What's New in Anesthesia and Analgesia: New Products, Techniques and Other Stuff

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NOTE: Other 'new' things may be presented in lecture that are not in the notes.

Abstract: New or new uses of anesthesia and analgesia drugs, techniques and equipment may be just what you need to elevate anesthesia and analgesia to the next level in your practice.

Keywords: anesthesia, analgesia, drug, equipment, monoclonal antibody, medetomidine + vatinoxin

New Pain Management Guidelines
2022 AAHA Pain Management Guidelines for Dogs and Cats (Gruen et al. 2022) open access at AAHA.org/Guidelines/
https://www.aaha.org/globalassets/02-guidelines/2022-pain-management/resources/2022-aaha-pain-management-guidelines-for-dog-and-cats_updated_041822.pdf

World Small Animal Veterinary Association (WSAVA)Pain Management Guidelines (Monteiro et al. 2022) open access at https://wsava.org/global-guidelines/global-pain-council-guidelines/.

2022 ISFM Consensus Guidelines on the Management of Acute Pain in Cats (Steagall PV et al.) open access at https://journals.sagepub.com/doi/pdf/10.1177/1098612X211066268

All three guidelines include not only pain management information but also descriptions of the newest *pain management scoring systems/scales*, including the Feline Grimace Scale.

New (or new-ish) FDA-approved Analgesic Drugs
Anti-nerve growth factor monoclonal antibodies (anti-NGFmAbs, Solensia® and Librela®)
Nerve growth factor is a potent pain generator and propagator, perhaps even more potent than prostaglandins. Monoclonal antibody drugs have several advantages over traditional pharmaceuticals, including injection rather than oral administration, long duration of action (4+ weeks) and elimination through protein catabolism and recycling rather than hepatic and/or renal clearance. The anti-NGFmAbs are species-specific for treatment of osteoarthritis pain in dogs (bedinvetmab, Librela®) and cats (frunevetmab, Solensia®) with minimal adverse effects. Both drugs are approved for their respective species in numerous countries, including the US.

Extended duration transdermal buprenorphine solution for cats (Zorbium®)
Buprenorphine is a moderately potent opioid with a high safety profile and a duration of action of 4-6 hours for surgical pain, with presumed slightly longer duration for mild pain. A high-concentration injectable formulation (Simbadol™) that provides analgesia for 24-hours is currently on the market. A new addition is a transdermal buprenorphine (Zorbium™) that provides analgesia for 4 days. Both are FDA-approved for cats only. Adverse effects are typical of opioids and include mild hyperthermia. Although both are approved for pre-surgical use, both can also be used for post-operative use. A common protocol is to use a more potent opioid as a premedication and follow with the longer duration opioid postoperatively. The timing of administration for the long-duration buprenorphine administration should be within 1-2 hours before the analgesic effects of the first opioid are predicted to wear off since both extended duration products take 1-2 hours for full effect. An advantage of the transdermal formulation is post-discharge analgesia without the need for the owner to administer the drug.

Simbadol® (long-duration buprenorphine)
Buprenorphine with 24-hour duration FDA-approved for use in cats for preoperative administration but the slow onset makes postoperative administration more practical in many instances. The label dose may cause sedation in patients that are receiving other analgesic drugs and in ill or old patients that are slow to metabolize the drug. We commonly use 75% of the label dose in patients that would receive low-end dosages of any other opioid that we use. Can be used off-label in dogs just like 'regular' buprenorphine at 0.02 mg/kg IV or IM – but poor uptake if used SQ at this dose. Simbadol administered to dogs at a dose of 0.02 mg/kg IM PLUS carprofen provided pain and sedation scores not significantly different from those proved by the same dose of 'regular' buprenorphine for 6 hours postoperatively (not tested beyond that time frame) – but 3 dogs in the regular group and 0 dogs in the Simbadol group required rescue analgesia postoperatively (Watanabe et al. 2018). Uptake at this route/dose is REALLY low after SQ administration but good IV or IM.

