Anaesthesia Mythbusters!
The VetEducation Online Veterinary Conference 2011

The Veteducation International Online Veterinary Conference 2011

Part of the Veteducation Live Online Web-Seminar Series

“Anaesthetic Mythbusters!”

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August 2011

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Introduction
Anaesthesia textbooks often state acepromazine is contraindicated in patients with a history of seizures, and many of us were taught not to administer this agent to Boxer dogs. Likewise, many veterinarians would consider the maintenance period the time of greatest risk for anaesthetic-related death. But are you sure? What evidence is there to support – or refute – these statements? Are they fact or fiction? This seminar will attempt to provide some perspective on these and other current anaesthetic “beliefs” by means of an evidence-based literature review. The inspiration for this seminar stems directly from the excellent paper – “Myths and Misconceptions in Small Animal Anesthesia” – published by Dr’s Wagner, Wright and Hellyer in 2003. While this publication debunked many interesting anaesthetic “folktales”, advances in clinical practice and the widespread use of the Internet (both as a means of disseminating and obtaining information), has lead to the development of new beliefs that also warrant critique. Likewise, publication of new, peer-reviewed information justifies re-visiting one or two of the “myths and misconceptions” previously reviewed by Wagner et al.

Evidence based medicine (EBM – also known as evidence based practice) is a term coined to describe a process whereby practitioners aim to apply the best available scientific evidence to clinical decision-making. In essence, EBM is a process of systematically reviewing, appraising and employing clinically relevant research as an adjunct to optimal patient care. This process seeks to assess the strength or validity of the available evidence – which may range from high powered meta-analyses and systematic reviews of large, prospective, double-blinded, placebo-controlled clinical trials, through to conventional “wisdom” or views posted on the Internet – and combine this with the clinician's personal clinical acumen to best manage a given patient. In an ideal world, treatment decisions would be based on the evidence gleaned from large scale, peer-reviewed meta-analyses of high quality clinical trials investigating specific aspects of small animal anaesthetic management, with evidence from “weaker” studies rejected. In reality, the veterinary literature contains a relative paucity of such material – the vast majority of small animal anaesthetic studies are performed in controlled research environments using healthy, often purpose-bred, dogs or cats. Study design and methodology often vary, making comparisons between experimental trials difficult. Investigations performed in dogs may not be repeated in cats: results may be conflicting and do not necessarily translate across species. For these reasons, “real world” decisions must often be based on “best level” information – such as that gleaned from textbooks, review articles, conference proceedings, web-based information systems (e.g. VIN), the advice of colleagues, or our own personal experience – understanding that “best level” may fall well short of high quality, rigorously critiqued evidence.

References

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**BELIEF No. 1:** The maintenance phase is the time of greatest risk for anaesthetic-related death in cats and dogs: Fact or fiction?

Relatively few studies examine this statement. Until recently, most of our knowledge of small animal anaesthetic-related mortality came from a 20-plus year-old British study published by Clarke and Hall in 1990. These investigators conducted a survey of 53 veterinary practices in which nearly 42,000 animals were anaesthetized over a two-year period in the mid-1980’s. In this study, the majority of anaesthetic-related deaths (55% of deaths in dogs and 39% of those in cats) occurred during the maintenance phase of anaesthesia. A similar – although much smaller – survey of private veterinary hospitals in Ontario, Canada, reported similar findings, with the majority of anaesthetic-related deaths occurring intraoperatively. But is this still the case? Is the maintenance phase still the period of greatest risk?

A number of recently published studies collectively form the Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF) – a large scale, multi-centre cohort investigation evaluating the risks of anaesthetic and sedation-related mortality in small animals. One hundred and seventeen private, referral, and university teaching practices in the United Kingdom collected data from more than 98,000 dogs and 79,000 cats over a two-year period from 2002 to 2004. Anaesthetic and sedation-related death was defined as “perioperative death within 48 hours of termination of the procedure, except where death was due solely to inoperable surgical or pre-existing medical conditions (i.e. anaesthesia and sedation could not reasonably be excluded from contributing to death).” Compared to the previous studies, CEPSAF revealed a clear shift in the timing of anaesthetic death with more than 50% of all deaths (47% of deaths in dogs and 61% of deaths in cats) occurring during the recovery phase – often within the first three hours. Although difficult to pinpoint a definitive cause of death in every case, many of the postoperative deaths were thought to be due to respiratory or cardiovascular complications, often occurring during periods when patients were unobserved.

