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Anaesthetic Case Challenges Mini Series

Session Three: Pain – when an NSAID and an opioid are not enough

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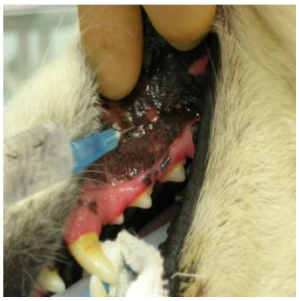

Acute Pain Management
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What is pain?

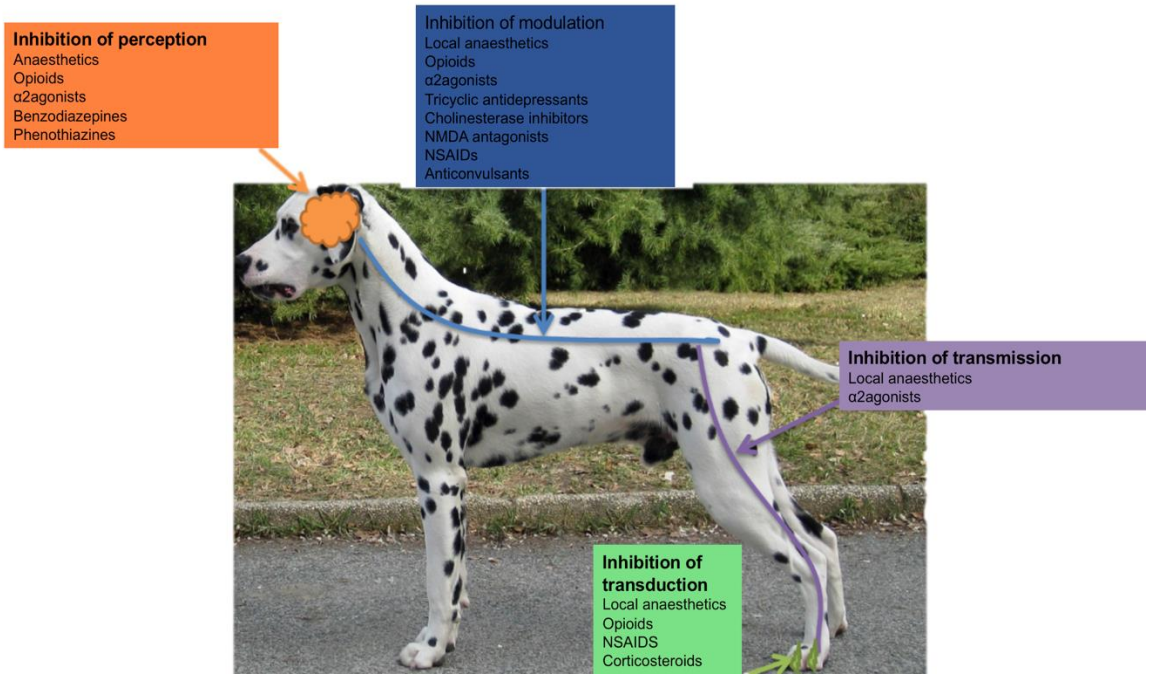
The International Association for the Study of Pain has defined pain as "*an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage*". Pain is therefore a subjective emotion.
The difficulty in veterinary medicine (and in non-verbal humans) is the inability of these patients to verbalise such emotions and in 2001 a note was added to the definition of pain. This states: "*the inability to communicate in **no way** negates the possibility that an individual is experiencing pain and is in need of appropriate pain relieving treatment*".
Molony and Kent in 1997 gave the following definition of pain in animals: "*an aversive sensory and emotional experience representing awareness by the animal of damage or threat to the integrity of its tissues…producing a change in physiology and behaviour directed to reduce or avoid the damage, reduce the likelihood of recurrence and promote recovery."* This definition already indicates that to assess pain in animals one must look for both physiological and behavioural changes.
There are different types (nociceptive, inflammatory, neuropathic and functional, cancer and post-surgical pain) and classifications (acute vs. chronic pain, somatic vs. visceral, superficial vs. deep) of pain, which reflect the complexity of this entity.
Acute pain is generally associated with tissue damage (or the threat of it). Acute pain has a protective purpose, it favours a change in the animal's behaviour and optimizes conditions in which healing can take place. This type of pain generally stops once healing has occurred. **Chronic pain**, which persists beyond the healing point, serves no purpose whatsoever and actually has a negative physical and psychological impact on the animal. Acute and chronic pain differ in aim but also in the ways of being assessed and their treatment.
Very often, in veterinary practice, pain is overlooked. The table below is from AAHA/AAFP pain management guidelines for dogs and cats which were published in 2007 and can be found online at www.aaha.org/professional/resources/pain_management.aspx and lists the most commonly overlooked painful conditions.

Type of Pain	Cause
Cardiopulmonary	Congestive heart failure (pulmonary edema and pleural effusion); pleuritis, cerebral vascular accident, thromboembolism (clot).
Oncologic	Any and all cancer.
Dermatologic	Otitis, severe pruritus, burns, chronic wounds; abscess, cellulitis, clipper burns, urine scalding, severe chin acne.
Dental	Oral tumors, feline oral resorptive lesions ("neck" lesions), fractures (no matter how small), tooth abscess, ulcers, stomatitis.
Gastrointestinal	Constipation, obstipation, obstruction, megacolon; anal sac impaction; hemorrhagic gastroenteritis, pancreatitis, gastric dilatation-volvulus (GDV), foreign body.
Musculoskeletal	Most often overlooked in cats. Muscular soreness, arthritis, degenerative joint disease, tendon or ligament injury, intervertebral disc disease, facet pain of spondylosis, osteodystrophy, dislocations.
Ocular	Corneal disease and ulcers, glaucoma, uveitis.
Urogenital	Uroliths, ureteroliths, queening/whelping, feline lower urinary tract disease/interstitial cystitis, acute renal failure, enlarged kidneys (capsular swelling), lower urinary tract infections, urinary obstruction, vaginitis (especially in obese cats).
Hospital procedures	Restraint (examination, obtaining blood and urine samples, radiographs, and ultrasound; even gentle handling and hard surfaces can increase pain in an already painful animal). Urinary/IV catheterization, bandaging, surgery, thoracocentesis, chest tube placement and drainage procedures, abdominocentesis. Manual extraction of stool and anal sac expression (especially in cats).
Surgical procedures	Ovariohysterectomy, castration, onychectomy,* growth removal, and all other surgical procedures.
Neurologic	Diabetic neuropathy.

If pain remains untreated, the stress response is initiated, with activation of the endocrine system and consequent increase in cortisol, catecholamines and inflammatory mediators. These will cause tachycardia, vasoconstriction, decreased GI motility, delayed wound healing, sleep deprivation and changes in the CNS with magnification and prolongation of the pain state.
In humans up to 10-50% of patient experience persistent post-surgical pain with 2-10% of these developing chronic pain.
In small animals the number of patient suffering form chronic pain is unknows but in a study in dogs, 1/3 of patients undergoing stifle stabilisation surgery experienced chronic pain.

In recent years, the concept of **preventive** analgesia is taking over the one of **pre-emptive** analgesia. The latter being an antinociceptive intervention that starts **before** surgical incision and is more effective in relieving acute postoperative pain than the same treatment starting after surgery. Preventive analgesia instead is aimed to **block** the development of sustained pain. A broader definition of preventive analgesia includes any regimen given at **any time** during the perioperative period that will be able to control pain-induced sensitization. Anyhow, the treatment of acute pain as effectively and soon as possible is paramount to avoid long term complications.

