Recognition and management of acute and chronic pain in horses has many challenges, as in all non-verbal animals assessment and objective measurement of pain that has in consideration the unique physiological and behavioural features of the species, breed, and individual variations is extremely difficult. Horses have specific challenges, as prey animals they are good at hiding painful behaviors which makes it very easy to overlook mild to moderate pain and undertreat painful conditions that can lead to wound up, sensitization and chronic pain conditions. There are also some misconceptions surrounding pain management and side effects of opioids and other analgesics in horses. For many years non-steroidal anti-inflammatories have been used as sole analgesic in multiple situations, now we know from multiple studies that multimodal analgesia provides more efficacious pain management than a single modality in most species, specially in chronic pain conditions.

**Recognition of pain in horses**

In the last years, efforts to develop and refine comprehensive and reliable multi-variable objective pain scales for use in various clinical applications have been made. No perfect pain scale has been developed yet but we understand now that pain is highly complex so the tendency has been to evolve and improve the most simple descriptive scale (SDS), visual analogue scores (VAS) and numerical rating scales (NRS) to more multi-dimensional scales that include evaluation of emotional, behaviour and physiological responses. Composite pain scales (CPS) are the most recent efforts to integrate all these parameters in an overall score, multiple authors have developed CPS to evaluate pain in different clinical conditions such as acute visceral (van Loon and Van Dierendonck 2015, Van Dierendonck and van Loon 2016), orthopaedic (Bussieres et al. 2008, Dutton et al 2009, Lindegaard et al. 2010), or surgical pain (Sellon et al. 2004, Sanz et al 2009). Recognition of pain based on changes in facial expression has been investigated lately and grimace scales have been developed in mice (Langford et al. 2010), rats (Sotocinal et al.2011), rabbits (Keating et al. 2012), lambs (Guesgen et al. 2016), and horses (Dalla Costa et al. 2014). The horse grimace score has been used to assess pain in acute laminitis, castration and acute colic (Dalla Costa et al. 2016, Dierendonck and van Loon 2016).

**Treatment of pain in horses**

Multimodal or balance analgesia involves administration of a combination of drugs with different mechanisms of action than often have additive effects, components of a multimodal analgesia often include systemic analgesics and anti-inflammatories, local or regional anesthetic techniques and in some cases alternative or physical therapies.

Among all drugs nonsteroidal anti-inflammatory drugs (NSAIDs) are still the most used drugs in horses in acute painful conditions and to treat pain associated with inflammation. There is also data suggesting that NSAIDs may be useful as part of protocols to treat chronic and refractory pain since prostaglandins have been linked to hyperalgesia and central sensitization (Driessen and Zrucco 2014). Opioids, specially μ-pure agonists are
the choice to treat moderate and severe pain in almost all species, some controversy exists about side effects versus benefits of using opioids in horses. Multiple opioids have proven anti-nociceptive effects in horses in different pain models and clinical situations although side effects such as decrease in gastrointestinal motility, opioid-induce hyperalgesia, and opioid tolerance should be considered when long-term therapy is planned. For these reasons lower doses of opioids combined with other drugs, administered intermittently or as a continuous rate infusion, as part of a balanced approach is the actual tendency. Combinations of α2-agonists, lidocaine, ketamine, NSAIDs and opioids are commonly used to prevent and treat peri-operative pain. Other drugs investigated with potential analgesic effects in horses are gabapentin, pregabalin, tramadol, and butylscopolamine. (Driessen and Zrucco 2014, Sanchez and Robertson 2014).

A good complement of systemic administration of analgesic drugs is the use of local or regional anesthesia techniques. When used properly they can be very effective to treat acute and chronic pain and reduce significantly doses and consequently side effects of systemic analgesics and anti-inflammatories. Single injections for blocking peripheral nerves are useful for standing procedures and to provide intra and post-operative analgesia locally. Single injections can be repeated but in some areas like the limbs the placement of continuous peripheral nerve block catheters is possible and allows (Ex; palmar nerves, ulnar nerve, median nerve) continuous or intermittent administration of local anesthetics close to the targeted nerve (Driessen et al. 2008, Zarucco et al. 2010). Epidural administration of local anesthetics can be used for regional anesthesia of the perineal area, anus, rectum, vulva, vagina, urethra and bladder, high volumes of local anesthetics can cause ataxia and weakness. For more proximal analgesia administration of epidural opioids, α2-agonists (for example morphine/detomidine) or ketamine can be used adjuvant treatment (exception: xylazine can also cause motor blockade). Placement of indwelling epidural catheters allows for intermittent or continuous administration of epidural drugs without repeated punctures. Intra-articular administration of morphine with or without local anesthetics is also effective to treat pain post-arthroscopy or in sinovitis models for at least 24 hours (Santos et al. 2009, Lindegaard et al. 2010).

