zafalon Ferreira, Renata Haddad Pinho, Paulo Sergio Patto Santos, Valéria Nobre Leal Souza Oliva

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One-lung ventilation (OLV) is technique that aims at separating different ventilation protocols to each side of the thorax. The aim of this study was to assess the implications of OLV in dogs undergoing different protocols of general anesthesia. Six healthy adult beagle dogs (two males and four females) weighing 11.5 ± 2.38 kg were anesthetized three times, comprising three experimental groups: constant rate infusion of propofol at 0.4 to 0.8 mg kg^{-1} $minute^{-1}$ (GP); isoflurane at 1 MAC (minimum alveolar concentration; GI1); and isoflurane at 1.5 MAC (GI1.5). Mechanical ventilation was initiated at a peak pressure of 15 cmH_2O, positive end-expiratory pressure of 5 cmH_2O and respiratory rate adjusted between 20 to 30 movements $minute^{-1}$. The subjects were maintained at an initial two-lung ventilation (TLV) for 30 minutes (TLV30i), then at OLV for 1 hour divided in 3 time points (OLV20, OLV40 and OLV60, respectively) and back to TLV for the final 30 minutes (TLV30f), comprising 2 hours of anesthesia. OLV was achieved using a double-lumen endotracheal tube placed in the left bronchus. At each time point, venous admixture (Qs/Qt in %), alveolar-arterial oxygen gradient ($P(A\text{-}a)O_2$ in mmHg), arterial carbon dioxide ($PaCO_2$ in mmHg) and tidal volume (V_T) were recorded. Data were analyzed for normal distribution, followed by analysis of variance for repeated measures and Tukey's test at 5% significance. There was significant difference between GI1 and GI1.5 at OLV60 in Qs/Qt and OLV40 in V_T. The $PaCO_2$ was significantly higher and V_T lower during OLV compared to TLV30i in all groups. There was an increase in $P(A\text{-}a)O_2$ and Qs/Qt during OLV compared to TLV30f in GI1.5. In conclusion, OLV with either propofol or isoflurane increases CO_2 in a similarly. However Qs/Qt and $P(A\text{-}a)O_2$ are more increased by the association of OLV and isoflurane at the higher concentration (1.5 MAC).

Table 1. Mean ± standard deviation of respiratory variables obtained from six dogs anesthetized with constant rate infusion of propofol (GP) or isoflurane at 1 or 1.5 MAC (GI1.0 and GI1.5, respectively) during two hours of anesthesia, divided in 30 or 20 minute intervals under two-lung (TLV) or one-lung (OLV) ventilation of the right lung.

Variável	Grupo	Momento de avaliação				
		VBP30	VMP20	VMP40	VMP60	VBP30
Qs/Qt (%)	GP	1.1 ± 0.49	1.6 ± 0.91	1.3 ± 0.92	1.5 ± 1.11	1.2 ± 1.04
	$GI_{1,0}$	1.2 ± 0.66	1.5 ± 0.97	1.5 ± 0.99	0.9 ± 0.44 *	1.3 ± 0.73
	$GI_{1,5}$	1.8 ± 0.77 ^{ab}	2.3 ± 1.31 ^{a}	2.2 ± 0.97 ^{ab}	2.3 ± 1.17 * ^{ab}	1.2 ± 0.60 ^{b}
$P(A\text{-}a)O_2$ (mmHg)	GP	111 ± 64.6	145 ± 75.9	127 ± 74.8	138 ± 80.6	97 ± 67.8
	$GI_{1,0}$	132 ± 55.6	156 ± 73.5	155 ± 78.1	119 ± 34.5	154 ± 90.6
	$GI_{1,5}$	170 ± 97.9 ^{ab}	215 ± 64.8 ^{ab}	222 ± 62.7 ^{a}	205 ± 77.7 ^{ab}	139 ± 72.0 ^{b}
$PaCO_2$ (mmHg)	GP	44.8 ± 7.42 ^{c}	53.2 ± 8.80 ^{ab}	54.6 ± 7.28 ^{ab}	56.0 ± 7.55 ^{a}	48.7 ± 7.23 ^{bc}
	$GI_{1,0}$	48.6 ± 10.26 ^{b}	64.0 ± 16.26 ^{a}	65.8 ± 4.67 ^{a}	65.6 ± 10.24 ^{a}	53.9 ± 11.39 ^{ab}
	$GI_{1,5}$	45.7 ± 3.48 ^{b}	54.7 ± 5.10 ^{ab}	57.5 ± 11.02 ^{a}	61.1 ± 10.26 ^{a}	53.0 ± 13.42 ^{ab}
V_T (mL kg^{-1})	GP	3.8 ± 1.09 ^{a}	2.3 ± 0.93 ^{b}	2.4 ± 0.75 ^{b}	2.3 ± 0.75 ^{b}	4.2 ± 0.99 ^{a}
	$GI_{1,0}$	3.7 ± 0.85 ^{a}	2.0 ± 0.77 ^{b}	1.9 ± 0.89 * ^{b}	1.9 ± 0.82 ^{b}	4.1 ± 0.51 ^{a}
	$GI_{1,5}$	4.1 ± 0.72 ^{a}	2.5 ± 0.49 ^{b}	2.8 ± 0.77 * ^{b}	2.8 ± 0.55 ^{b}	4.5 ± 0.75 ^{a}

