Along with body temperature, pulse rate, respiratory rate and arterial blood pressure (ABP), pain is now considered “the fifth vital sign” and should be regularly assessed in all patients – not just those undergoing surgery. A sound understanding of pain – how it occurs, how to assess it, and how to treat it – greatly enhances our ability to provide excellent patient care. Yet this may be easier said than done. Despite decades of intensive research and significant advances in some areas, there are still many gaps in our knowledge and a great number of unknowns concerning effective management of small animal pain – particularly in cats. Pain and its management are vast, continually expanding, and sometimes controversial topics. It is impossible to cover “all things new” in small animal pain management in a short lecture. Instead, this review will highlight some key developments in the management of acute perioperative pain that represent noteworthy advances, are clinically relevant, and may readily be implemented into clinical practice.

**What’s new in managing pain: Information resources**

Much of our current knowledge of small animal pain has been summated in the “World Small Animal Veterinary Association (WSAVA) Global Pain Council’s Guidelines for the Recognition, Assessment and Treatment of Pain”, recently published as a free-access electronic document.\(^1\) At just under 60 pages, these comprehensive guidelines provide excellent reviews of pain pathophysiology and analgesic agent pharmacology, in addition to detailed descriptions of the recognition, assessment and treatment of both acute and chronic pain in cats and dogs. This useful resource was designed for clinical use; and is packed with valuable, easy to implement information including suggested analgesic protocols for a variety of routine procedures, and a detailed section on loco-regional anaesthetic agents and techniques. Recommendations for pain management in specific scenarios – including analgesia for lactating patients, pain management in the very young, and management of cancer-related pain – are also included. These are guidelines – not an exhaustive text – but a substantial reference list is also provided for those wishing to explore a particular topic in greater detail.

**What’s new in managing pain: Recognizing and assessing pain in cats**

Three pain recognition and assessment tools – two Composite Measure Pain Scales (CMPS) and a facial “grimace” scale – have recently been developed for use in cats.\(^2,6\) To understand why this represents a major advance in small animal pain management, it’s useful to review the current standing of pain recognition and assessment in cats and dogs.

While human pain is often said to be “what the patient says hurts”, small animal pain is largely determined by what we as caregivers think it is, given the inability of our patients to self-report. Signs of pain in cats and dogs may include: - (1) loss of normal behaviours, (2) adoption of abnormal behaviours, (3) reaction to gentle touch or palpation of the painful area, and (4) changes in physiologic parameters. Pain behaviours are species-specific, often subtle, and may be difficult to detect – and interpret – particularly in patients recovering from anaesthesia. For these reasons, assessment frequently becomes a subjective process; biased by our understanding of pain, our familiarity with how painful a given procedure or condition is likely to be, and our ability to recognise pain in an individual. Acute pain may be localized or generalized, and may range in severity from mild discomfort to excruciating agony but normally responds well to appropriate treatment. “Appropriate treatment”
however, depends on our ability to recognise pain and assess it correctly (i.e. the location, degree and nature of pain, and whether or not it improves following treatment). Although we can predict pain and can make broad assumptions about anticipated pain levels following different procedures, we still need a reliable means of recognising and “quantifying” pain in an individual. Likewise, even though we have a wide range of analgesic agents at our disposal and can administer these in various ways according to our knowledge and experience; a method of evaluating the effectiveness of therapy in a given patient is still required to treat pain successfully. The development of a “tool” that would allow us to accurately recognise and “measure” pain – particularly in cats where this can be notoriously difficult – would represent a major advance; allowing us to better identify and evaluate painful patients, and to use the drugs we already have to treat their pain more effectively. From a broader perspective, a tool that can reliably quantify pain, accurately assess the efficacy of analgesic interventions, and allow valid comparisons across research studies and between clinical trials, can only benefit pain research and – ultimately – individual patient care.