The last 20 years has seen the introduction of new anaesthetic agents and techniques, and – perhaps more importantly – employment of trained veterinary nurses/technicians and the use of advanced monitoring devices such as non-invasive blood pressure (NIBP) monitors and pulse oximetry, which tend to reduce the risks of intraoperative death. Improvements in one area of practice invariably highlight deficiencies in another. Although CEPSAF showed a notable reduction in the overall mortality rate compared to the Clarke and Hall study, the timing of death has now moved to the recovery period. These findings clearly identify the recovery period as the time of greatest risk for anaesthetized cats and dogs, and highlight the importance of continued, vigilant monitoring and support during this phase of anaesthesia.

**References**

BELIEF No. 2: Low doses of potent alpha2-agonists such as medetomidine produce minimal cardiovascular effects: Fact or fiction?

Common sense suggests that as the side effects of anaesthetic agents are typically dose-dependent in nature, low doses of potent alpha2-agonists such as medetomidine should result in minimal cardiovascular effects. But is this the case? Can low dose medetomidine be used in patients who may be intolerant of the cardiovascular effects typical of “standard” doses? This question was also addressed by Wagner et al; however, increasing use of this agent and a growing body of scientific literature addressing the cardiopulmonary effects of medetomidine justify re-visiting this issue.

The alpha2-agonist medetomidine is an equal mixture of two optical enantiomers: - dexmedetomidine and levomedetomidine – the latter of which is considered to be pharmacologically inactive. Package insert doses vary somewhat from country to country but are generally in the range of 10-80 micrograms/kg in dogs (with higher doses recommended in smaller- compared to larger dogs) and 50-150 micrograms/kg in cats, with the lower end of the dose ranges recommended when the agent is used as a premedicant. However, use of “micro-doses” of medetomidine (e.g. 1-10 micrograms/kg) has become increasingly popular. The haemodynamic effects of medetomidine in dogs have been reviewed extensively in both the veterinary and human literature (because the dog is a common model for cardiac research). In contrast, there are comparatively few studies investigating the cardiovascular effects of this agent in cats.4-6. The cardiovascular effects of the alpha2-agonists are often described as “potent”, and include a biphasic arterial blood pressure response with decreases in heart rate and cardiac output, increases in systemic vascular resistance and central venous pressure, and varying effects on cardiac rhythm. Studies in both dogs and cats show clinically recommended doses of medetomidine produce these typical “alpha2-agonist” effects, although blood pressure responses are variable (hypotension has not been reported in dogs) and it does not appear to be as arrhythmogenic as other members of this class. But are these effects dose-dependent?

A single, small, research-based study specifically addresses this question – at least in dogs. Medetomidine was administered to 25 conscious dogs at doses of 1, 2, 5, 10 and 20 micrograms/kg IV, and the haemodynamic effects assessed. Significant haemodynamic changes (including marked reductions in heart rate and cardiac output) were noted with all doses studied. Although the changes were slightly less severe with the two lowest doses studied, near maximal changes were seen with doses as low as 5 micrograms/kg: increasing the dose above this increased the duration of these effects but did little to affect their severity. The authors concluded that “a reduction of the recommended dose of up to six times does not significantly influence the degree of cardiovascular effects and will not reduce the undesirable effects” of medetomidine.7. These findings are supported by the results of a more recent study, investigating the haemodynamic effects of medetomidine constant rate infusions (CRIs) in dogs.8. The haemodynamic effects of medetomidine at doses of 1, 2 or 3 micrograms/kg/hr were evaluated over a 60-min period in six conscious, instrumented dogs, in this small, placebo-controlled trial. Clinically significant increases in systemic vascular resistance and decreases in heart rate and cardiac output were detected with all doses. Although the changes trended towards a dose-dependent relationship, dose-dependency was not demonstrated statistically.

Our best level evidence suggests that (1) the cardiovascular effects of medetomidine are not dose dependent, and (2) that small doses may produce clinically significant changes in haemodynamic function. While these changes may be well
tolerated in healthy individuals, medetomidine should be avoided or used with extreme caution in patients with cardiovascular compromise or instability – even when employed in small doses.

References
BELIEF No. 3: Drug choice (i.e. the selection of an appropriate anaesthetic protocol) is the major determinant of anaesthetic outcome in cats and dogs – particularly in compromised patients: Fact or fiction?