* Means followed by an asterisk on lines (groups) or letters on columns (time points) are significantly different according to Tukey test ($p<0.05$). MAC = minimum alveolar concentration; Qs/Qt = venous admixture; $P(A\text{-}a)O_2$ = alveolar-arterial oxygen gradient; $PaCO_2$ = arterial carbon dioxide tension; V_T = tidal volume.

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P-50 Effects of the epidural administration of three different doses of tiletamine-zolazepam in dogs

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Epidural administration of drugs is commonly used to provide regional anesthesia and analgesia. The aim of this study was to evaluate the anesthetic effects of the epidural administration of three different doses of Tiletamine-Zolazepam (TZ) in dogs.

Forty healthy dogs (20 males and 20 females) (3.5+/-1.5 years old) (14.2+/- 2.3 kg BW) were included in a randomized, prospective, controlled, blinded experimental study. After induction with propofol (6 mg/kg IV) an epidural catheter was placed in the lumbosacral epidural space. Once the dogs recovered from propofol anesthesia, animals were administered with one of the following treatments, (5 males and 5 females/group): Control (CS) (Saline 0.9%, 0.25 mL/kg, n=10), TZ-2.5 (Tiletamine-Zolazepam 2.5 mg/kg, n=10), TZ-5 (Tiletamine-Zolazepam 5 mg/kg n=10), and TZ-10 (Tiletamine-Zolazepam 10 mg/kg n=10). All the doses were adjusted to a final volume of 0.25 mL/kg with saline 0.9%. Heart rate (HR), Respiratory rate (RR), arterial oxygen saturation of hemoglobin (SPO_2, mean arterial blood pressure (MAP) and rectal temperature (RT) were evaluated throughout 6 hours of evaluation. Data were analyzed by ANOVA ($P<0.05$).

HR increased in treated groups 15 minutes after administration of TZ ($P<0.05$), RR increased in TZ-2.5 from minute 40 to 120 when compared with CS. There were no differences among groups for MAP, SPO_2 and RT. Onset of epidural analgesia (from epidural injection to absence of response after tail clampling) were not different among treated groups: TZ-2.5 (4.8± 1.5 min), TZ-5 (3.1±1.8 min), TZ-10 (1.5 ±0.8 min). Analgesia time and time to standing were longer ($P<0.05$) in TZ-10 (95±2 – 252.3±54.2 min respectively) than in TZ-5 (59.6±18.2 – 182.9±54.7) and in TZ-2.5 (33.7±13.6 – 93.5±18 min). Sedation was present in all groups, but signs of light general anesthesia were only evident in TZ-10. (28±8.5 min duration).

It is concluded that lumbosacral epidural 2.5, 5 and 10 mg/kg of Tiletamine-Zolazepam induces dose-related analgesia and recovery times in dogs.