The veterinary literature is replete with attempts to identify scientifically objective methods of pain assessment. Various observer-based pain “scales” and scoring systems have been developed in an attempt to create a robust and reliable pain assessment tool. These include simple but relatively insensitive methods such as pre-emptive scoring and simple descriptive scales, in addition to better (albeit still not ideal) tools such as visual analogue- and numerical rating scales. Pain expression is a multidimensional phenomenon so tools that evaluate multiple ”domains” tend to be more sensitive than those only evaluating pain “intensity”. CMPS – sometimes referred to as Multi-dimensional Composite Pain Scales (MDCPS) – therefore represent a further improvement in design. These can be thought of as “up market” numerical rating scales where greater weight is given to parameters thought to be more reliable “pain detectors” (e.g. The University of Melbourne Pain Scale for dogs, which combines physiological data and behavioural responses). To be useful, a pain assessment tool must be valid, reliable, responsive (i.e. able to discriminate between clinically relevant differences in patient status) and practical. Its value escalates if the scale has a defined “intervention value” to aid clinical decision-making, and a set protocol to ensure consistency of the assessment process. Differences in pain behaviours and expression dictate the need for species-specific tools. Because of their importance in pain research, various pain scales have been designed for use in mice and rats; but to date, those developed for small animals have focused almost exclusively on dogs.

Pain however, is an abstract construct. Pain is not just about “how it feels” but is also about “how it makes you feel”; and is influenced by factors such as age, breed, sex, temperament, the duration of the pain, and the patient’s environment.1 Psychometrics is the science of measuring complex, intangible constructs such as motivation, intelligence, and quality of life. The Glasgow CMPS for dogs (2001) was the first pain recognition and assessment tool in veterinary medicine designed using psychometric principles. It was later refined into a short form (CMPS-SF, (2007)) – with an emphasis on ease and speed of completion – for use in general clinical practice.6 The CMPS-SF meets all the requirements of a “useful” pain assessment tool, and is generally accepted as the clinical standard for measuring acute pain in dogs. Until recently, only two pain scales had specifically been developed for use in cats (The Colorado State University Feline Acute Pain Scale and the French “4aVet”), with neither tested for validity or reliability. However, validation of the Brazilian UNESP-Botucatu MDCPS (English-version) and the recent publication of the Glasgow CMPS-Feline and facial “grimace” tools, represent significant advances in our ability to recognise and assess pain in cats and herald a new era in the management of acute pain in this species.
The UNESP-Botucatu Multidimensional Composite Pain Scale for cats

The Brazilian UNESP-Botucatu MDCPS was designed specifically as a research tool for assessing acute postoperative pain in cats following ovariohysterectomy. A pain recognition and assessment tool that has been validated in one language is not automatically valid in another, as meaning and intent can be lost in simple translation. However, both the original Brazilian-Portuguese- and subsequent English versions of this CMPS have been shown to be valid, reliable and responsive – at least when used by veterinary anaesthetists and anaesthetic technicians to assess pain post-ovariohysterectomy.

The English version of this psychometric principles-based CMPS uses ten “pain detection domains” – posture, comfort, activity, attitude, miscellaneous behaviours, reaction to palpation of the abdomen/flank, reaction to palpation of the surgical wound, ABP, appetite, and vocalization – contained within three specific subscales: (1) Pain Expression, (2) Physiological Variables, and (3) Psychomotor Change. The “miscellaneous behaviours” domain contains a number of specific behaviours and facial expressions including squinted eyes, tail wagging, contracting and extending the hind limbs, contracting the abdominal muscles, and licking/chewing the wound. Evaluation during the development phase of the MDCPS showed basic physiological parameters such as heart and respiratory rate, pupil size, and temperature to be inaccurate indicators of pain in cats – just as they are in children – with only systolic ABP remaining in the final version. Descriptors within each domain are carefully defined and ranked according to increasing pain intensity. The assessment follows a set protocol with the assessor observing and interacting with the cat in a described fashion before choosing the score for each domain that best describes the cat’s behaviour/response or appearance. Each of the ten domains is ranked on a score of 0-3 (where 0 = no change or normal), giving a final score out of 30 (where 30 = maximal pain possible). The “global pain score” is the sum of the three subscale scores, with scores ≥ 8/30 indicating the need for rescue analgesia.