The pathways responsible for producing pain involve four main steps. Noxious stimuli (mechanical, thermal, electrical or chemical) stimulate peripheral receptors and are transformed into electrical signals (transduction), which are then transmitted (transmission) to the spinal cord where they are modulated (modulation) and then relayed (projection) to the brain where they are finally processed and produce awareness of that painful stimulation (perception). As different drugs inhibit pain at one or more of these steps, often a combo of drugs should be used to effectively provide analgesia.



Pain assessment

Pain assessment is a fundamental tool to ensure good quality analgesia and to avoid acute pain turning into chronic.
Several factors influence how the patients will express pain. Age, species, the individual itself and its genetical variation in the number and distribution of opioids, as well as sedation levels are all important (and not the only) factors.
To assess pain in animals, both physiological and behavioural parameters should be considered.
Physiological signs include heart rate, blood pressure, pupil dilatation. These are common to pain and stress, hence are difficult to use in an – very likely stressed – hospitalised patient.

Behavioural signs are more reliable. Loss of normal behaviour or the development of a new abnormal behaviour can be good indicators of pain, but again could indicate a stressful situation.
Discomfort or dysphoria can often be confused with - or occur simultaneously to - pain. It is important to make sure the patient's bladder is empty, that the patient is on a comfortable bedding, in a good position and that both its body and ambient temperature are adequate. To distinguish pain from discomfort it is important to interact with the patient. If the patient calms down it is likely to be in pain. In doubt, analgesia should be administered and if the patient's status improves then the patient was likely to be in pain. Otherwise it was dysphoria and a sedative such as acepromazine or medetomidine should be administered unless contraindicated.
Recently several categorical ways of assessing pain have been validated in both cats and dogs.
Pain scales should be used as an adjunct to physical evaluation and are important to ensure pain is assessed and treated in every patient.
There are several more or less complex or and more or less objective pain scales for assessment of acute pain in small animals. In recent years several have been validated in cats and dogs. Amongst these, the most commonly used in the UK are probably the *Definite Revised Glasgow Composite Measure Pain Scale (2014) for cats* and the *Glasgow Composite Measure Pain Scale - Short Form for dogs*. These scales can be found online and downloaded for free from: http://www.aprvt.com/uploads/5/3/0/5/5305564/cmp_feline_eng.pdf and https://www.wsava.org/WSAVA/media/PDF_old/Canine-CMPS-SF_0.pdf .
The use of these pain scales will allow analgesia to be tailored to the patient. Analgesics will be given only If the patient is painful and overtreatment is avoided. On the downside, patients will need to actually experience pain so that it can be identified and treated. These scales also require staff time, regular disturbance of the patient and of its rest and finally in stoic patients it is likely that analgesia will be withheld when it is instead necessary.
Because of the limitations that co-exist with every pain scale, analgesia should not be denied if the pain score of a patient is low but the procedure is likely to be painful. In this case a test dose of analgesic should be administered and the patients' response should be assessed.
Sedated or critically ill patients may not be able to express adequate pain behaviours and, also in these cases, a test dose of analgesics should be administered. Increased awareness to surroundings can be considered as a positive response to the analgesic treatment.
It is also fundamental to keep in mind that pain experience can alter rapidly, and pain assessments should be performed frequently. Sometimes, as mentioned above, the best tool for accurate diagnosis of pain is the actual administration of an analgesic. The patient will then need to be re-assessed, analgesic efficacy will need to be re-evaluated and finally analgesia will need to be re-administered appropriately as assessment requires.

Analgesic drugs:

Several drugs are used nowadays to treat pain in our companion animals. Many are licensed and some are used off license. These notes contain both licensed and commonly used unlicensed drugs. The reader is referred to the UK and the cascade legislation for the off license use of these drugs

Non-steroidal anti-inflammatory drugs (NSAIDS):

This class of drugs includes molecules that specifically inhibit the formation of prostaglandins and of thromboxanes from arachidonic acid. To achieve this, NSAIDS inhibit cyclo-oxygenase (COX) enzymes. There are two isoforms of this enzyme. COX 1 which is said to be constitutively expressed in many tissues and COX 2 which is inducible by inflammation in many tissues.
COX 1 is normally called the good "housekeeping" enzyme and much effort was put in producing drugs which were COX 2 selective (i.e inhibited only the COX 2). However, recent data demonstrates that COX 2 is constitutively expressed in the kidney and repairs gastric erosions, and COX 1 products may also contribute to the inflammatory response. In the light of this, nowadays drugs which inhibit preferentially COX 2 and also a little bit of COX 1 should be preferred. Most veterinary NSAIDS (i.e meloxicam) are COX 2 selective rather than specific.
Unless contraindicated NSAIDS should be the first line of any analgesic regimen. Several drugs and several formulations of NSAIDS are licensed for both acute and chronic pain in cats and dogs.
NSAIDS have anti-inflammatory, antipyretic, analgesic and anti-endotoxic effects. Some (meloxicam and carprofen for example) also have chondroprotective effects.

They can be used as sole analgesic against inflammatory pain or in the case of very mild pain. Usually they are used in conjunction to an opioid.
From a pharmacological point of view NSAIDS are weak acids and they are well absorbed both via the oral and the subcutaneous routes. They are highly protein bound and should be used with care in the hypo-proteinaemic patient. NSAIDS are metabolized mainly by the liver and excreted in the urine. Because metabolism (as potency) varies in the different species, the half-life will vary a lot in between different animals and dosing should be based on data for the species in consideration.
A peculiarity of most NSAIDS is that the duration of anti-inflammatory effects is considerably longer than the plasma half-life and this is due to the fact that leakage of proteins in the inflamed tissue will "trap" NSAIDS which will tend to accumulate in the inflamed tissue.
The response of patients to the variety of NSAIDS available is not only very subjective but also differs according to the condition. If one NSAID does not seem to provide the desired effects, it is worth trying another one but allowing at least 48 hours (not scientifically determined) of "washout" period. The only study looking at the washout period showed that an interval of up to 1 week between beginning treatment with firocoxib and cessation of treatment with a different NSAID was not associated with any increased risk of adverse events.

In spite of being widely used in veterinary (and human) medicine, NSAIDS have some side effects which are worth mentioning.
-Gastrointestinal effects: By inhibiting the production of PGI2 and PGE2 (COX 1 products) which have anti-acid effects, NSAIDS can increase the risk of gastric ulceration.
-Renal effects: PGE1 and PGE2 are vasodilator and are responsible of maintaining renal blood flow constant during periods of hypotension and/or hypovolaemia. They are not the primary responsible of renal blood flow in normal individuals, therefore no negative effects are seen in patients in which kidney function is adequate and in which blood pressure is maintained within normal limits.
- Hepatic effects: Because the metabolism and excretion of NSAIDS varies within species, it is difficult to determine their level of hepatotoxicity. Absolutely avoid the use of paracetamol in the cat. There has been a case report of acute hepatic dysfunction in Labradors after administration of carpofen but the pathogenesis was not clear.
- Platelet effects: TXA2 promotes platelet aggregation, meanwhile PGI2 inhibits it. Non-selective COX inhibitor increase the risk of intra-operative haemorrhage. In a recent paper oral administration of some COX 2 selective NSAIDS (carprofen, meloxicam and deracoxib) caused detectable alterations in platelet function in dogs and therefore individual assessment of platelet function is advised when administering these drugs prior to surgery, particularly in the presence of other risk factors for bleeding.
- Reproduction: PG are widely involved in ovulation, embryo implantation, normal labour and closure of the ductus arteriosus. The safety of NSAIDS has not been determined in the pregnant, lactating and breeding animal.
- Respiratory system: NSAIDS are not recommended in asthmatic patients as, by inhibiting COX enzyme, they shunt more arachidonic acid down the 5-lipoxygenasee pathway, producing more leukotrienes which can enhance bronchial reactivity.
- Cartilage: Although some NSAIDS are chondroprotective, others decrease proteoglycan synthesis and have chondrodystrophic effects.