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P-51 Volumetric capnography during low (10 mL/kg) and high (15 ml/kg) tidal volume in healthy anesthetized dogs

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The study was aimed to determine the impact of a low and high (10 and 15 mL/kg) tidal volume on gas exchange and respiratory mechanics, in healthy anesthetized dogs.
Six healthy adult beagle dogs were anesthetized twice, with a two-week washout period, under a constant rate infusion of propofol (20 ± 5 mg/kg/hr), remifentanil (20 mcg/kg/hr) and vecuronium (50 mcg/kg. Animals were ventilated in dorsal recumbency for 30 minutes under volume-controlled mode, with a respiratory minute volume (V_E) of 3.33 (1.76 - 6.74) L/min and an inspired oxygen fraction of 0.4. Tidal volume (V_T) of 10 and 15 mL/kg were used in the first and second anesthesia, respectively. Gas exchange (arterial sample), dynamic compliance (C_{dyn}), expired CO_2 volume (V_TCO_2), expired CO2 pressure ($PETCO_2$), alveolar tidal volume (V_{Talv}), physiological dead space (V_D/V_T) and oxygen saturation were measured 30 minutes after initiating ventilation.
Non parametric data were analysed by a Wilcoxon test, and presented as median (range) ($p< 0.05$).
The increase in V_T from 10 to 15 mL/kg resulted in a significant decrease in $PETCO_2$ (from 48.5 to 39 mmHg), $PaCO_2$ (from 49.5 to 41 mmHg) and V_D/V_T (from 0.78 to 0.68) with a concurrent significant increase in *pH* (from 7.29 to 7.37), V_{Talv} (from 27 to 81 mL) and V_TCO_2/*breathe* (from 1.56 to 3.26 mL/breathe). Neither V_E nor C_{dyn} presented significant differences between both groups.

A decrease in V_T from 15 to 10 mL/kg and a consequently augmented dead-space volume, hindered CO_2 elimination per breath and thus promoted hypercapnia and acidosis. It is concluded that variations in V_T resulted in significant changes on respiratory variables and thus on gas exchange and homeostasis. It is therefore recommended to determine the best V_T for each animal under general anesthesia.

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P-52 Ultrasonographic anatomy of the caudal lumbar spine in cats

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The objective of this study was to describe the ultrasonographic anatomy of the caudal lumbar region in cats.
Twenty-four adult cats, scheduled for a therapeutic procedure where neuraxial anesthesia was indicated, were anesthetized and positioned in sternal recumbency. A transverse and parasagittal two-dimensional ultrasonographic (US) scan was performed over L7-S1, L6-7 and L5-6 intervertebral spaces. Transverse ultrasound images were obtained by orienting the probe perpendicular to the vertebral column, centered on the neuraxial midline and tilted cephalad to improve visualization of the structures inside the vertebral canal. Parasagittal images were obtained by rotating the probe 90°, displacing it laterally and also angling it toward the midline.
Postprocedural image analysis consisted of the measurement of the midline distances between the identified structures, from the skin to the floor of the spinal canal.
Data were checked for normality and expressed as mean (SD).
A quick US identification of all the intervertebral spaces studied was feasible in all the cats. Ultrasound scanning allowed high visibility of the lumbar bony prominences and the following structures inside the spinal canal (from superficial to deep): interarcuate ligament, epidural space, dorsal dura, intrathecal space, dorsal piamater, ventral piamater, ventral dura, dorsal longitudinal ligament and vertebral body. Measured distances are presented in the table.
This is the first study to describe in detail the ultrasound anatomy of the caudal lumbar region in cats. Measurements obtained can be useful to determine the relationship between involved structures when performing neuraxial anesthesia.

Table Transverse and parasagittal ultrasound-measured distances (cm) between structures from the skin to the floor the spinal canal in cats. Data are presented as mean (SD).