The English-version validation study showed the tool possessed sufficient responsiveness to discriminate between different analgesic treatments in the immediate recovery period; could identify those cats requiring additional pain relief; and could document improvements in an individual’s pain levels over time. Disadvantages of this scale include a relative lack of utility – assessment is fairly complex, time-consuming, and requires some technical skill (i.e. the ability to measure ABP) – and that validation has been demonstrated only when the scale is used to assess post-ovariohysterectomy pain by personnel specifically trained in anaesthesia. Studies testing the validity, reliability and responsiveness of this tool for assessing other types of pain, and/or its utility/practicality in general practice are lacking. However, Subscale 1 (miscellaneous behaviours, reaction to touch/palpation of flank, reaction to touch/palpation of wound, and vocalization) is a valid “stand alone” instrument, and may prove useful as a “short form” tool. An intervention level of ≥ 3/12 has been determined for this subscale in the face of ovariohysterectomy-related pain. The UNESP-Botucatu “Animal Pain” website is a useful resource, containing downloadable versions of the MDCPS, links to peer-reviewed MDCPS-related publications, video footage demonstrating the various behaviours evaluated in the scale, and a number of helpful practice/self-assessment videos.

Facial signs of acute pain in cats: A feline facial “grimace” scale

Facial expression is considered a sensitive indicator of pain in people, with “grimace” scales proving a reliable and accurate means of recognising and assessing acute pain in babies. Recently, veterinary researchers have also looked to facial expression to aid pain detection and measurement in animals, with the development of species-specific grimace scales in mice, rats and rabbits. These tools have focused on facial features such as the eyes, ears,
mouth/muzzle area and whiskers; defining specific signs that constitute a “painful face” such as “orbital tightening”, “cheek bulging”, and “combined nose and cheek flattening”, in addition to specific ear and whisker positions. These scales have been shown to be valid and reliable indicators of various causes of pain in these species. A study reporting the development of a similar equine grimace scale was also published recently.

In late 2014, the same group responsible for the development of the Glasgow CMPS and CMPS-SF for dogs published a prototype facial grimace scale for cats.4 The tool presently consists of “cartoon-caricatures” of painful and pain-free cat faces, created using a complex process of feature identification and digital mapping. Initially, 59 “face-on” photographs of healthy, pain-free cats were collected from various sources including veterinary clinics, cat breeders and the general public. Guidelines for restraining and photographing the cats were provided, and the resulting images cropped and standardized using a computer software package. The investigators then mapped 78 readily identifiable anatomical landmarks on each facial image, and measured 80 specific distances between various landmarks. Similar photographs of 28 cats hospitalised post-surgery, or for traumatic or painful medical conditions, were obtained and digitally mapped with the same anatomical landmarks. Both groups included images of domestic shorthair-, domestic longhair- and some purebred (Siamese and Persian) cats. Using a mathematical model, the investigators examined the “movement” of defined facial features between painful and pain-free cats by using the measured distances between landmarks to compare areas of “facial expression” (e.g. the eyes and ears) which might be representative of a painful face. Initial evaluation identified discriminating features of the eyes, ears, and muzzle region; however, the eye-features were later excluded due to concerns about possible drug-effects on eye position and shape in cats. An artist was consulted for creation of the cartoon caricatures and two pictorial panels were produced: one for ear position and the other for nose/muzzle shape. Each panel depicts three faces of increasing pain intensity, with pain scores ranging from 0-2.

In a clinical setting, a scale that only discriminates between pain and no pain has limited value; however, facial grimace scales may also be embedded into multidimensional CMPS, complimenting other behavioural, postural and physiological items and increasing overall responsiveness. It is expected that a version of this grimace scale will be incorporated into the newly developed Glasgow CMPS for cats (CMPS-Feline, see below).