Liposome Encapsulated Bupivacaine (*Nocita®)*
Not completely new but new information on storage. The liposome encapsulated bupivacaine Nocita® is approved for incisional injection for stifle surgery in dogs and peripheral nerve block for manus desensitization in cats. However, the drug is widely used off-label for other incisional, wound and peripheral nerve blocks. Liposome encapsulation increases the duration (72 hours) and safety as small amounts of bupivacaine are slowly released. Research shows that the liposomes maintained integrity and there was no bacterial or viral contamination for 4 days after Nocita® vials were **aseptically** punctured (Carlson et al, 2020). Using the drug for a longer time will allow easier division of the drug (and the costs) among patients. If the surgery includes an implant that could get infected, opening a new vial is recommended.

New Medical 'Devices' for Joint Injections

A veterinary medical device is defined by the FDA as a product that provides function without pharmacological, chemical, or metabolic action.

Naturally derived collagen and elastin

Spryng™ is an intra-articular device that is 'indicated for use in both horses and small animals to aid in the management of lameness issues, joint pain and osteoarthritis from loss of cartilage or tissue-bone mechanical malfunction caused by joint dysfunction not associated with infection.' The product is a 'shock-absorbing matrix that works with synovial fluid to mimic the protective form and function of natural, healthy joint cartilage.' Provides up to 1-year of action. (Reference: https://www.sprynghealth.com/small-animal-how-it-works)

Radioactive Tin

Synovetin OA® is approved for intra-articular treatment of osteoarthritis elbow pain in dogs. The device uses 'novel, conversion electron therapy using Tin (117mSn)' The product 'emits low-energy electrons that cause targeted elimination of inflamed synovial cells'. Used off-label in joints other than the elbow. Provides up to 1-year of pain relief. (Reference: https://www.synovetin.com/how-synovetin-oar-works)

Other New/New(ish) Drugs

Ketamine infusions and subcutaneous injections

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist and plays a role in both anesthesia & analgesia. Activation of the NMDA receptors in the dorsal horn of the spinal cord are, in large part, responsible for the pain of central sensitization (or 'wind up'). By antagonizing these receptors, the pain pathway can be returned to 'normal'. Meaning that the patient may still feel pain (thus ketamine must be part of a multimodal protocol) but that the pain is not exaggerated and is more likely to be controlled by traditional analgesic drugs like NSAIDs and opioids. To best achieve this effect, ketamine should be administered as an infusion. The analgesic effects in chronic pain patients have been well-documented in humans (Remerand et al. 2009; Sigtermans et al. 2009; Cohen et al. 2018), although, as with any treatment of any chronic condition, a ketamine infusion does not always produce analgesia (Sen et al. 2009). This may be because the pain in those patients is not caused or augmented by central sensitization. In veterinary medicine, ketamine improved postoperative analgesia after forelimb amputation for up to 3 days (Wagner et al. 2002). There are no publications to guide ketamine infusions in dogs and cats for chronic pain but an infusion of 5-15 microg/kg/min following a loading bolus of 0.2-**0.5 mg/kg** (preferred) is a common protocol. The duration of the infusion is not known. Ideally, the infusion would be administered until the patient demonstrates decreased pain but this is unlikely to be practical. Anecdotal reports include everything from 2 to 24 hours but the common range is 2-6 hours. The infusion is repeated 'as needed', which could be anything from never to weekly – or even every 2-3 days for severe pain. As stated, this is part of a multimodal protocol

and the goal is to return quality of life to the patient but not necessarily to eliminate other analgesic therapies.
Anecdotally, ketamine administered at **0.5 mg/kg subcutaneously** at monthly intervals may control pain. However, this may be a 'maintenance' protocol once pain is controlled. Initial dosing used by the author is weekly, or if pain is severe, every 2-3 days, until pain relief is noted. Then the dosing interval is slowly extended and once monthly can be achieved. The pain relief is not as rapid or likely as profound as that achieved with the infusion but is more practical to administer. As with humans, neither route of ketamine administration will decrease pain in all patients. The only predictable, profound pain-relieving drugs are the NSAIDs and the antiNGF-mAbs.