Selection of an anaesthetic protocol/technique should be based on consideration of the following: - (1) patient factors (e.g. species, breed, age, temperament, and relevant history and physical examination findings), (2) the procedure to be performed (e.g. invasive versus non-invasive and minor versus major procedure, estimated duration, body site, anticipated pain etc), (3) the available drugs, equipment and facilities, and (4) the knowledge and experience of the individual veterinarian. In addition, a plan for a compromised patient should also consider: - (1) the physiologic consequences of the disease or injury process, (2) the basic pharmacology of anaesthetic agents and how this may alter in the face of disease or dysfunction, and (3) personal familiarity with the technique. Unfortunately, we are yet to develop the perfect anaesthetic agent: likewise, we still lack an anaesthetic agent that is perfect for all situations. There are relative and absolute contraindications for all commonly used anaesthetic agents, and these recommendations guide our selection of a particular agent for a particular patient. Without question, selection of an appropriate anaesthetic protocol for a given patient is important, but is it the major determinant of anaesthetic outcome?

Few anaesthetic mortality studies have been able to identify a major association between a single anaesthetic agent or drug-class and anaesthetic-related death in cats and dogs. Studies of this nature require large numbers to provide sufficient statistical power for analysis, and few veterinary investigations meet these requirements. In addition, a statistical link between a given drug and mortality does not necessarily imply cause and effect, as the causes of anaesthetic-related death are usually complex and multifactorial. None-the-less, Clarke and Hall (1990) identified an association between the alpha2-agonist xylazine and increased risk of anaesthetic-related death in both dogs and cats – an association that was also noted (in dogs, but not in cats) by Dyson et al (1998). Clarke and Hall’s small animal anaesthetic mortality study was performed in the mid-1980s. It noted an increase in mortality in dogs receiving xylazine as a premedicant and in cats given xylazine-ketamine combinations, in comparison to other agents. Notably, the anaesthetic-related deaths in dogs all occurred in practices in which xylazine was used infrequently, while all anaesthetic deaths in cats receiving xylazine-ketamine combinations occurred during periods when patients were unobserved. Other identified risk factors in dogs included halothane and thiopentone, while those in cats included induction of anaesthesia with a volatile agent, thiopentone, ether, ketamine and nitrous oxide.

When Dyson et al performed their anaesthetic mortality study about ten years later the picture had changed somewhat. Although they also detected a link between premedication with xylazine – a known arrhythmogenic agent – and anaesthetic-related death in dogs, most deaths occurred in dogs receiving additional arrhythmogenic agents (e.g. thiopentone and halothane) as part of their anaesthetic protocol, or in those with likely elevations in circulating catecholamine levels (e.g. dogs that were violently struggling at the time of death). This suggested that inappropriate use of xylazine – rather than the drug per se – was a contributing factor to mortality in these patients. No other links between a single anaesthetic agent and death in dogs were noted. In addition, Dyson et al did not find an association between xylazine-ketamine combinations (or any of the other, previously identified agents) and anaesthetic death in cats. In fact, this combination was reported to be “comparable in safety to other regimens”. The authors surmised that (1) improved anaesthetic training of veterinary graduates, (2) increased familiarity with the combination and awareness of appropriate use (e.g. restricting use to fit healthy patients only), and (3) employment of trained veterinary nurses/technicians to better monitor anaesthetized patients (a factor associated with a significant reduction in risk), all
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contributed to the apparent improvement in outcome associated with xylazine/ketamine combinations in cats in this study compared to that of Clarke and Hall.

The Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF) was performed over a two-year period from 2002-2004, an additional 10 years after Dyson et al’s work. Based on the findings outlined above, the authors hypothesized that medetomidine – a potent, highly specific alpha_2-agonist – would also be associated with an increased risk of anaesthetic death. This did not prove to be the case. No increase in odds of death was detected when this agent was compared to other premedicants, and in fact medetomidine trended towards reduced odds of anaesthetic-related death in both cats and dogs. The authors deduced that specific drug differences (medetomidine is markedly less arrhythmogenic than xylazine) and improved understanding of appropriate use of this drug class had resulted in this “change of fortune” for alpha_2-agonist use. Furthermore, CEPSAF was unable to identify a clear association between any individual induction or maintenance agent and anaesthetic-related death in cats, suggesting that factors other than basic drug effects were now more important with respect to outcome. Interestingly, increased odds of death were detected in dogs induced with an injectable agent and maintained with halothane and in those undergoing total inhalational anaesthesia (isoflurane or halothane), compared to those induced with an injectable agent but maintained with isoflurane. This finding also suggests that the manner in which agents are employed (i.e. technique) is more important than choice of an individual agent (within reason), as the odds for death with isoflurane “flip-flopped” depending on how the agent was used.