The Glasgow Composite Measure Pain Scale for cats
The Glasgow CMPS-Feline (Glasgow CMPS-F) was created using similar psychometric methods to those developed for the highly successful Glasgow CMPS-SF for dogs.5,6 The psychometric approach to scale design is complex but follows an established process of item selection, scale/questionnaire construction, and testing for validity, reliability and responsiveness. Initially, various words describing cats in acute pain were collected from a range of 30 individuals including veterinarians, veterinary nurses, cat-breeders, rescue workers and cat owners. These individuals were also given the pain descriptors appearing in the canine CMPS-SF, and asked if they felt these words were also applicable to cats experiencing acute pain. The resulting list was reduced from 115 to 40 “items”, which were then grouped into six “behavioural categories”: - vocalization, activity/posture, attention to wound, response to people, response to touch, and demeanour. The categories were arranged in a specific sequence (as listed above) to form the basis of the assessment protocol, and “items” within each category were ranked in order of increasing pain intensity. Ranking was achieved via an on-line survey in which 630 English-speaking veterinarians from 23 countries were presented with all possible combinations of word pairs and asked which of each pair they felt represented the most pain. The results were used to create a scoring system based on rank. A revised version of the pain assessment tool (rCMPS-F) was developed following initial analysis of the CMPS-F prototype and user feedback. In this

Machon, R. Anaesthesia - what's new in managing pain
Proceedings of the 4th AVA/NZVA Pan Pacific Conference, Brisbane 2015
version, less-sensitive items were dropped, and the “behavioural categories” were changed to six questions that are answered as the assessor observes and interacts with the cat according to the set protocol.

Validation and responsiveness were tested in two studies in which a range of assessors – including various veterinary nurses and veterinary interns, residents and specialist level clinicians – scored pain levels in >120 cats of varying sex, age, breed and clinical status, experiencing acute pain related to surgical, traumatic and medical conditions. The rCMPS-F was able to detect statistically significant improvements in the pain scores of individual cats following analgesia administration, and was also able to accurately distinguish between cats that did and did not require additional pain relief.5

The rCMPS-F has been designed for use in a clinical setting, where acute pain may arise from various sources in addition to surgery, and where assessment may be performed by caregivers with varying levels of proficiency and experience. Time for completion of the questionnaire and computation of the pain score is relatively short, with the tool reported to receive positive user feedback regarding its utility. The rCMPS questionnaire is simple and self-explanatory. The assessor is instructed to observe and interact with the cat in a specific manner while working through the six questions i.e. “look at the cat in its cage”; “approach the cage, call the cat by name, and stroke along its back from head to tail”; and finally, if the cat has a wound or painful area, to “apply gentle pressure 5 cm around the site”. They then choose the most appropriate descriptor for each question – selecting the higher ranked score if more than one expression applies to the cat – and total the question scores to calculate the overall pain score. The rCMPS-F has a maximal value of 16, and a determined intervention value of ≥ 4/16.

Although there are many similarities in design, content and structure between the Glasgow rCMPS-F and the UNESP-Botucatu MDCPS pain recognition and assessment tools, the Glasgow pain scale offers some clear and practical advantages, particularly for use in general practice. None-the-less, the UNESP-Botucatu MDCPS can provide valuable information (albeit under specific circumstances) while some aspects of the assessment (e.g. appetite evaluation) might be useful as “adjunct” pain indicators. Further testing and refinement of the rCMPS-F is likely as the authors acknowledge this is still “a work in progress”, with future versions expected to incorporate the feline grimace scale (to improve responsiveness). Until then, all three tools are accessible, can be implemented in clinical practice, and should help us to better recognise and manage pain in this species.