As a general rule NSAIDS are contraindicated in patients which are dehydrated or hypovolaemic, with impaired renal or hepatic function, patients with gastrointestinal ulcers or erosions, coagulopathies or patients which are pregnant or lactating.
Because of the risk of hypotension during anaesthesia, many prefer to administer NSAIDs after then end of surgery, others instead prefer pre-surgical administration of NSAIDs (preventive analgesia). The choice is case sensitive and depends on several factors such as possible contraindications (is the patient hypovolaemic or dehydrated, is he at risk of hypotension or haemorrhage during surgery?). Also, the human and veterinary literature gives conflicting results on the MAC sparing or pre-emptive analgesic effects of NSAIDs.

<u>Carporfen:</u>
COX 2 specific NSAID. It is licensed in the injectable form for both dogs and cats and orally only in dogs.
After oral administration, peak plasma concentration is achieved in 1-3 hours from administration and the plasma half-life is reported to be between 10 hours in the dog and up to 49 hours (generally 20 hours) in the cat. The duration of effect in dogs is reported to be 12-18 hours.

The injectable formulation is licensed for pre-operative administration in dogs and cats and when administered pre-operatively, the analgesic effects were superior than when administered post-operatively.
Numerous studies have also demonstrated carprofen to be an effective analgesic against osteoarthritis in dogs.
Although there has been a case report of carprofen associated hepatotoxicity in Labrador dogs, data from the FDA suggest that the incidence of hepatotoxicity related to carprofen is no higher than the one from other NSAIDS

Meloxicam:
COX 2 specific NSAID. It is licensed in the injectable form and in the oral form as a palatable syrup or chewable tablets for both dogs and cats.
The half-life of meloxicam in both dogs and cats is prolonged (20-30 hours) therefore it is administered only once daily.
Unlike the majority of NSAIDS which are metabolised by glucuronidation in the liver, meloxicam is metabolised by oxidation. Because cats have a relative deficiency of glucuronyl transferase enzymes, the different metabolic pathway favours the chronic use of meloxicam in this species.
As for most NSAIDS the analgesic dose is higher than the anti-inflammatory one. When used for peri-operative analgesia, higher doses should be used compared to when meloxicam is used for chronic pain relief.
Pre-operative meloxicam has been shown to have no negative effects on renal function in dogs, also in the presence of mild hypotension. This said, blood pressure should still be monitored when administering an NSAID pre-operatively.
Meloxicam is an effective analgesic for chronic osteoarthritis. It is the only NSAID licensed for chronic use in the cat. The dose should be tapered to the lowest effective dose. Due to the inter-cat variability, daily dosing (at a dose often lower than the licensed one) may be necessary for some cats meanwhile longer intervals may be enough for others. Often cats with osteoarthritis are old and may have chronic kidney disease (CKD). In the USA, meloxicam has been black boxed for causing kidney disease, but research has shown that long-term treatment with oral meloxicam did not appear to reduce the lifespan of cats with pre-existent stable CKD. Analgesia with NSAIDS should not be denied in old cats with renal disease.

Firocoxib:
Selective COX 2 inhibitor NSAID. It is licensed in the oral formulation for the relief of pain and inflammation associated with osteoarthritis in dogs and for the relief of post-operative pain and inflammation associated with soft-tissue, orthopaedic and dental surgery in dogs.
In dogs undergoing ovariohysterectomy, firocoxib produced better post-operative analgesia than butorphanol. And in another study firocoxib was shown to be effective in managing pain associated with osteoarthritis for 90 days in geriatric dogs inducing minimal biochemical changes and adverse drug events.

Ketoprofen:
Non-specific COX inhibitor NSAID. Available in the injectable and oral formulations for both the dog and the cat.
Ketoprofen can be used for chronic pain management but it is not licensed for pre-operative use because it has been reported to cause clotting problems. Because newer, more specific and safer NSAIDS are now licensed for use in cat and dogs, ketoprofen does not really have a place in veterinary medicine anymore.

Robenacoxib
Selective COX-2 inhibitor. Available in the injectable and oral formulations for both dogs and cats.
Robenacoxib is licensed for the treatment of pain and inflammation associated with orthopaedic or soft tissue surgery in dogs and cats and for the treatment of chronic osteoarthritis pain in the dog.
Robenacoxib is highly bound to plasma proteins (>99%) and is extensively metabolised by the liver in cats and dogs. Peak blood concentrations are attained rapidly after subcutaneous injection or oral administration (0.5 hours).
After subcutaneous administration, the terminal half-life from blood was 1.1-1.7 hours.
As with other NSAIDS, robenacoxib persists longer and in higher concentrations at sites of inflammation than in blood and, for this reason, in spite of its short terminal half life, it only needs to be administered once daily.

Robenacoxib is excreted predominantly via the biliary route in cats (~70%) and dogs (~65%) and the remainder via the kidneys. Repeated subcutaneous administration at dosages of 2-20 mg/kg produced no change in the blood profile.
Unlike other NSAIDS robenacoxib has been shown to decrease the MAC of sevoflurane in the dog.

Paracetamol:
Classified as an NSAID although it acts in a slightly different manner. Paracetamol inhibits a COX 1 variant present in the CNS, called COX 3 and possibly also COX 2. It is also thought to act as a pro-drug, its active form being a cannabinoid which provides analgesia.
In dogs paracetamol is mainly metabolised by glucuronidation and less by sulphation in the liver. When these pathways are exhausted, the oxidative pathway becomes predominant and this results in the production of N-acetyl-P-benzoquinoneimine (NAPQI) which is a highly reactive oxidant species. Because in cats the glucuronidation and the sulphonidation pathways are less active, even small doses of paracetamol can cause an excessive amount of NAPQI and paracetamol toxicity.
Paracetamol should not be used in the cat.