Although CEPSAF was unable to identify a clear association between a single anaesthetic agent or drug class and anaesthetic-related death, other major risk factors were identified. Factors increasing the odds of death in both dogs and cats included: - (1) poor health status (i.e. increasing ASA grade), (2) increasing procedural urgency, (3) procedures of increasing complexity (4) small size, (5) low body weight, and (6) elderly patients (i.e. increasing age). Increasing the intended duration of the procedure was also identified as a major risk factor for anaesthetic-related death in dogs. Additional risk factors for death in cats included obesity, endotracheal intubation, and the use of fluid therapy, while simple monitoring techniques (measurement of pulse rate and use of pulse oximetry) significantly reduced the odds of anaesthetic-related death.

It seems the picture has changed again. Selection of an appropriate protocol for a given patient is clearly important: all agents have relative contraindications and it is important to select an appropriate protocol (including dose rates and routes of administration) for a given patient. That aside, all modern anaesthetic agents are extremely “safe” – at least when used appropriately. CEPSAF provides high quality evidence to support the view that the manner in which those drugs are used and the overall approach to patient management have now become the critical factors in determining outcome, rather than drug choice per se (within reason).

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BELIEF No. 4: Sevoflurane is a superior inhalant to isoflurane. It has become the inhalant of choice in human anaesthesia and should do likewise in small animal anaesthesia, given its superiority: Fact or fiction?

Wagner et al also reviewed this topic in their “Anesthetic Myths and Misconceptions” paper. At the time (2003), sevoflurane was a relatively new agent in Australasia – few practitioners could have chosen to use this agent routinely. However, increasing availability and the publication of a growing body of work investigating the use of sevoflurane in small animals justify revisiting this statement.

Sevoflurane was developed in the 1960’s but was not fully evaluated and marketed at that time, and was instead “shelved” until its “rediscovery” in the late 1980’s. Sevoflurane was first approved for human use in Japan in 1990, where it has become the inhalant of choice in human anaesthetic practice. It was approved for veterinary use in the US in 1999 and has been available to veterinary practitioners in Australasia for some years. Sevoflurane is a sweet-smelling, volatile agent – not dissimilar to isoflurane – that produces classical anaesthesia and is delivered via a conventional, agent specific vaporizer. The biggest advantage of sevoflurane is its low blood: gas partition coefficient (0.69 compared to 1.4 for isoflurane) i.e. the agent is very insoluble. Theoretically, this should produce faster mask inductions, more rapid changes in depth following a change in vaporizer setting, and more rapid recoveries than those seen with isoflurane. Sevoflurane has become popular in human anaesthesia because: (1) its low blood: gas partition coefficient, pleasant smell, and lack of airway irritability help speed mask inductions (common in both adults and children), (2) its rapid recovery allows day-case patients to be discharged from hospital quickly (a significant cost-saver in the human health care environment), and (3) it avoids the problems of “halothane hepatitis” – relatively common in people, but very rare in domestic species. But do these “advantages” translate to veterinary anaesthetic practice? Should we consider sevoflurane a superior inhalant to isoflurane? Is there evidence in the veterinary literature to support the view that sevoflurane should become the small animal inhalant of choice?

The single greatest disadvantage of sevoflurane in veterinary anaesthetic practice is its cost – the agent is significantly more expensive than isoflurane on a ml per ml basis. Sevoflurane is also less potent than isoflurane with a reported minimum alveolar concentration (MAC) of 2.1-2.58% in small animals, although values as low as 1.78% have been reported in dogs. All other factors being equal (e.g. circuit type, fresh gas flow rate etc), higher vaporizer settings are therefore required to maintain anaesthesia with sevoflurane compared to isoflurane. This results in further expense because a greater volume of the liquid agent (more expensive than isoflurane to begin with) will be used on a per minute basis.