While these new instruments represent a major advance in our ability to recognise and assess acute pain in cats, it’s important to remember that animal pain scales will never be perfect. The inability of our patients to accurately self-report denies us a “gold standard” to measure these tools against. All animal pain scales rely to some extent on the recognition and/or interpretation of various behaviours (which may prove difficult in patients recovering from anaesthesia), have a subjective component, and are subject to some degree of observer error and bias. A patient should never have to “prove” they are painful – by means of achieving an intervention score or otherwise – in order to receive pain relief. Surgical and trauma-related pain is 100% predictable. Clinical judgement and common sense are still important factors in deciding if a given patient requires analgesia: in cases of uncertainty, a positive response to a “test dose” of a rapidly acting analgesic agent may be easier to assess, and may serve as a pragmatic indicator of pain and the need for further treatment.

**What’s new in managing pain: Hot research topics**

Regional anaesthesia is widely employed in both people and large animals, but is still relatively under-utilized in cats and dogs. However, the last 5-10 years has witnessed a
surge of interest in small animal loco-regional anaesthesia, with numerous studies appearing in the literature. Current research focuses on the development of new techniques (often modifications of those used in people), new approaches to well-established techniques (e.g. brachial plexus blocks), and methods for improving the efficacy of blockade (e.g. use of ultrasound- or nerve locator-guided needle placement to allow accurate injection of local anaesthetic agent (LAA)). Promising techniques include new alternatives to epidural anaesthesia such as femoral- and sciatic nerve blockade, the “RUMM” (radial, ulnar, median and musculocutaneous) block for forelimb anaesthesia, and the transversus abdominus plane or "TAP" block for procedures such as mastectomy. Many of these techniques are complex, technically demanding, and require specific training and/or the use of specialized equipment for their delivery. Others are still in the developmental stage and require clinical evaluation. However, the idea underpinning this upswing of interest – i.e. that loco-regional anaesthesia is a valuable addition to general anaesthesia, and that it may improve intraoperative patient management, patient outcome, and comfort in the recovery period – is one that can readily be implemented into small animal practice.

LAAs produce reversible blockade of signal transmission along nerve fibres, causing temporary loss of sensory and/or motor function. Unlike opioids or NSAIDs, these agents produce complete – albeit short-lived – analgesia by blocking nociceptive input from a given area. LAAs are voltage-gated sodium (Na+) channel blockers, producing conduction blockade via inhibition of the normal Na+ ion influx responsible for action potential generation (and propagation) within nerve axons. Blockade is completely reversible, with normal conduction returning as the agent is redistributed and metabolised. Variations in Na+ channel density and LAA binding affinity between different nerve fibres results in the phenomenon of differential blockade: - small fibres (e.g. autonomic and pain) are blocked before larger fibres (e.g. sensory and motor), while myelinated fibres are blocked before non-myelinated fibres of similar diameter. Blockade therefore results in loss of sensation in the following order: pain, cold, warmth, touch, deep pressure, and finally, motor function.

LAAs including lidocaine, mepivacaine, bupivacaine and ropivacaine, provide useful and effective perioperative analgesia. Loco-regional blocks are particularly useful in conjunction with general anaesthesia; as they allow a marked reduction in the dose of maintenance agent, may produce pre-emptive analgesia (e.g. epidural blockade), and may contribute to pain relief in the immediate recovery period. However, blocks can also be performed at the conclusion of a procedure in preparation for the recovery phase. LAAs are extraordinarily versatile. Routes of administration include: - topical, local infiltration or installation, perineural, neuraxial (i.e. epidural/subarachnoid), intra-articular, interpleural/intraperitoneal, intravenous (e.g. Bier blocks or constant rate infusions (CRIs)), and transdermal (e.g. EMLA cream). While generally considered very safe, complications – including injection related problems such as infection, haematoma formation and nerve laceration/injury; and various drug-related toxicities – accompany their use. A variety of blocks have been developed and are well described. While many are simple, others are technically demanding, can be time-consuming and are associated with known complications. Relatively simple techniques for peri-operative pain management include the various dental blocks, epidural and intra-articular blockade, and the use of “soaker” (or wound) catheters. These techniques are detailed in various textbooks, the WSAVA Global Pain Council guidelines, and in a number of easy-access electronic articles (see Appendix). Blocks can be repeated in conscious patients; however, injections are often painful and require patient tolerance.