Drug	Use	Dose, route
Carprofen	Surgical pain Chronic pain	Dog: 4 mg/kg IV, SC preop once Can be continued PO - 4 mg/kg/day for up to 5 days, then at 2 mg/kg/day Cat: 4 mg/kg SC single dose at induction Dog: 4 mg/kg/day PO for up to 7 days, then at 2 mg/kg/day
Meloxicam	Surgical pain Chronic pain	Dog: 0.2 mg/kg SC, PO as a single dose. Can be followed by 0.1 mg/kg PO q 24hr Cat: 0.2 mg/kg SC as a single dose. Can continue treatment after 24hr with 0.05 mg/kg PO – up to 5 days Single injection of 0.3 mg/kg SC Dog: 0.2 mg/kg SC, PO as a single dose. Can be followed by 0.1 mg/kg PO q 24hr Cat: Initial oral dose of 0.1 mg/kg PO q 24hr, followed by 0.05 mg/kg PO q 24hr up to 14 days if no improvement is apparent. Use minimum effective dose
Firocoxib	Surgical / chronic pain	Dog: 5 mg/kg PO q 24hrs up to 3 days
Ketoprofen	Surgical / chronic pain	Dog: 2 mg/kg IV, SC, IM 1 mg/kg PO post-operative then once daily for up to 3 days 0.25 mg/kg PO for up to 30 days. If continued treatment required, re-examine the dog first DO NOT GIVE PRE-OP Cat: 2 mg/kg IV, SC, IM 1 mg/kg PO post-operative then once daily for up to 5 days
Robenacoxib	Surgical pain/acute musculoskeletal Chronic pain	Dog: 2mg/kg SC followed by 1 mg/kg PO once daily Cat: 2mg/kg SC followed by 1 mg/kg PO once daily for up to 6 days – use lowest effective dose Dog: 1mg/kg PO
Tepoxalin	Chronic pain	Dog: 10 mg/kg PO once daily
Paracetamol	Acute/chronic pain	Dog: 10-15 mg/kg PO or 10 mg/kg IV over 15 min q 8-12hr DO NOT USE IN CATS

Opioids:

Although the aim of this seminar is to discuss analgesic drugs other than opioids, for centuries the opium poppy has been used to provide analgesia and it remains the mainstay of most analgesic regimens. For this reason, opioids will still be discussed in depth in these notes.
Opioids are considered to be more effective for dull rather than sharp pain but in clinical practice they are successfully used for all types of pain.

Opioids available in veterinary medicine are classified as Schedule 2 or 3 drugs and undergo more or less strict regulations.
This class of drugs acts by binding to opioid receptors that are widespread throughout the body. The main opioid receptors are called μ, κ and δ. The combination of an opioid with one of these receptors provides analgesia but also other effects. These side effects are reduced when an opioid is administered to an animal in pain.
- Respiratory depression: the sensitivity of the respiratory centre to changes in carbon dioxide is reduced. In small animals, mostly when awake, this does not seem to be such a big problem as it is in humans. Pure μ agonists can cause panting due to changes in the central thermoregulation set point. Butorphanol and fentanyl have potent antitussive effects.
- Cardiovascular effects: Most opioids (with the exception of pethidine) cause bradycardia secondary to increased vagal tone. This is atropine responsive. Some opioids (pethidine and morphine) can cause histamine release with consequent tachycardia and hypotension. Etorphine and carfentanil can cause severe hypotension.
- Gastrointestinal effects: Opioids (with the exception of pethidine) decrease peristaltic activity of the GI tract (in reality they increase motility but this is uncoordinated). Defecation is common in the first phase. Again, with the exception of pethidine (which is spasmolytic), pure μ agonists, increase sphincter tone, including the pyloric and the biliary sphincter (Oddi). This means that pure μ agonists are not recommended for duodenal endoscopy and have been avoided in animals with biliary obstruction. The latter concept is now abandoned in dogs as it is unlikely this species has a sphincter of Oddi.
Opioids act both on the chemoreceptor trigger zone (CTZ) in the medulla to cause emesis and on the vomiting centre (VC) to cause anti-emetic effects. The CTZ is not protected by the blood brain barrier but the VC is. For drugs which are more fat soluble (i.e methadone compared to morphine) and can cross the blood brain barrier faster, the emetic effects of the CTZ are offset by the antiemetic effects of the VC and no vomiting occurs. This explains why animals given morphine will vomit meanwhile animals given methadone will not. Vomiting can be reduced if acepromazine is administered 15 minutes prior to intramuscular morphine.
In cats excessive salivation can be observed.
- Other effects: μ agonists cause miosis in the dog (stimulation of the cell bodies in the oculomotor nuclear complex) and mydriasis in the cat (catecholamine induced). Mydriasis increases sensitivity to light and care should be taken when handling cats which have received μ agonists.
In dogs, opioids decrease the thermoregulatory set point in the CNS and cause panting. In cats instead, opioid induced hyperthermia is common.
μ agonists increase urethral sphincter tone and inhibit the voiding reflex. Often, if the bladder is not expressed, there will be urine overflow and this can be mistaken for incontinence.

Effect	μ	κ	δ
Analgesia - supraspinal	+++	-	-
- spinal	++	+	+
- peripheral	++	++	-
Respiratory depression	+++	-	++
Gastro-intestinal effects	++	+	+
Sedation	++	++	-
Effect on pupil	Miosis dog Mydriasis cat	Miosis	Mydriasis
Euphoria	+++	-	-
Dysphoria	-	+++	-

Opioids are classified based on the receptors they act on and on their effects on that receptor (agonists vs antagonists)

Opioid	μ	κ	δ
Morphine	+++	+/0	+/0
Methadone	+++	0	0
Pethidine	+++	+/0	0
Fentanyl	+++	0	0
Remifentanil	+++	0	0
Buprenorphine	++	--	+/0
Butorphanol	-	++	0
Naloxone	---	--	-

+ agonist, - antagonist, 0 no action

Pure μ agonists:

- Morphine: 0.1-0.6 mg/kg q 4-6 hours IV, IM, SC –
Not licensed for use in small animals
This is the "gold standard" of the opioids (to which all the other opioids are compared). It is not licensed for use in small animals. The IV route must be used with caution as if administered too fast, morphine can cause histamine release. Morphine can also be administered intra-articularly, epidurally and spinally (the preservative free form being preferred in this case). Absorption of orally administered morphine is poor. It is not very protein bound (30%). Morphine causes vomiting by acting on the CTZ. This opioid is metabolised by glucuronidation to morphine-3-glucuronide and morphine-6-glucuronide. The latter is an active metabolite, more potent than the parent compound. Because cats have low glucuronidation capabilities, they produce less morphine-6-glucuronide.
Morphine can be used as a CRI at 0.1-0.3 mg/kg/hr.

- **Methadone:** 0.1-0.6 mg/kg q 4-6 hours IV, IM, SC
This opioid is licensed for use in small animals. It has very similar potency to morphine but because it is more liposoluble it does not cause vomiting and may have a quicker onset. Methadone does not cause histamine release.
This opioid has NMDA antagonistics effects.
In dogs, methadone alone produces mild sedation and a high incidence of panting. A greater level of sedation is achieved when methadone is used in combination with acepromazine or an alpha$_2$agonist. In a study comparing the effects of morphine, methadone, butorphanol or tramadol in combination with acepromazine, methadone appeared to provide better sedation than the other drugs.
When comparing morphine and methadone's effects on the cardiovascular parameters in conscious dogs, methadone is a more potent cardiovascular depressant agent than morphine and its effects seemed to be dose related.
Methadone can accumulate after prolonged use in humans but in small animal patients CRIs have been used with no clinically obvious cumulative effects. The recommended dose is 0.1-0.3 mg/kg/hr.