Physical therapies and rehabilitation are currently an active area of clinical research in equine medicine and may play a role in recovery and rehabilitation especially for recovery after orthopaedic surgery or chronic musculoskeletal conditions.
REFERENCES


PERI-OPERATIVE MANAGEMENT OF THE “DIFFICULT” PATIENT: STRATEGIES TO MANAGE THE ANXIOUS/AGGRESSIVE DOG OR CAT
Andrea Sanchez, DVM, DVSc, ACVAA candidate

Visiting the clinic is a stressful experience for many pets but it becomes particularly difficult to animals and owners when patient exhibits behavioural problems such as extreme anxiety or hyperactivity. In cases of dogs or cats showing severe aggressive behaviors, the problem involves not only the patient and the owner but it also represents a safety hazard for all the staff members and other hospital patients. Probably the most complicated situations arise when owners have poor control over their pets or patients need to stay hospitalized for the post-operative period. One of the objectives of this talk is to provide some strategies and therapeutic options to plan and facilitate the process of examination, surgical procedure and hospitalization of anxious patients and to review sedation protocols that can help us to safely diagnose and treat the highly aggressive or non-cooperative patient.

Oral protocols: oral sedation is a useful strategy to attempt mild sedation or anxiolytic effect prior to hospital visits, if the owner feels comfortable with the concept, or to facilitate cage rest or exercise restriction post-operatively. The objective is not to achieve heavy sedation and under no circumstances potent sedatives/tranquilizers should be given at home without veterinarian supervision, but some drugs or combination of drugs can facilitate the transport of the patient to the hospital, placement of a muzzle or administration of more potent drugs by parenteral route with less struggle.

Trazodone: this is a drug used as antidepressant in human medicine and part of the selective serotonin reuptake inhibitors (SSRIs) drug class that also have anxiolytic and hypnotic properties. At higher dosages, trazodone also acts as an antagonist at postsynaptic 5HT2C receptors. Its active metabolite m-chlorophenylpiperazine is a potent direct 5-HT agonist. When used alone, anxyiolisis and mild sedation with high individual variability are expected in dogs and cats.

- Cats: Two different studies in small cat populations have proven that doses of 50-100 mg, PO appear to be safe in healthy cats (Stevens et al 2016, Orlando et al. 2006). At these doses trazodone alone appears to decrease anxiety during transportation and examination and cause sedation characterized by decrease in activity (46-83%). Peak effects were observed 2-2.5 hours after administration. No side effects or changes in physiological variables were seen in theses studies but at this time no studies providing pharmacokinetic or detailed cardiovascular effects are available in the literature.

- Dogs: trazodone at doses of 3-10 mg/kg every 8-12 hours has been tested to facilitated post-surgical confinement after orthopedic surgery with 90% success (Gruen et al. 2014). In this study onset of sedative effects was seen at 31-45 minutes after administration although pharmacokinetic data in dogs has proven high bioavailability (84.6±13.2%) and very variable time to peak plasma
concentrations of 445 ± 271 min (Jay et al. 2013). Trazodone can cause some degree of cardiac depression in dogs anesthetized so caution is advice in animals with cardiovascular disease until more information is available. Reduction in dose is also recommended when trazodone is administered with other drugs that act on the serotonin pathway such as tramadol, phenothiazines, trycyclic antidepressants or other SSRIs due to risk of developing serotonin syndrome.

**Gabapentin:** a structural analogue of GABA commonly use as anti-epileptic or to treat chronic and neuropathic pain. The most commonly reported side effect is sedation. Despite lack of prospective studies, the author finds this drug particularly useful in aggressive cats to facilitate physical exam and intramuscular injection of elected pre-medication. Given as a dose of 50-100 mg per cat PO 2 hours prior to arrival alone or in combination with 3-5 mg/kg of trazodone. Oral absorption is near complete in cats (88.7 +/- 11.1%) (Siao et al. 2010)

**Acepromazine:** It is one of the most widely used sedatives in veterinary medicine, when given parentally provides a dose-dependent reliable sedation primary by blockade of dopamine receptors. When given orally in dogs, only 20% of the dose is absorbed and present in plasma (Hashem et al. 1992). Doses recommended in the literature range from 0.5-2.2 mg/kg PO but the author finds this drug not effective and cats and very variable and unreliable in dogs when given alone.

**Benzodiazepines:** These drugs exert their CNS depressant actions by enhancing endogenous GABA (inhibitory neurotransmitter) binding to its receptor that leads to sedation, anxiolysis and muscle relaxation. Despite all these positive properties, administration of benzodiazepines alone can be associated with paradoxical responses in dogs and cats that lead to excitement and disinhibitory behaviors. Consequently, their use is preferred for highly anxious or frighten dogs but they are not recommended in very aggressive patients. Among all benzodiazepines probably the most useful for oral sedation in dogs and cats is alprazolam but lorazepam and oxazepam have been also used. All these drugs can have large individual variability so a test dose a couple of days prior to the visit to find the effective dose for each patient is recommended. Alprazolam can be administered orally at 0.125 to 0.25 mg per cat and 0.02 to 0.1 mg/kg in dogs the night before and then 1-2 hours prior to visit alone or in combination with trazodone, tramadol or gabapentin.