What’s new in managing pain: Novel dosing strategies and cool ideas

1. Lidocaine patches
The recent development of a lidocaine patch offers new possibilities for postoperative pain management in various species. The patch appears to work by producing local analgesia –

Machon, R. Anaesthesia - what's new in managing pain
Proceedings of the 4th AVA/NZVA Pan Pacific Conference, Brisbane 2015
rather than anaesthesia – via differential blockade of pain and sensory nerve fibres. It is thought the patch delivers concentrations of lidocaine sufficient to block Na⁺ channels in small, unmyelinated pain fibres but insufficient to block transmission in larger sensory fibres; resulting in analgesia without numbness or loss of sensitivity to touch, pressure or temperature. Patch application therefore produces analgesia without loss of sensory function in the skin or loss of motor function in underlying musculature. Because systemic uptake is low (peak plasma lidocaine concentrations are reported to be 100 times lower than those in the skin and muscle beneath the patch), the risks of toxicity are small.⁸

These patches differ from transdermal fentanyl patches in several aspects, the most important being that lidocaine patches act locally rather than systemically. Additional differences include: (1) patch application: lidocaine patches must be applied close to the site of injury, (2) patch technology: lidocaine patches may be cut to size without altering the drug delivery system, and (3) economics: lidocaine patches are less expensive than fentanyl patches yet provide a similar duration of analgesia (i.e. about three days), while unused portions of the lidocaine patch may be stored and used later on other patients.⁸ However, both patches are associated with individual variability in systemic absorption and may be ingested, potentially resulting in toxicity. Lidocaine patches are clean but not sterile, and it is suggested wounds be closed and the patch then applied over a non-adherent sterile dressing or gauze. Patches are self-adhesive and come with a protective liner that should be removed before application.

2. **Long-acting transdermal fentanyl solution**

A new long-acting transdermal fentanyl solution – employing novel, innovative Australian-designed drug-delivery technology – has been developed for use in dogs.⁹ Marketed overseas as Recuvyra™, this solution is best thought of as a “patch-less” fentanyl patch. The topically applied solution is rapidly absorbed percutaneously and passes into the stratum corneum where it resides; acting as a reservoir from which fentanyl is slowly released into the bloodstream. Effective plasma concentrations are achieved 30 min post-administration and for up to four days after a single application. There is no need to clip hair and the new technology avoids many of the pitfalls of patch application such as prolonged onset of effect, variable uptake, patch adhesion issues, the effects of temperature-induced changes in fentanyl release, and patch ingestion.⁹

Recuvyra™ is supplied as a highly concentrated 50mg/ml solution, and comes with purpose-designed needless adaptors, syringes and applicator tips for drawing up the drug and applying it to patients. The shelf life is reported to be 3 years, with a use-by-time of 30 days after the vial is first opened. The solution is applied as a “single” small-volume dose (divided into one or more 0.5 ml aliquots) in the dorsal scapular area – much like the topical parasiticides – using a purpose-designed two-pronged applicator. At present, European veterinarians must complete a mandatory on-line training session before being able to order and use the product. The training module features information on the presentation, correct preparation and handling of the product, and appropriate handling and care of patients following treatment (including management of the dog at home).