A low blood: gas partition coefficient offers several potential benefits as outlined above. As predicted, many small animal investigations report sevoflurane mask inductions to be faster than with isoflurane, although not markedly. A study in 8 healthy Beagles reported induction times (to a point permitting intubation) of 5.7 min and 8.6 min for sevoflurane versus isoflurane, respectively. This study employed the “low-to-high” induction method (i.e. beginning with low concentrations of inhalant (0.5 MAC) and increasing the delivered concentration by 0.5 MAC increments every 15 sec to a final concentration of 2 MAC). These findings were supported by another speed-of-induction study performed in 6 healthy, non-premedicated Pointers, in which both agents were initially delivered at high concentrations (approximately 3 x MAC), rather than using the “low-to-high” technique. Sevoflurane induced anaesthesia more rapidly than isoflurane in this study, the induction was considered smoother, and the dogs were noted to be more...
tolerant of the mask with sevoflurane compared to isoflurane (due, perhaps, to the agent’s low pungency). However, a prospective clinical trial of mask inductions in 71 premedicated dogs undergoing routine de-sexing, showed no difference in speed or quality of induction when both agents were administered at maximum vaporizer settings (i.e. 8% (3.4 MAC) and 5% (3.8 MAC) for sevoflurane and isoflurane, respectively). Similar findings were also noted in a small, research study in 8 dogs using the same “maximal vaporizer setting” induction technique.

Less information is available for cats. A clinical study in 28 healthy, premedicated cats presenting for routine de-sexing, showed mask inductions to be faster with sevoflurane (time to intubation was about 4 min with sevoflurane versus nearly 5 min with isoflurane), although the overall quality of induction was reported to be the same with both agents. In contrast, a research-based study in 42 cats premedicated with atropine and ketamine was unable to show any difference in the speed of mask inductions between the two agents. Collectively, these studies suggest that mask inductions with sevoflurane are generally rapid, smooth and well tolerated; however, other factors in addition to solubility – such as induction technique, the actual concentration delivered, premedication, and individual patient factors – also influence the speed and quality of mask inductions in the clinical environment, and may off-set some of the perceived benefits of sevoflurane over isoflurane.

Conflicting information has also appeared about the recovery properties of sevoflurane with some studies reporting quicker, better quality recoveries in comparison to isoflurane; others reporting abrupt, stormy recoveries in some species and some individuals; others reporting a better quality of recovery with sevoflurane compared to isoflurane but no difference in speed of recovery; and still others reporting no significant differences in recovery speed or quality between the two agents. From a clinical perspective, it would appear that both the speed and quality of recovery in dogs and cats are generally very good following use of either agent, and that sevoflurane offers little benefit over isoflurane in this regard despite its lower solubility.

The introduction of isoflurane was hailed as a breakthrough due to the clear advantages it offered over halothane, particularly in terms of its cardiovascular effects. Although some contradictory results appear in the literature, the cardiopulmonary effects of sevoflurane appear very similar to those of isoflurane. Both agents are reported to produce dose-dependent respiratory depression due to centrally mediated actions and impaired diaphragmatic function, resulting in reductions in respiratory rate and tidal volume with corresponding increases in PaCO₂ levels and the production of a respiratory acidosis. However, a recent study reported the anaesthetic index of sevoflurane in dogs (3.45) to be higher than that of isoflurane (2.61), suggesting the former produces comparatively less ventilatory depression in this species (although both agents produce greater ventilatory depression than halothane). The cardiovascular effects of the two agents are also very similar with dose-dependent reductions in ABP, cardiac output, stroke volume and systemic vascular resistance, and increases in heart rate, reported in dogs and cats. Clinically significant reductions in ABP are observed with both agents when delivered in concentrations ≥ 2 MAC. These reductions were noted to be larger in dogs receiving sevoflurane compared to isoflurane at comparable MAC values in two studies, although the opposite effect was seen in another study in cats. The arrhythmogenic potential of both agents is comparable small (and markedly less than that of halothane). A recent, prospective, multi-centre clinical trial of sevoflurane as a maintenance agent in 196 ASA grade I-III dogs undergoing a variety of diagnostic and surgical procedures, reported hypotension (defined as a MAP less than 60 mmHg) and apnoea (defined as no ventilatory effort for greater than 30-60 sec), in 46% and 12% of
dogs, respectively: no arrhythmias were observed. The authors concluded that sevoflurane appeared a safe and effective maintenance agent in clinical canine patients.

While small animals appear relatively resistant to “halothane hepatitis”, hepatic metabolic burden and potential toxicities should also be considered when evaluating an inhalant. About 3-5% of a total administered dose of sevoflurane undergoes hepatic metabolism. This compares to about 20-25% for halothane and 0.17% for isoflurane (i.e. the metabolic burden on the liver is much less than that seen with halothane but significantly greater than that seen with isoflurane). Notably, although a larger amount of sevoflurane undergoes hepatic degradation compared to isoflurane, sevoflurane cannot be degraded to the acyl halide molecule thought to be responsible for “halothane hepatitis” in people. The effects of sevoflurane on hepatic function seem very similar to those of isoflurane – at least in those species studied to date. An experimental study investigating the effects of 60 min of inhalational anaesthesia on hepatic function in 24 clinically normal dogs (premedicated with xylazine and induced with propofol) reported comparable results for isoflurane and sevoflurane. Both agents produced small elevations in aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT) serum levels immediately after, and for a period of up to 7 days, following anaesthesia. Clinical signs of hepatic disease or dysfunction were not detected in the 14-day follow-up period. Similar results were reported for cats receiving 90 min of sevoflurane or isoflurane anaesthesia. Both agents produced mild increases in serum AST levels 24 hr after anaesthesia but these values, along with those for ALT and BUN, did not differ significantly from baseline for the remainder of the 7-day follow-up period.