- **Pethidine:** 2-5 mg/kg IM, SC q 1.5-2 hours
Pethidine is licensed for use in small animals. It has about 1/10th of the potency of morphine. It must not be administered IV as it will cause histamine release. As mentioned earlier - unlike the other opioids - pethidine has vagolytic (increases the heart rate) and spasmolytic effects.
Pethidine also has local anaesthetic-like and NMDA antagonistic activity. Furthermore pethidine also inhibits noradrenaline and serotonin reuptake. Pethidine should be used with caution in patients taking monoamine oxidase inhibitor (MAO) (selegiline), sympathomimetics (phenylpropanolamine, ephedrine) or tricyclic antidepressants (clomipramine) which also increase circulating adrenaline and serotonin levels and can cause consequent possible serotonin syndrome.
Although not scientifically proven, pethidine seems to be very useful in "taking the edge off" nervous patients in which an opioid is chosen as the sole premedication agent. The patient will not seem sedated but is often easier to handle.

-**Fentanyl**: 1mcg/kg-7 mcg/kg IV, IM, SC
Fentanyl is a very potent μ agonist (100 times the efficacy of morphine), it is licensed for IV use in small animals.
This drug has a very fast onset of action (1-2 minutes) and a short duration of action (up to 20 minutes after a bolus, longer after a prolonged infusion). As for the efficacy, also the respiratory depression and the bradycardia caused by this drug will be important. Mostly when given under general anaesthesia, the patient will require ventilatory support and sometimes the administration of an anticolinergic. Fentanyl used as a CRI (0.1-0.5 mcg/kg/min) during surgery will allow to decrease the amount of inhalant anaesthetic used (MAC sparing effect). It should be kept in mind that after prolonged infusions fentanyl may accumulate.

- **Remifentanil, Alfentanil and Sufentanil** are synthetic analogues of fentanyl. These are respectively 50, 20 and 1000 times more potent than morphine. They are rarely used in veterinary medicine. The only one with is used more often is remifentanil as it has the peculiarity of being metabolised by red blood cell cholinesterase and not from the liver. Its use can therefore be justified in patients with severe liver disease. These drugs are not licensed for use in small animals

-**Tramadol:** 1-5 mg/kg IV, PO, q 6hrs
Not licensed for use in small animals
Tramadol is classified as an atypical μ agonist. It is available both in the injectable and oral formulation. It has 1/10 the potency of morphine. Analgesia is provided by action on μ receptors from the parent drug and its metabolite (100 times more potent than the parent compound). Analgesia also occurs via inhibition of noradrenaline and serotonin reuptake and via its weak alpha$_2$agonistic effects. As for pethidine, tramadol should be used with caution in patients taking monoamine oxidase inhibitor (selegiline), sympathomimetics (phenylpropanolamine, ephedrine) or tricyclic antidepressants (clomipramine) which also increase circulating adrenaline and serotonin levels and can cause consequent possible serotonin syndrome.
Side effects include vomiting and drowsiness.

Partial μ agonists
-**Buprenorphine** 0.01-0.02 mg/kg IV, IM, SC, OTM q 6-8 hours
This opioid is licensed for use in the dog and cat. Buprenorphine has a very strong affinity for μ receptors but only partial agonist activity. This means buprenorphine will occupy the μ receptor but will not exert full action (the effect will always be less than maximal) on these receptors.
The time of onset is slow (20-45 minutes depending on the route of administration). A peculiarity of buprenorphine is that, in the cat it is well absorbed via the oral transmucosal route (different from oral route!). This does not happen in the dog as they have a different salivary pH.
When administered to non painful cats, buprenorphine tends to cause euphoria (rather than dysphoria). Although euphoric cats may be extremely friendly, placing an IV cannula in a rolling, purring, continuously grooming cat may be difficult.
The analgesia provided by this opioid has a characteristic bell-shaped curve, where higher doses produce less analgesia than lower doses.
Also it is worth highlighting that as the affinity of buprenorphine for the μ receptor is higher than that of the pure μ agonists, if a painful procedure (i.e. ex lap, fracture repair) is planned in the next 6-8 hours, then the use of buprenorphine should be avoided and a pure μ agonist should be used instead.

Agonist-antagonists:
-Butorphanol 0.1-0.4 mg/kg IM, IV, SC q 2hrs
This opioid, licensed for use in cats and dogs is agonist on the κ and antagonist on the μ receptors. This means that the analgesia provided by this opioid is minimal and its use should be reserved for non painful procedures. The onset of action is short (a few minutes to 30 minutes depending on the route of administration) and so is the duration of action (45 min to 2 hrs). It is a potent antitussive.

Opioid	Potency	Dose	Duration of action (hr)
Morphine	1	0.1-0.6 mg/kg	4-6
Methadone	1	0.1-0.6 mg/kg	4-6
Pethidine	0.1	2-5 mg/kg	1.5-2
Fentanyl bolus **CRI**	100	0.001-0.007 mg/kg 0.1-0.5 µg/kg/min	0.3
Remifentanil CRI	50	0.1 µg/kg/min	
Buprenorphine		0.01-0.02 mg/kg	6-12
Butorphanol		0.1-0.4 mg/kg	0.7-2
Tramadol		1-5 (start with lower doses) mg/kg	6-12
Naloxone		0.002-0.04 mg/kg	0.5-1

NMDA- antagonists:

Ketamine 0.2-0.5 mg/kg IV, IM, SC
Ketamine is an un-competitive NMDA receptor antagonist. It is licensed as an anaesthetic in the cat and the dog but can be used under the cascade for analgesia. Ketamine is a Schedule 2 controlled drug.
Although this is becoming controversial because the evidence is scares, the use of ketamine should be avoided in those patients where a rise in intracranial or intraocular pressure is not wanted
The analgesic dose of ketamine is lower than the anaesthetic dose (sub-anaesthetic). Beneficial effects including improved appetite and lower pain scores have been shown after soft tissue and major orthopaedic surgery. In trauma patients treatment should begin as soon as possible after initial triage.
Ketamine's effects on the NMDA receptor can occur only if the receptor is activated, hence from a physiological point of view, ketamine should be more effective in chronic pain statuses or at least when the painful stimulus is already present.
Doses as little as 0.2-0.5 mg/kg IV, IM, SC as a one off or repeated as necessary are enough to provide analgesia. Ketamine can also be used as a CRI (1-20 µg/kg/min). When ketamine is administered under general anaesthesia (mostly if administered IV), a decrease in respiratory rate and/or blood pressure can be seen. This will not happen because of the ketamine but because of the potent MAC sparing effects of this drug. The inhalant anaesthetic should therefore be decreased after the administration of ketamine.
Ketamine indirectly stimulates the sympathetic system and can be useful to maintain heart rate and blood pressure when needed. Because of its action on NMDA receptor, ketamine is highly recommended in patients with neurological pain or in patients in which chronic pain may be an issue (amputation, spinal patients). Recently it has also been shown that ketamine limits opioid dependence and opioid induced hyperalgesia.

Local anaesthetics:

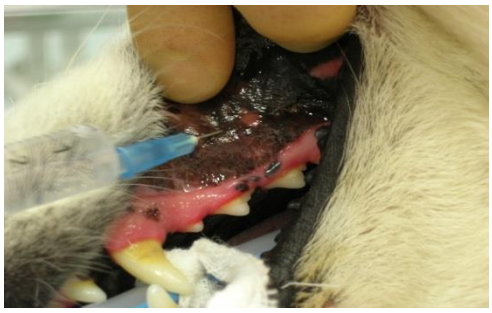
This class of drugs is very useful in controlling pain. Local anaesthetics can be administered via most routes. They exert their action by blocking voltage gated sodium channels and therefore preventing membrane depolarisation. The local anaesthetics most commonly used in veterinary medicine belong to the amide linked category.
When using local anaesthetic in cats, always use the lower dose as this species seem to be more sensitive to this class of drugs.