QUICK CALCULATION Ketamine CRI: Add 60 mg (0.6 mls of 100 mg/ml) ketamine to a 1-L bag and run at 2 mls/kg/hr to provide 2 microg/kg/min or at surgical fluid rate (10 ml/kg/hr) to provide 10 microg/kg/min (intra-op dose). Or deliver the ketamine using a

Pregabalin
The mechanism of action of pregabalin is the same as that for gabapentin but the drug undergoes linear pharmacokinetics, making dosing easier. Pregabalin is widely used in human medicine for treatment of a variety of chronic pain conditions. Research in animals is limited but has, for example, been shown to alleviate central pain from syringomyelia in Cavalier King Charles Spaniels (Thoefner et al. 2019 & 2020; Sanchiz-Mora et al. 2019). Pharmacokinetic studies suggest dosages of 1-2 mg/kg BID in cats (Esteban MA, et al. Front Vet Sci 20;5:136, 2018) and 4 mg/kg BID in dogs (Salazar V, et al. Vet Anaesth Analg 36(6):574-80, 2009). Pregabalin may also be a better anxiolytic than gabapentin and there is an approved pregabalin anti-anxiety product for cats (Bonqat) approved in Europe/UK.

Local Blocks
Local blocks aren't new, but some techniques may be new to your practice. Here are two of my favorites:
Peritoneal lavage for ovariohysterectomy and other abdominal surgeries

1. Desensitize the incision site by injecting local anesthetics into the tissues. Incise the skin and linea.
2. Inject (or 'instill' or 'squirt') a standard dose of local anesthetic drug into the abdomen through the incision using a sterile syringe (no needle). Standard drugs/dosages: Lidocaine 2-4 mg/kg cat; 4-6 mg/kg dog; bupivacaine or ropivacaine 1-2 mg/kg cat; 2 mg/kg dog. Upper end of dosing range is recommended. If necessary, dilute local anesthetic with sterile saline to achieve a total volume of 0.4-0.6 ml/kg.

3. The drug can be injected immediately after the abdominal wall is incised (more effective) or immediately prior to closing the abdominal incision (maybe more practical since the drug isn't absorbed by sponges used to control bleeding).
4. At completion of the OHE, close the incision per routine surgical protocol, leaving the drug in the abdomen.
5. In human medicine, intraperitoneal lavage is used not only for hysterectomies but also to decrease intraoperative nociception and postoperative pain from other abdominal surgeries, including caesarean section. Intraperitoneal lavage is commonly used for these surgeries in veterinary medicine. Although no research is yet published for any surgeries other than ovariohysterectomies, experts commented that 'it is our consensus that these techniques [incisional and intraperitoneal local anesthetic administration] should be used for any type of abdominal surgery'. (Open Access: Steagall PVM, Benito J, Monteiro B, Lascelles D, Kronen PW, Murrell JC, Robertson S, Wright B, Yamashita K. Intraperitoneal and incisional analgesia in small animals: simple, cost-effective techniques. 2020;1(1):19-23.)


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Intraperitoneal and incisional analgesia in small animals: simple, cost-effective techniques

P. V. M. Steagall, J. Benito, B. Monteiro, D. Lascelles, P. W. Kronen, J. C. Murrell, S. Robertson, B. Wright, K. Yamashita

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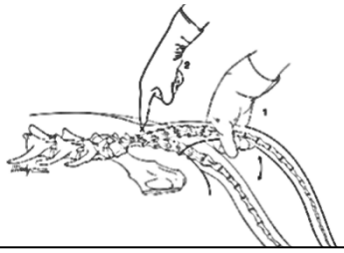
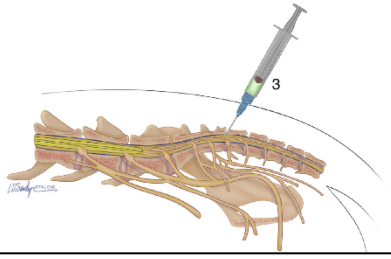
Sacrococcygeal or intercoccygeal epidural for surgery in the perineal area