Concerns have also been raised about the nephrotoxic potential of sevoflurane. Sevoflurane-induced nephrotoxicity may arise via one of two main mechanisms: - (1) the degradation of the agent to fluoride ions (a similar problem to that seen with methoxyflurane), and (2) the production of Compound A – a product that arises via interaction of sevoflurane with CO₂ absorbents (e.g. soda lime), especially in the face of low-flow anaesthesia. Despite these theoretical concerns, nephrotoxicity has not proved a clinical problem in either human- or veterinary patients receiving sevoflurane. Part of the reason for this may lie in the fact that nephrotoxicity appears highly species dependent – rats are very sensitive to these toxicoses but it appears dogs are considerably less sensitive than other species, although it is harder to find data for relative sensitivity in cats. A study investigating the production of fluoride ions in dogs undergoing sevoflurane anaesthesia reported small serum concentrations of the ion at levels markedly less than those seen in dogs undergoing a comparatively shorter period of methoxyflurane anaesthesia. In similar fashion, studies in both the human and veterinary literature have failed to show clinically significant levels of Compound A in dogs undergoing low-flow or closed circuit anaesthesia with sevoflurane. Although Compound A was detected, the levels were well below those known to be nephrotoxic in rats.

While sevoflurane offers advantages over isoflurane in human anaesthesia, it appears these factors are not as relevant in cats and dogs. Sevoflurane is undoubtedly a safe, useful and effective inhalant in cats and dogs, and may prove the agent of choice in some individuals under some circumstances. However, current evidence does not justify the view that this agent is “superior” to isoflurane.

References


BELIEF No. 5: Acepromazine is contraindicated in patients with a history of seizures and in those undergoing potentially seizure-genic procedures (e.g. myelography). It is also contraindicated in Boxer dogs: Fact or fiction?