Drug	Dose (mg/kg)	Onset of action (min)	Duration of action (hours)	Toxic dose (mg/kg)	Comments
Lidocaine	1-2	5-20	1-2	8-10	Some solutions (including the licensed one) may contain adrenaline
Bupivacaine	1-2	10-20	4-5	4	Not licensed
Ropivacaine	2-3	10-20	3-5	5	Not licensed. Slightly less potent than bupivacaine but also less cardiotoxic.

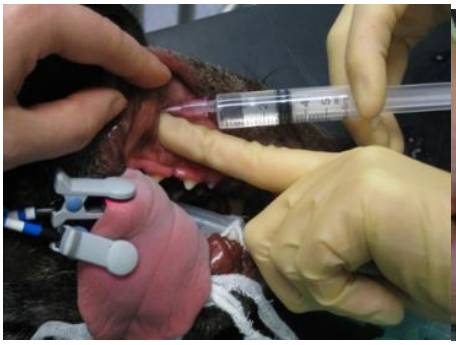
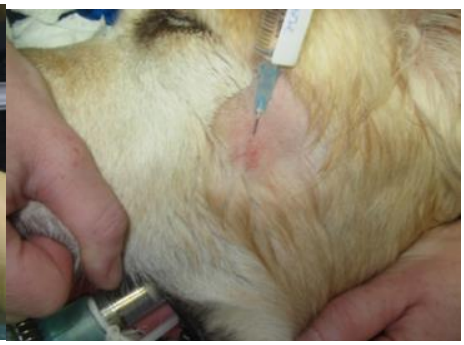
Local anaesthetics can be applied topically on mucous membranes, on the conjunctiva and the cornea, intra-articular, intra-pleural, intra-peritoneal and as splash blocks. Also, they can be infiltrated in the surgical wound with the aid of a needle or of a wound soaker catheter.
Local anaesthetics are well known for their use for specific nerve blocks and for their use in epidural anaesthesia.
The main blocks which can be performed in private practice are described below. Always draw back before injecting a local anaesthetic to avoid intravascular administration and if too much resistance is perceived on injection, draw the needle back slightly to avoid the risk of intraneural injection
Some local blocks can be performed blindly, others require the use of a nerve stimulator or of an ultrasound machine.
To use a **nerve stimulator**, the nerve which is located must have a motor component and special needles should be used. These needles are completely insulated except for their tip, so that the conduction of the stimulus occurs only at the tip. These needles are both connected to the nerve stimulator and to a port allowing local anaesthetic to be delivered. The area of interest should be clipped and prepped, and the needle inserted according to the landmarks for the determined block. Once the needle is inserted in muscle, a current of 1mA, 2Hz is provided and until a strong muscle twitch corresponding to the nerve stimulated appears. The current is then slowly decreased, and the needle repositioned until the muscle twitch is present at about 0.5-0.4 mA but absent at 2 mA (otherwise the needle is too close to the nerve in question). At this point, after withdrawal to check for the absence of blood (indicating intravascular injection), local anaesthetic can be injected. The muscle twitch will disappear as soon as a few mL of local anaesthetic are injected.
The use of an ultrasound machine in conjunction (or not) to a nerve stimulator is becoming always more frequent. This US allows to visualise the nerve (also located through electrical stimulation) and to ascertain that the local anaesthetic is being deposited all around the nerve (donut effect).

Nerve blocks of the head

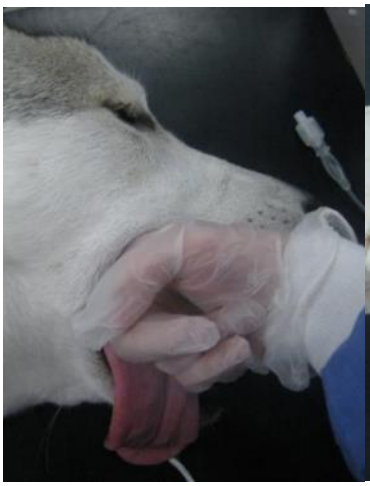
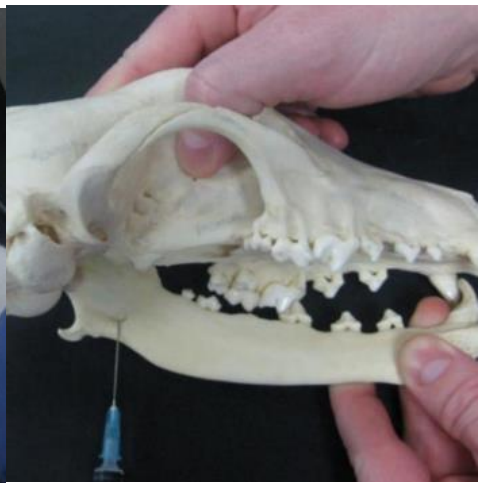
Nerve blocks performed on the head are easily performed, very useful mostly with the ‘old patient’s dental’ and do not require the use of a nerve stimulator.
-Infraorbital nerve block: This block aims to desensitize the nose, the upper lip, the skin and the teeth rostroventral to the infraorbital foramen. The block can be performed intra-orally or extra-orally (through the skin). The infraorbital nerve is blocked with a 25g needle at the level of the infraorbital foramen which can be palpated midway between the rostral border of the zygomatic arch and the canine tooth on the same side. Very little local anaesthetic is required and a dose of 0.05-0.1 ml/10kg is sufficient.



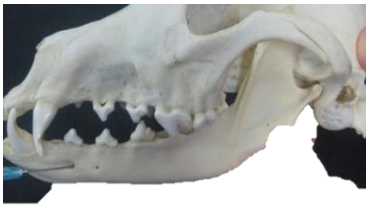
-Maxillary nerve block: This block aims to desensitize the nasal planum, the upper lip and teeth, the maxilla and the palate. The maxillary nerve is blocked proximally when it enters the infraorbital canal by performing a “deep” infraorbital block. For this approach, to avoid nerve damage, it is recommended to use an IV cannula.
Other approaches to this nerve can be the extraoral approach, when a 23g needle is inserted caudal to the zygomatic arch, approximately 1 cm caudal to the lateral canthus of the eye and with the needle directed towards the pterygopalatine fossa.
A third approach to this nerve is the intraoral approach, where the nerve is blocked inserting the needle behind the last upper molar
A dose of 0.5-1 ml/10 kg of local anaesthetic is sufficient to block this nerve

-Mandibular nerve block: This desensitizes the lower teeth, the mandible, the skin and the mucosa of the lower lip. The mandibular nerve can be blocked on the medial surface of the mandible, by inserting a 23 g needle just in front of the angular process of the mandible. By inserting a finger in the mouth of an anaesthetised patient, the nerve can be palpated as a “guitar string” on the medial side of the lower angle of the jaw.

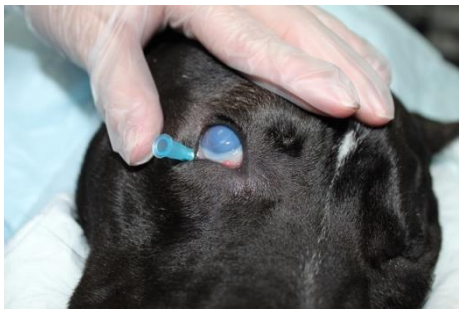



-Mental nerve block: This desensitizes the lower lip, teeth and chin rostral to the site of the block. The (medial) mental foramen can easily be palpated one third of the distance from the ventral border to the dorsal border of the mandible at the level of the root of the second premolar.