1. Move the tail up and down in a 'pumping' motion while palpating the sacrococcygeal region of the patient. The first movable space at the caudal end of the sacrum is either the sacrococcygeal or intercoccygeal space. Either site is appropriate for injection.
2. Insert a 22-G needle through the skin ON MIDLINE at a 45-degree angle to the skin surface.
3. Proceed slowly until needle enters the space (generally hit bone and 'walk off' the bone).
4. Hanging drop technique may work. Should have no resistance on injection.
5. Use lidocaine for the most rapid onset or bupivacaine or ropivacaine for longer duration.
6. Dose is 0.1-0.2 ml/kg of any of the drugs. Note **mls** not mgs.
7. Opioids can be added (same as for lumbosacral epidural) to extend the duration of the analgesia but won't achieve the 24-hour duration of morphine injected into the lumbosacral space. Don't inject air, air bubble may cause incomplete block since this is a very small space.
8. This block is often used to provide analgesia for placement of urinary bladder catheters for relief urethral obstructions in cats but should not be niched to only this species or only this use. The block is widely used in large animal medicine and is appropriate for both dogs and cats for any surgery/procedure in the perineal area, including urethrostomies, tail amputations, anal gland removal, deobstipation, assisted vaginal delivery of puppies or kittens, etc.





Diagrams open access download from https://www.aaha.org/aaha-guidelines/2020-aaha-anesthesia-and-monitoring-guidelines-for-dogs-and-cats/local-anesthetic-techniques/

Pain score your patients! We can't know if our patients are painful unless we look for pain. They aren't going to tell us – we have to 'ask' them if they are in pain! The newest pain scale for cats (the Feline Grimace Scale) is validated by research (Evangelista et al. 2019) and is super easy to implement. Get the open access article AND training manual from PubMed or go straight to the training manual: https://static-content.springer.com/esm/art%3A10.1038%2Fs41598-019-55693-8/MediaObjects/41598_2019_55693_MOESM1_ESM.pdf

New Anesthesia Guidelines

Download the open access **2020 AAHA Anesthesia and Monitoring Guidelines** (Grubb et al. 2020) and use the on-line resource center (see drop down menu on right of screen at the website listed below) for guidelines on local anesthetic blocks, anesthesia equipment set-up, assessment and maintenance recommendations, checklists, etc… https://www.aaha.org/aaha-guidelines/2020-aaha-anesthesia-and-monitoring-guidelines-for-dogs-and-cats/anesthesia-and-monitoring-home/

Download the open access **AAFP Feline Anesthesia Guidelines** (Robertson et al. 2018) https://journals.sagepub.com/doi/pdf/10.1177/1098612X18781391

New (or new-ish) Sedative, Anesthetic or Support Drugs

Medetomidine + Vatinoxan (Zenalpha®)

Zenalpha® is the alpha-2 agonist medetomidine combined with the peripherally-acting alpha-2 antagonist vatinoxan. With this drug the central effects of medetomidine (sedation and analgesia) are maintained while the peripheral effects (vasoconstriction, bradycardia, etc…) are prevented or at least diminished.

Propofol

Not new – but have you ever used a 'propofol sandwich'? Administration of 1.0 mg/kg propofol prior to administration of 0.25 mg/kg midazolam followed by propofol 'to effect' until intubation was possible resulted in smoother inductions (midazolam often causes excitement when used first) and lower overall propofol dosages that administering the midazolam first. (Sanchez et al. Veterinary Anaesthesia and Analgesia 2013;40(4):359–366.

Alfaxalone (Alfaxan®)
Alfaxalone is a new-ish induction drug ('neuroactive steroid'), DEA Class IV. It can be used IV for anesthesia induction or IM for mild to moderate sedation in cats and very small dogs (otherwise the volume is too large). How to use it: 1) As an induction drug in exactly the same way that you would use propofol. Dose: 2-3 mg/kg IV in dogs, up to 5 mg/kg in cats. 2) For IM sedation in cats that may not be able to metabolize acepromazine and/or have cardiovascular disease that precludes the use of alpha-2 agonists. Administer 0.5-2 mg/kg with an opioid.