Although references are usually lacking, many anaesthetic textbooks report that acepromazine lowers the seizure threshold in vulnerable patients and caution against the use of this agent in patients at risk for seizures.\textsuperscript{1-5}. Acepromazine is classified as an aliphatic phenothiazine – a drug class used extensively as psychotropic medicants in people.\textsuperscript{1, 2, 5, 6}. Some members of this class (most notably chlorpromazine) have been shown to reduce the seizure threshold and induce epileptic-like EEG discharge patterns in rats and other research animals including dogs.\textsuperscript{5-7}. Clinical use of chlorpromazine has also been linked to seizure provocation in epileptic people and dogs.\textsuperscript{7}. However, analyses suggest that psychotropic medication induced seizures are influenced by many factors including the specific drug, dosage, rate of titration of the drug, concurrent use of other drugs (particularly those altering pharmacokinetics), and the patient’s underlying disease and seizure history: many phenothiazines do not carry the same risk as chlorpromazine.\textsuperscript{5-6}. Phenothiazines are anti-dopaminergic agents. Dopamine is thought to act as an inhibitory neurotransmitter, and it is postulated that blockade/inactivation of central D\textsubscript{2} receptors may precipitate seizure activity in vulnerable individuals. However, while the human literature acknowledges that some phenothiazines may precipitate seizures in epileptic patients, the precise mechanism by which this occurs is still the subject of much debate.\textsuperscript{6}. Interestingly, early veterinary textbooks note the anticonvulsant properties of acepromazine, while pre-treatment with chlorpromazine has been documented to reduce experimentally induced seizure activity in rats.\textsuperscript{2, 6}. A recent (2006) retrospective study evaluated the effects of acepromazine administered to 36 dogs with a history of seizures.\textsuperscript{5}. In addition, acepromazine was specifically given to decrease seizure activity in a further 11 dogs also included in this study. No seizures were seen within 16 hr of acepromazine administration in any of the 36 dogs with a seizure history; while seizure activity was abated (1.5-8 hr), or did not recur, in 9/11 dogs that were actively fitting when they received acepromazine (although most of these dogs also received additional anti-seizure medications). A similar study reviewed the administration of acepromazine to 31 dogs, with a history of seizures, admitted to a specialist emergency practice.\textsuperscript{6}. “Seizure” was the presenting complaint in 28/31 dogs. 22/31 dogs had a prior history of seizures, and 15 of these were currently receiving anti-seizure medication at the time of admission. Seizures were seen in 4 of the 31 dogs, although in one of these, the seizure occurred > 10 hr after acepromazine administration (i.e. well outside the expected duration of action of this drug). The authors concluded that there was no clinical evidence that acepromazine is associated with increased seizure activity in dogs presenting with seizure disorders.\textsuperscript{6}. Acepromazine has also been contraindicated in patients undergoing potentially seizure-genic procedures – most notably, contrast myelography.\textsuperscript{8, 9}. This recommendation arose from anecdotal reports of post-myelographic seizures following the use of the now outdated contrast medium metrizamide in patients who had also received acepromazine, and was strengthened by the results of a myelographic research-based trial in Beagles in which 5/5 of dogs anaesthetized with a protocol that included acepromazine, convulsed on recovery.\textsuperscript{10}. Since that time, at least two clinically based retrospective reviews of post-myelographic seizures have suggested there is no link between the anaesthetic agents employed and increased seizure risk in dogs undergoing myelography.\textsuperscript{11, 12}. Despite these findings, authors continued to caution against the use of acepromazine stating that this agent increased seizure prevalence.\textsuperscript{13}. Two retrospective analyses of contrast myelography in small animals specifically examined the proposed link between acepromazine administration and post-
myelographic seizures in dogs.\textsuperscript{8, 9} The first study compared clinical patients receiving iohexol with those undergoing metrizamide or iopamidol myelography.\textsuperscript{8} Acepromazine was administered as a premedicant to 68 dogs prior to myelography, but post-myelographic seizures were not noted in any of these dogs. Similar results were documented in a recent (2011) retrospective study of the incidence of, and risk factors for, seizures after iohexol myelography in dogs.\textsuperscript{9} Records for 503 dogs were reviewed. Acepromazine was administered to 145 dogs, either as premedication or as recovery medication or both. Seizures were documented in 15/503 dogs. Although six of these dogs had received acepromazine, 139/488 dogs that did not seizure had also received this agent. Statistical analysis failed to reveal a causative link between use of acepromazine and post-myelographic seizures.\textsuperscript{9}

Many veterinary students are also taught that acepromazine is contraindicated in Boxer dogs. Hall and Clarke\textsuperscript{4} state that “the Boxer dog is renowned for fainting after very small doses of acepromazine given by any route”, but do not supply references or data to support this statement. A recent Pubmed search (August 2011) failed to find any references supporting this view. Review of the retrospective seizure studies discussed above, showed 4/36 dogs with a history of seizures receiving acepromazine to be Boxers: no adverse effects of acepromazine administration were noted in these animals.\textsuperscript{5} Likewise, none of the various small animal anaesthetic complication- or morbidity and mortality studies outlined in other sections of this paper,\textsuperscript{14–21} mentions an association between acepromazine and any anaesthetic-related complication in Boxers – including Clarke and Hall’s own survey from the 1980’s.\textsuperscript{14}

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Belief No. 6: The use of advanced monitoring techniques such as pulse oximetry, arterial blood pressure monitoring, and capnometry significantly reduces patient morbidity and mortality: Fact or fiction?

Anaesthetic complications can only be recognised by patient monitoring (i.e. performing frequent, regular assessments of the patient); understanding the signs and stages of anaesthesia; and being able to differentiate “normal” from “abnormal”.1 While there is no question that simple monitoring techniques provide essential, baseline information about anaesthetic depth and vital organ function, “hands on” methods are limited in the sense that they lack subtlety: changes in parameters may indicate function is “inadequate” but do little to quantify the degree of impairment. In contrast, devices such as non-invasive blood pressure (NIBP) monitors, capnometers and pulse oximeters, provide information about respiratory and cardiovascular function that is difficult, if not impossible, to gain in anaesthetized patients using physical techniques alone.1, 2 Common sense suggests these techniques should aid in the recognition of anaesthetic complications, and by allowing early intervention, should reduce anaesthetic-related death – but does the literature support this view?