-Retrobulbar block: This desensitizes the eye, eyelids and most of the upper face. Because this block is associated with some potential risks (damage to the eyeball, to the optic nerve, retrobulbar haemorrhage, increased intraocular pressure, injection of local anaesthetic within the optic nerve meningeal sheath, retrobulbar haemorrhage and occurrence of the oculocardiac reflex) this block is often reserved for enucleations. There are many ways of performing this block but the most effective has been shown to be the inferior temporal palpebral where the block is performed midway between the lateral canthus and the middle of the lower eyelid along the inferior eyelid at the level of the orbital

rim. (Fig 2). The needle is directed along the floor of the orbit and then redirected dorsally and towards the nose to reach the apex of the orbit.



Fore Limb

Brachial plexus nerve block: This block can be performed blindly, with a nerve stimulator (91% success) or US guided. Several approaches have been described, including the paravertebral, subscalenic, axillary approach with the latter being the easiest to perform and the one described here. The use of a nerve stimulator non only increases the success rate of this block but also the area covered by the block. The area desensitised with this block covers the limb, distal to the distal third of humerus (or distal to elbow if performed blindly). The needle (spinal needle in dogs)'s length is first measure to the level of the first rib. The needle is then inserted at the level of the point of shoulder (acromion), medially to the scapula and advanced up to first rib in a ventro-caudal direction, parallel to the vertebral column. If performed blindly then, after withdrawal to exclude intravascular injection, local anaesthetic can be injected. If a nerve stimulator is being used, biceps contraction and elbow flexion will be the response we are looking for as a result of stimulation of the musculocutaneous nerve. After having blocked this nerve, the needle is inserted deeper to block the rest of the plexus and extension of the elbow, carpus and digits should be seen before injecting.
A total volume of 0.3 ml/kg should be injected. Complications associated with this block can be intravascular puncture, nerve damage, pneumothorax and there is also one report of atrial fibrillation in a dog in which the needle penetrated the chest.

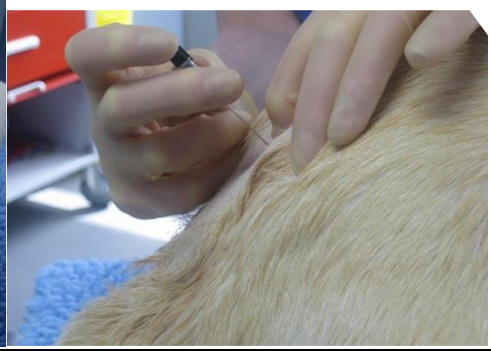
RUMM block This block can be performed blind, with a nerve stimulator or US guided. The radial nerve is located by the lateral aspect of the mid-humeral region between triceps and brachialis mm. If a nerve stimulator is used an extension of the carpus should be seen. A dose of 0.1 ml/kg of local anaesthetic can be injected at this point
The ulnar, medial and musculocutaneous nerves are located on the medial aspect mid-humeral region. At this level, once the brachial pulse is palpated between the biceps brachialis and the triceps mm the needle is inserted caudal to brachial artery. If a nerve stimulator is used, then flexion antebrachium (median nerve) and paw flexion (ulnar nerve) should be noticed. Here a volume of 0.15 ml/kg of local anaesthetic can be injected.

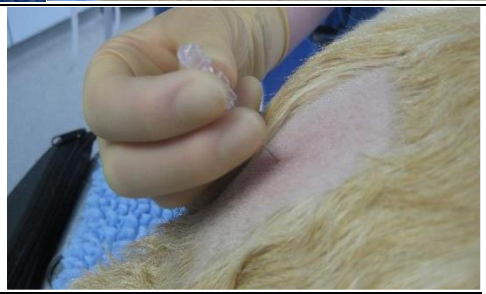
Interdigital block: Does not require a nerve stimulator. This block is performed to desensitise the digit and consists of an interdigital subcutaneous bilateral infiltration of the said digit. A 23g needle can be used to insert 1-2 ml of local anaesthetic in total.

-Intra-articular anaesthesia: This block can easily be performed by injecting local anaesthetic in an articulation. Chemical synovitis following this block has been reported but this is no worse than inflammation following saline. The main concern of this block is the possibility of some chondrotoxic effects of the local anaesthetics, but this still needs to be asserted.

Hind limb

Epidural anaesthesia- is performed without the use of a nerve stimulator. This technique provides bilateral anaesthesia to the pelvic limbs, caudal abdomen and the perineal region. The patient is positioned in sternal recumbency with the legs pulled forward (easier) or, if pathologies do not allow this, in lateral recumbency with the legs slightly pulled forward. After clipping and aseptically preparing the area, the wings of the ileum are palpated with the thumb and the middle finger. Creating a triangle with the index finger pointing towards the tail, the spine is palpated, and the lumbosacral space can be felt as a depression in line with the spine, just caudal to the wings of the ileum. A spinal needle is inserted at that level and as soon as it is through the skin the stylet is removed, and a drop of saline is placed in the hub of the needle (hanging drop). The needle is inserted further until a 'pop' sensation is felt. This is the needle going through the ligamentum flavum. At this point, the drop of saline should be 'sucked' into the needle (this does not always occur and even less if the epidural is performed with the patient in lateral recumbency), confirming the tip of the needle is in the epidural space. After confirming the absence of CSF or blood, drugs can be slowly injected at this point. There should be no resistance to injection. The lack of resistance can also be confirmed by leaving an air bubble in the needle and confirming this bubble does not compress during injection. Drugs normally used are preservative free morphine at a dose of 0.1 mg/kg and bupivacaine/ropivacaine at a dose of 0.5 mg/kg. The maximum volume of drugs to be administered epidurally is of 6 ml and doses should be reduced in pregnant, obese and older patients. The use of morphine only will provide analgesia for up to 24h. The use of local anaesthetic will provide anaesthesia for up to 6-8 hr.





Contraindication to epidurals are infection of the injection site, coagulopathies, anatomical distorsion (pelvic fracture, obesity) and possibly sepsis. Some complications are associated, albeit rarely to epidural injection of local anaesthetic and morphine. These include hypotension, motor blockade, urinary retention, pruritus and slow (or different) hair growth.

Femoral and sciatic nerve block: Several approaches have been described to block the femoral and the sciatic nerves. A nerve stimulator or an ultrasound are necessary to perform this block. The femoral nerve innervates the medial aspect of the hindlimb, distal to just below the stifle. The sciatic nerve and its branches, innervates the remainder of the hindlimb. The sciatic nerve is approached between the greater trocanter and the ischiatic tuberosity. Once the area is clipped and prepped, the needle is inserted perpendicular to the skin and the digital flexors or extensor muscles are stimulated, causing flexion or extension of the digits. After withdrawal to ascertain no blood is present, 0.05 to 0.1 ml/kg of local anaesthetic is injected. The femoral nerve is located inguinally at the level of the femoral triangle. Once the area is clipped and prepped, the femoral artery is palpated and the needle inserted cranially to said artery, as proximally as possible. The quadriceps muscle is stimulated, causing extension of the stifle. After withdrawal to ascertain no blood is present, 0.05 to 1 ml/kg of local anaesthetic is injected.