	L7-S1		L7-L6		L6-L7	
	Transverse	Parasagittal	Transverse	Parasagittal	Transverse	Parasagittal
S-IL	**0.99 (0.18)**	1.14 (0.22)	**1.09 (0.15)**	1.14 (0.15)	**1.04 (0.16)**	1.14 (0.18)
S-DLL	**1.47 (0.24)**	1.62 (0.24)	**1.66 (0.17)**	1.70 (0.21)	**1.73 (0.21)**	1.81 (0.16)
IL-DLL	**0.48 (0.11)**	0.49 (0.11)	**0.58 (0.07)**	0.57 (0.06)	**0.67 (0.08)**	0.69 (0.13)
IL-DD	**0.04 (0.02)**	0.03 (0.02)	**0.03 (0.01)**	0.04 (0.01)	**0.04 (0.01)**	0.04 (0.01)
DD-VD	**0.30 (0.07)**	0.32 (0.07)	**0.39 (0.06)**	0.40 (0.04)	**0.52 (0.10)**	0.54 (0.13)
DD-DP	**0.07 (0.02)**	0.07 (0.02)	**0.07 (0.02)**	0.08 (0.02)	**0.09 (0.02)**	0.08 (0.03)

S: skin. IL: Interarcuate ligament. DLL: dorsal longitudinal ligament. DD: dorsal dura. VD: ventral dura. DP: dorsal piamater.

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P-53 Intermittent indirect oscillometric blood pressure measurement incorporating pulse transit time on cuff pressure in anesthetized dogs: comparison to direct arterial blood pressure

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Indirect or noninvasive blood pressure (NIBP) measurement was compared with direct or invasive BP (IBP) measurement in fifteen anesthetized dogs. A multiparameter veterinary patient monitor, Vetland V12, using oscillometric method employing a novel algorithm incorporating pulse transit time (PTT) on measured values of cuff pressure (CP). The BP cuff was placed non-invasively over the mid metatarsal area of hindlimb, and direct BP was measured from a pre-placed catheter into a dorsopedal artery in the hindlimb with no cuff. Systolic arterial BP (SABP), diastolic arterial BP (DABP), and mean arterial BP (MABP) data were analyzed using correlation regression analysis and Bland Altman plots to compare the degree of agreement between the two measurement methods. The correlation between the two measurement methods was strong in medium pressure group (n=86, systolic 90-120 mmHg) and in high pressure group (n=71, systolic above 120 mmHg), but weak in low pressure group (n=47, systolic below 90 mmHg). In medium pressure group, the correlation coefficient (r2) ranged from 0.77 for mean pressure and 0.85 for diastolic pressure. A high correlation was also observed for mean pressure (r2=0.73) in high pressure group. Correlation coefficient for all systolic, diastolic and mean pressures in low pressure group was low with r2 ranging from 0.2 to 0.4. Calculated bias and precision of blood pressure readings were representative of these observations and assessment in the degree of agreement between the two methods as indicated from values of the correlation coefficient. These data demonstrated mean pressure measured between 60 and 150 mmHg from indirect BP method using oscillometric principle incorporating a novel algorithm employing pulse transit time on measured values of cuff pressure correlates highly with that from direct BP method in anesthetized dogs. However, mean BP readings measured from the indirect method falling outside these ranges may require additional validation of accuracy for consequential clinical interpretation in anesthetized dogs. The noninvasive blood pressure monitoring method based on oscillometric principle incorporating a novel algorithm in this study can be particularly useful to alert abrupt and sudden changes in BP from undesirable anesthetic depth and associated cardiovascular abnormalities.

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P-54 Perioperative effects of epidural and combined femoral and sciatic nerve blocks, assisted with or without peripheral nerve stimulator in dogs undergoig stifle surgery