3. **Long-acting liposomal bupivacaine**

Although the LAAs provide true analgesia, their short duration of action limits their usefulness to the immediate postoperative period. Conventional bupivacaine is considered a long acting LAA but at 3-8 hr, its duration of action is still limiting. A new, novel, slow-release bupivacaine formulation – liposomal bupivacaine – has recently been released. Designed for single-dose infiltration during wound closure, this new formulation reportedly provides effective analgesia for up to 72 hr. The extended effect is achieved by encapsulating the bupivacaine within microscopic carrier molecules known as liposomes, which are “trapped” in

the tissue and slowly release the drug over time. Traditional liposomes consist of a phospholipid bilayer with an aqueous core, and can be used to deliver either hydrophilic drugs (contained within the core) or hydrophobic agents (contained in the lipid bilayer). However, this new technology employs “multivesicular” liposomes. These are complex spherical particles composed of a honeycomb-like structure of numerous, tiny, internal aqueous chambers – each containing encapsulated bupivacaine – separated by lipid membranes. The lipid membranes erode in a predictable manner over time, resulting in sustained drug release. Although most of the bupivacaine is contained within the liposomes, a small amount is also present in the solution as free bupivacaine. This allows a rapid onset of effect followed by prolonged blockade as the liposomes begin to erode. Toxicity is reported to be no greater than for traditional bupivacaine.

Liposomal bupivacaine is marketed as a preservative-free aqueous suspension in a single use vial, but is currently extraordinarily expensive. To date, approval has only been granted for use in people as outlined above; however, use in other loco-regional techniques (e.g. various perineural blocks and intra-articular blockade) holds much promise.

4. **MK-467**

Medetomidine is commonly employed as a sedative- and preanaesthetic agent in cats and dogs. This alpha2-agonist produces predictable, reliable and dose-dependent sedation, muscle relaxation and analgesia; is reversible; and can be administered via a variety of routes – all desirable factors that contribute to its popularity in general practice. It has useful analgesic potential, and interest continues to grow in the use of medetomidine for its MAC-sparing properties; as a component of various anaesthetic and analgesic CRI protocols; and in its delivery via novel routes (e.g. epidural and intra-articular administration). Unfortunately, use is also associated with significant, potentially deleterious cardiovascular changes including marked peripheral vasoconstriction, dramatic increases in ABP, and significant decreases in heart rate and cardiac output. Although these effects are generally well tolerated in normal healthy animals, use of medetomidine (and other alpha2-agonists) is cautioned in compromised patients (e.g. geriatrics and paediatrics) and in those with cardiovascular disease. Various strategies to prevent or offset these undesirable changes (e.g. concurrent administration of anticholinergics and simple reduction of the administered dose) have proven ineffective. Likewise, although reversal or “partial reversal” with a traditional alpha2-antagonist such as atipamezole will improve cardiovascular function, it does so at the expense of alpha2-agonist-induced sedation and analgesia, which are also reversed.10

MK-467 (also known as L-659,066) is a peripherally acting alpha2 adrenoceptor antagonist, which is unable to cross the blood-brain barrier and is therefore excluded from the central nervous system. Studies in a number of species including sheep, horses and dogs have demonstrated the ability of this unique agent to attenuate (but not completely offset) the undesirable cardiovascular effects of medetomidine without compromising the degree or quality of sedation.10 This is possible because unlike sedation – which is a centrally mediated effect – the majority of medetomidine’s cardiovascular changes are mediated via interaction with peripherally located alpha2-adrenoceptors. Early investigations examined the effects of medetomidine in patients pre-treated with intravenous MK-467 – an impractical strategy for the real world. However, a recent study in dogs was also able to show the effectiveness of MK-467 in reducing medetomidine-induced changes in cardiovascular function – while still preserving medetomidine-induced sedation – when both agents were concurrently administered intramuscularly.10 Studies are yet to examine whether medetomidine-induced analgesia is also preserved with MK-467, and if its beneficial effects on cardiovascular function extend to vulnerable patient groups such as the very old and those with cardiovascular disease. In the meantime, MK-467 offers hope of improved

Machon, R. Anaesthesia - what’s new in managing pain
Proceedings of the 4th AVA/NZVA Pan Pacific Conference, Brisbane 2015

645
cardiovascular function in patients receiving medetomidine (or other potent alpha2-agonists), and that a wider patient population may also be able to benefit from the potentially useful analgesic properties of this popular agent.

References


Appendix