Other areas

Intercostal nerve block: can be performed for thoracotomies, rib fractures or when chest drains are in place. The artery, vein and nerve run at the back of the rib and this is where the needle needs to be inserted. Two sites cranially and 2 sites caudally to the site of interst should be blocked as well.

Interpleural block: can be performed via chest drain. The efficacy of this block is controversial with some studies showing it to be ineffective and others comparable to morphine analgesia.

Intraperitoneal block: again, the efficacy of this block is controversial, depending on when the block was performed (pre-op superior to intra-op and post-op) or on what drug was used (bupivacaine better than lidocaine).

Wound soakers: These can be used post amputation, TECA surgery, removal or large masses. They are associated to minor complications (catheter disconnection, seromas, inflammation and infection). Lidocaine CRI can be administered via the wound soaker or more simply bupivacaine can be injected in boluses give every 6-8 hr. In cats the CRI is not recommended.

Intra-testicular block: This block performed in dogs has shown to be effective in having MAC sparing effects but was not useful to decrease post-operative pain scores.

Auriculotemporal/auriculopalpebral block: indicated for TECA surgery. No studies in dogs have shown effectiveness (or lack of). A splash block performed at the moment of surgery is probably easier to perform and more effective. In one study, the addition of a continuous, local infusion of bupivacaine did not significantly increase the degree of postoperative analgesia in dogs that underwent total ear canal ablation and were given morphine at the end of surgery.

TAP block (Transversus abdominis plane) is a block which is performed under ultrasound guidance. This block must be performed bilateral to the abdominal midline and depending on the site of surgrey, at the level or the cranial or caudal abdomen (or both).

Systemic lidocaine

-Intravenous lidocaine: 20-80 µg/kg/min IV
Lidocaine is often used as a CRI to provide perioperative analgesia, mostly for gastro-intestinal surgery. Other than its well known anti-arrhythmic properties, lidocaine has good analgesic and MAC sparing effects but it is also known for its prokinetic and anti-inflammatory properties.
A recent publication showed that a lidocaine CRI used during septic patient's anaesthesia decreased short term mortality. Also early treatment with IV lidocaine bolus of 2 mg/kg , followed by CRI of lidocaine of 50 mcg/kg/min for 24hr post presentation may decrease the occurrence of cardiac arrhythmias, acute kidney injury and hospitalization time period significantly in lidocaine-treated dogs with GDV compared to untreated historical controls. These results are controversial as a previous study showed no effect, other than an increase in hospital stay in GDV patients treated with lidocaine. Do not use the lidocaine solution containing adrenaline!

MLK

The combination of morphine (or methadone), lidocaine and ketamine is often used as it provides a multimodal approach to analgesia. The MLK combination (with morphine) has also been shown to decrease the isoflurane requirements in dogs of up to 45%.

There are several recipes for the MLK CRI and the amount of drugs to be added in the bag depends on the rate at which the fluids will be run.

It is preferable to prepare the MLK so that a rate of 0.5-3 ml/kg/hr will be administered, so not to interfere with the fluid therapy plan of the patient.

Although there are some studies published about the use of lidocaine in the cat, it is preferable not to use lidocaine as a CRI in this species.

Hartmanns' (or saline)	Methadone (or morphine)	Lidocaine	Ketamine
500 ml	50 mg (5 ml of the 10 mg/ml solution)	750 mg (37.5 ml of the 20 mg/ml solution)	75 mg (0.75 ml of the 100mg/ml solution)
1 L	100 mg (10 ml of the 10 mg/ml solution)	1500 mg (75 ml of the 20 mg/ml solution)	150 mg (1.5 ml of the 100 mg/ml solution)

Before adding the drugs to the bag, remove an equivalent volume of solution from the bag.

Giving a bolus of the drug before starting the MLK infusion will help achieving effective plasma concentrations in less time. Therefore, the slow administration of methadone 0.1-0.3 mg/kg IM or IV, ketamine 0.2-0.5 mg/kg IM or IV and lidocaine 0.5 mg/kg IV are recommended before the beginning of the CRI.

This CRI can be run at 0.5-3 ml/kg/hr

When running at 1 ml/kg/hr this will provide:

- Methadone (or morphine): 0.1 mg/kg/hr
- Lidocaine: 25 µg/kg/min
- Ketamine: 2.5 µg/kg/min

It is preferable to decrease the rate over time and according to the response of the patient. Pain assessments should be carried out and the cardiovascular status (presence of bradycardia), the temperature and mentation of the patient should be assessed on a regular basis and the CRI adjusted accordingly.

A single drug, a combination of any two of the three agents (not lidocaine in cats) or the three agents can be selected to be administered as an infusion. The amount of drug and the dose to be used will not change.

Alpha$_2$agonists:

This class of drugs produces sedation, muscle relaxation and analgesia. Although the analgesic effects are short lived compared to the sedative effects, they can be used as part of a multimodal approach to analgesia and as an aid to reduce stress response. Alpha$_2$agonists should not be used a sole analgesic in any case other than mild pain. These drugs bind to different alpha$_2$adrenoceptors subtypes in the dorsal horn of the spinal cord (spinal analgesia), cerebral cortex and locus ceruleus (sedation and supra-spinal analgesia) which are present on noradrenergic and non-noradrenergic neurons. The analgesia provided by alpha$_2$agonits is mostly visceral.

Because alpha$_2$agonists have several side effects (bradycardia and bradyarrhythmias, decreased cardiac output, hyper/hypotension, respiratory depression, increased urine output, hyperglycaemia and emesis) their use should be reserved for younger, healthy or aggressive patients. The effects of alpha$_2$agonists can be antagonised by atipamezole.

Medetomidine (or its pure enantiomer dexmedetomidine) can be used as part of the premedication protocol or as a CRI during anaesthesia. Either way the administration of these drugs will allow an important MAC sparing effect.

The analgesic doses are much lower than the doses used for sedation.

Medetomidine: 1-2 µg/kg and a CRI of 1-2 µg/kg/hr

Dexmedetomidine 0.5-5 µg/kg/hr and a CRI of 0.5-1 µg/kg/hr

Nitrous oxide:

This is a gaseous inhalant anaesthetic used as an analgesic rather than an anaesthetic. Other than analgesia, other advantages of nitrous oxide are the second gas effect (faster anaesthetic uptake at the beginning of inhalational anaesthesia) the MAC sparing effect and the sympathetic stimulation.
Nitrous oxide diffuses into gas filled pockets and should be used with caution in patients presenting for example with pneumothorax of gastric dilation. Also, the inflation of the cuff of the endotracheal tube should be checked regularly as it can increase in volume.
Care should be taken to have an inspired oxygen of at least 33% and if inspired oxygen cannot be monitored then a maximum level of 50% of nitrous oxide should be used (to avoid a hypoxic mixture). On recovery, adequate oxygen should be provided to prevent hypoxia caused by the nitrous oxide re-diffusing into the alveoli and diluting oxygen levels. Supplemental oxygen should be administered for at least 10 minutes after the discontinuation of nitrous oxide.

Conclusions:

With the multitude of drugs available to relieve pain in small animal patient, the only decision left to take is which drug or combination of drugs to use. The use of multimodal analgesia is extremely useful to ‘attack pain from more sides’.
An active effort should be made to assess pain, tailor the analgesic protocol and then re-assess the effects of the drugs administered. Wherever possible pain scales should be used.
Treating acute pain is essential to avoid the development of chronic, maladaptive pain.