Dopamine and dobutamine (not necessarily new but new to some)
These are positive inotropic drugs used to treat hypotension by increasing myocardial contractility.
How to use them: As an infusion to improve blood pressure. It is an obvious choice in patients with cardiovascular dysfunction but should also be considered in patients who are hypotensive in spite of decreasing the inhalant dose and increasing the fluid rate. The inhalants cause hypotension by both vasodilation and decreased myocardial contractility, so even patients with healthy hearts might need to receive dopamine to improve blood pressure during general anesthesia.

Equipment
'Pop-Off' occlusion valve (or 'occlusion button')

Instead of completely closing the pop-off (or 'pressure relief') valve to give the patient a breath, just push this button for temporary closure of the valve. When you release the pressure on the button, the valve is automatically open. This prevents accidental prolonged closure of the valve – which can cause rapid pressurization of the breathing system and patient's the airway. Over-pressurization can cause cardiovascular collapse, pulmonary barotrauma, and death in a very short time (minutes).
Advantages: EASY, cheap. Will prevent an accident that can cause dire consequences.
Disadvantages: Takes two hands to give a patient a breath (small price to pay for safety); some models supposedly leak inhalant anesthetic (might be due to failure of the button to close the orifice all the way).
Source: Multiple companies, eg, Surgivet and JD Medical.

Bain 'Block' or 'Mount

Block or mount for attachment of a pressure manometer and scavenging system to the rebreathing system. This allows the pressure generated by a positive-pressure breath to be MEASURED, which decreases likelihood of barotrauma (pressure too high) or inadequate ventilation (pressure too low). Also decreases

contamination of room with waste gas because of attachment to scavenging system.
Source: Multiple companies

Syringe pumps or other volume-limiting devices
Use these for administration of drugs (analgesic CRIs, dopamine, etc…) AND for delivery of IV fluids to cats. A great way to avoid under- or over-hydration (the latter is a fairly common problem in really small patients). Over-hydration can lead to edema in a variety of tissues, most notably pulmonary edema.
Advantages: EASY to titrate drugs and fluids at an accurate dose.
Disadvantage: Some pumps are expensive; you have to learn to program them – which isn't all that hard but is something else to learn.

TIP: If you don't want syringe pumps, use buretrols (or any other fluid limiting device) when administering fluids to really small patients. OR, my favorite if equipment isn't available, just pull up the amount of fluid that the patient needs over the expected surgery duration into a syringe and have the anesthetist titrate it in a couple of mls at a time while they are monitoring the patient. Not a continuous method of delivery but close enough to continuous - and avoids overhydration. So for example, a 3 kg cat that needs 5 ml/kg/hour IV fluids that will be anesthetized for 2 hours, we draw up 3 kg x 5 ml/kg/hr x 2 hours = 30 mls of fluid into a syringe. It is easy to see 30 mls in a syringe – but really hard to determine 30 mls in a 1-liter bag of fluids.
Source: Multiple companies

Flexible foam cat mouth gags (use hair rollers!)
We don't use mouth gags for anesthesia but, of course, mouth gags are commonly used in anesthetized patients. Unfortunately, opening the mouth of a cat too wide causes decreased blood flow in the maxillary arteries (Martin-Flores et al. Vet J. 2014;200(1):60-4), which are the main blood source for the retinae and brain in the cat. The decreased blood flow secondary to mouth gag use has been implicated in post-anesthesia blindness and neurologic deficits. These deficits may resolve - but may be permanent and may result in euthanasia (Stiles et al. Vet J. 2012;193(2): 367-73).

Advantages: CHEAP! Doesn't force the mouth open excessively wide.
Disadvantages: May not open the mouth wide enough for some procedures in the caudal oral cavity. Can still open the mouth wider – but don't leave it that way too long!
TIP: Rollers can be rinsed off and re-used but just throw them away if the cat's mouth is particularly nasty or if the cat has any communicable disease. They are cheap!