Although complications of anaesthesia have been well described3-5, few studies report the incidence of “every day” complications in small animals. However, Dyson et al’s anaesthetic morbidity and mortality study (performed in > 16,500 small animals in the mid 1990’s), reported anaesthetic complications in 2.1% of dogs and 1.3% of cats.6 Patients in this study were monitored at least intermittently in about 85% of cases, although monitoring was limited to fairly simple techniques (e.g. physical assessment, stethoscope or apnoea monitor) with ABP monitoring performed in < 0.2% of cases. In contrast, a study examining 2556 dogs and 683 cats anaesthetised by the anaesthesia service of a large University Veterinary Teaching Hospital (also performed in the mid 1990’s), reported various complications including hypotension, hypoxaemia and hypoventilation in 12% of dogs and 10.5% of cats, when patients were monitored with more advanced techniques such as NIBP monitors and pulse oximetry.7 While it could be argued that the higher incidence of complications in the teaching hospital- versus the private practice based study was the result of a sicker patient population (studies suggest ASA III to V patients represent only 5-10% of the caseload in private practice versus 20-40% of the caseload in referral practice)8, a higher incidence of complications was also noted in private practice patients that were monitored more intensively, highlighting the importance of monitoring with respect to problem recognition.6, 7 A recent (2007) retrospective study of cardiopulmonary complications in 1281 anaesthetized dogs undergoing a variety of diagnostic and surgical procedures, supports this view.9 Hypoxia, bradycardia, hypotension and hypoventilation were identified in approximately 16%, 36%, 38% and 63% of patients respectively, when monitoring devices – including ABP monitors, pulse oximetry and capnometry – were employed. It would appear the use of monitoring devices helps in the detection of problems, but does this translate to a reduction in anaesthetic-related mortality?

Studies investigating critical incidents in anaesthetised people have conclusively demonstrated the use of minimum monitoring standards (i.e. a set of published guidelines or recommendations that document the baseline level of acceptable care) to significantly reduce patient morbidity and mortality.2, 11, 12 Routine monitoring of ABP, arterial saturation and end-tidal CO₂ values (ETCO₂) is now considered a minimum standard in human anaesthesia.2, 11 An Australasian study of 2000 critical incidents in anaesthetised people showed a monitor of some sort was the first indicator of a problem in 52% of reported incidents and complications.13 The authors of this study were able to predict the theoretical “usefulness” of various monitors in a typical anaesthetic procedure. Based on these predictions, pulse
oximetry would have detected 82% of all problems and would have warned of nearly 60% of problems prior to the potential for organ damage. The addition of capnography would have raised these figures to 88% and 65% respectively, while the addition of ABP monitoring would have resulted in detection of 93% of complications – providing warning of 65% of these – before the potential for organ damage had occurred. Based on this analysis and after consideration of costs, the authors created a “priority sequence for monitor acquisition” for those with limited resources. The “usefulness” ranking of the monitors (in descending order) was as follows: - (1) stethoscope, (2) NIBP monitor, (3) pulse oximeter, and (4) capnometer, suggesting that ABP monitoring was particularly useful in detecting complications and reducing risk in anaesthetized patients.

Dyson et al's small animal anaesthetic morbidity and mortality investigation was the first veterinary study to demonstrate that the presence of technician/nurse to monitor an anaesthetized patient significantly reduces the risk of anaesthetic-related death. More recently, the Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF) showed a significant (p < 0.001), 3-4-fold reduction in the odds of death when pulse rate and pulse oximetry were routinely monitored in anaesthetized cats. Assessment of the success (or failure) of other monitoring devices to reduce the risk of anaesthetic related death was not possible, because strategies such as ABP monitoring were performed in < 10% of patients. Current evidence therefore supports the view – but does not conclusively demonstrate – that employment of minimum anaesthetic monitoring standards (including use of monitoring devices such as NIBP monitors, pulse oximeters and capnometers) aid in problem recognition and reduce the risk of anaesthetic-related death (understanding that use of these methods does not guarantee outcome).

References
Conclusion

Many areas of small animal anaesthetic practice are open to debate and this paper has attempted to address just a few of these by means of an evidence based literature review. The following statements are current, often polarizing topics, and are provided as food for thought – you may enjoy researching these yourself, or debating these within your practice or with other colleagues!

Statement No 1: Because isoflurane is so inert in comparison to halothane, there is no longer any need to employ strategies for reducing staff exposure to waste anaesthetic gases when using this agent: Fact or fiction? Statement No. 2: Although it was once used routinely as a premedicant in dogs and cats, routine use of atropine is now considered unjustified and should be avoided: Fact or fiction?