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AIM: to compare the perioperative efficacy of epidural and combined femoral and sciatic nerve blocks, carried out with or without peripheral nerve stimulator assistance.
DESIGN: prospective randomized blinded clinical study.
ANIMALS: 29 dogs undergoing stifle surgery
METHODS: Animals were randomly assigned into three treatments: PD (n = 10): epidural; PN (n = 10) femoral and sciatic nerve blocks performed with peripheral nerve stimulator; RA (n = 9): femoral and sciatic nerve blockade using anatomical landmarks. Dogs were premedicated with fentanyl (3 mcg/kg) combined with acepromazine (0.03 mg/kg).Anesthesia was induced with propofol (5 mg/kg) and maintained with isoflurane. Fentanyl (3.0 mcg/kg) was given if there was observed increase in HR, SBP or MAP (more than 20% of baselines values). Pain and sedation were evaluated in the moments M1, M2, M4, M6, M8, M10, M12 and M24 after surgery. Pain assessment was performed using a Glasgow modified scales (GMS), scale of the Colorado State University (CSU) and Visual Analog Scale (VAS). Rescue analgesia was performed with morphine (0.5 mg/kg IM). Statistical analysis was performed by analysis of variance for the parametric variables, Kruskal-Wallis test To compare treatments, Friedman test to compare moments. The backlog of rescues was adjusted in a Logistic regression. A 5% significance level was adopted.
RESULTS: Epidural abolished the need for intraoperative rescue analgesia, differing from the PN and RA treatments. RA required more trans-operative analgesics than PN, however, this difference was not statistically significant. Post-anesthetic rescues analgesia, PN did not differ from the others, however, the amount of rescue analgesia was significantly lower in PD than RA. The percentages of animals requiring more than one morphine administration were higher in RA compared to PN and PD.
CONCLUSION: Epidural anesthesia inhibited the analgesic requirements during the surgical procedure and required less postoperative rescue analgesia. A peripheral nerve stimulator does not decrease the need for rescue analgesia during surgery, nor in the post-operative period.

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P-55 Clinical investigation about the allergic reaction of propofol in dogs

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Propofol is an anesthetic agent those solutes include egg yolk lecithin and soybean oil. Therefore, there is concern about the use of propofol on patients that are allergic to these substances. We examined the association between the use of propofol and the presence or absence of adverse events in allergic dogs. Based on an allergen-specific immunoglobulin E (IgE) test, 14 dogs with high levels (high-IgE group) and seven dogs with low levels (control group) of IgE were included in this study. We compared the incidence of anaphylactic reactions and the plasma histamine levels under general anesthesia maintained with isoflurane throughout surgery, following intravenous induction with propofol in both groups. A Chi-squared test was used to compare frequency of the incidence of anaphylactic reactions, a Students *t*-test was used to compare the plasma histamine levels. In both tests, statistical significance was set at $p < 0.05$. The anaphylactic reactions such as blush, hypotension and respiratory depression were recognized. And some of them were expressed at the same time. The average incidence of anaphylactic reactions after the use of propofol was 21.4% and 14.3%, and the plasma histamine level (mean ± standard deviation) was 167.9 ± 94.5 nM and 65.7 ± 40.3 nM in the high-IgE group and the control group, respectively. No shock-like symptom was observed in either group. These results revealed that risk of specific adverse events were low and propofol may be used relatively safely, although careful perioperative anesthesia monitoring and standby protocols are required when using propofol in dogs with a history of allergic diseases or with high chicken- or soybean-specific IgE levels.

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P-56 Sciatic and femoral nerve block in cats: a preliminary anatomical study

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Loco-regional anesthesia is used for the treatment of perioperative pain. This study evaluated methylene blue solution (MBS) staining after its injection over the sciatic (ScN) and femoral (FN) nerves in cats.
Ten pelvic limbs of five cadavers were used. The approach for the ScN block was performed by inserting a 30 X 0.7 mm needle between the femoral greater trochanter and ischiatic tuberosity. The approach for the FN block was performed by using a ventral (inguinal) approach. The femoral triangle was identified. The puncture site was located cranial to the femoral artery and the needle was inserted either 1 or 0.5 cm. For the ScN approach, 1 mL of the MBS was injected in the first limb whereas 0.1 mL/kg of dye was injected in the other nine limbs. For the FN approach, the MBS (0.1 mL/kg) was injected in six limbs whereas 0.1 mL of dye was injected in the other four limbs. Cadavers were dissected and the sciatic and femoral nerves were photographed to evaluate MBS staining which was considered to be successful when MBS was observed over the target nerves.
The ScN was stained in 100% of injections. The 1 mL dye injection in the first limb was excessive and a large area adjacent to the ScN was stained. The smaller volume (0.1 mL/kg) resulted in adequate staining. The FN was not stained (six injections) when the needle was inserted by 1 cm (either using 0.1 mL or 0.1 mL/kg). However, it was stained (four injections) when the needle was inserted by 0.5 cm (either using 0.1 mL or 0.1 mL/kg)
This preliminary study showed that the depth of needle insertion may be an important factor for the successful blockade of the FN.