**Oral transmucosal (OTM) protocols:** this route allows the administration of more potent sedatives and, when the appropriate drug protocol is chosen, effects are, generally, more profound and reliable than the oral route. With the exception of buprenorphine alone, the administration of more potent drugs such as detomidine, dexmedetomidine or ketamine should be performed in the clinic. Profound CNS and cardiovascular effects of these drugs makes close motorization crucial to prevent complications. This is especially important in highly aggressive older patients or animals with unknown cardiovascular status due to inability to perform complete physical examination when using potent drugs.
- Cats: one study suggested that the mucosal route of administration should be as effective as intravenous and intramuscular injections in cats (Robertson et al. 2003). Buprenorphine alone at 0.02 mg/kg, or in combination with any of the above mentioned oral drugs, can be given in the oral mucosa 60 minutes prior to visit to obtain mild/moderate sedation. For more profound sedation, a combination of buprenorphine at 0.02 mg/kg with dexmedetomidine at 0.02-0.04 mg/kg has proven to provide enough sedation to allow catheter placement or at least facilitate administration of IM injection of additional drugs in highly aggressive cats, despite lower and slower absorption than intramuscular route (Santos et al. 2010, Porters et al. 2014, Porters et al. 2015). Ketamine at 3-10 mg/kg can be added to this combination but it tends to cause severe hypersalivation. Intranasal administration of midazolam/buprenorphine or ketamine/midazolam can also produce effective and atraumatic sedation in cats. (Marjani et al. 2015)

- Dogs: detomidine gel administered by the OTM route at 0.35-1 mg/m² provided sedation suitable for a short, minimally invasive procedure in healthy dogs (Messenger et al. 2016), with peak effect detected 30-60 minutes after application. Injectable dexmedetomidine formulation has been also used to produce sedation through administration in buccal pouch at 0.02-0.04 mg/kg (Cohen and Bennett 2015). In the author’s experience, a combination of dexmedetomidine 0.04 mg/kg and ketamine 5 mg/kg can be squirt in the oral cavity or mixed with a small amount of “sticky food” such as peanut butter or marshmallow melt and applied in the oral pouch with a tongue depressor; this combination provides moderate sedation in most patients.

**Injectable protocols:** Administration of drugs by subcutaneous or intramuscular routes can be a challenge in the very anxious/aggressive patient. For very anxious dogs the administration of oral drugs prior to visit for mild sedation or anxiolysis is very useful. Additionally, the injection should be quick and atraumatic and the patient should be left in a quite place for drugs to take effect. Some mild sedation in the recovery period to make the transition from general anesthesia to consciousness is also recommended and the oral protocol chosen for pre-operative management can be used for hospital stay and post-operative period. When the animal is extremely aggressive parenteral administration becomes more critical and profound sedation may be needed for catheter placement prior to general anesthesia. The drugs and doses used for profound sedation or temporal immobilization may have profound cardiovascular effects, so ideally a complete physical exam should be performed prior to their use but sometimes this may not be possible in this type of patients. It is always very important to understand and be comfortable with the effects of every drug used. Reversible drugs are preferred, while oxygen supplementation and close monitoring are highly recommended. Some examples of protocols for injectable immobilization in healthy animals (note that the low end of the dose range should be used for older or debilitated patients despite signs of aggressive behaviour):

- Cats:
1. Dexmedetomidine 0.01-0.04 mg/kg (half of the dose if medetomidine is used instead) + Opioid (the election of the opioid is based on the procedure happening after sedation)
   - Butorphanol for non-invasive procedures or diagnostics
   - Buprenorphine for mild/moderate painful procedures
   - μ-pure opioid agonists such as hydromorphone, methadone, morphine, oxymorphone, or fentanyl among others if more invasive/procedure or pre-existing painful condition.
2. Alfaxalone 3-5 mg/kg + Dexmedetomidine 0.01-0.02 mg/kg IM +/- Opioid (volume of injection is high with alfaxalone, opioid can be given after if necessary)
3. Dexmedetomidine 0.01-0.02 mg/kg + Ketamine 1-5 mg/kg IM + Opioid

   - Dogs:
     1. Dexmedetomidine 0.01-0.02 mg/kg + Opioid (the election of the opioid is based on the procedure happening after sedation) IM
     2. Acepromazine 0.02 mg/kg + Dexmedetomidine 0.01 mg/kg + Ketamine 1-3 mg/kg IM
     3. Dexmedetomidine 0.01 + Ketamine 1-3 mg/kg + Opioid

Notes:
- These protocols are suitable for healthy animals, protocols have to be tailored to the individual patient and pre-existing diseases/conditions considered
- Atipamezole should always be available when α2-adrenergics are used and naloxone is also recommended
- Careful when approaching very aggressive animals after sedation, with some of this protocols the patient may appear heavily sedated but still be arousable and reactive, safety first!
- Opioid/α2-adrenergics combination may cause vomit, careful with closed muzzles and keep in mind risk of aspiration
- Some of these combinations may cause severe respiratory depression, always provide oxygen if anesthetic induction and endotracheal intubation are not performed immediately after sedation
- Heart rate, SpO2 and blood pressure monitoring is highly recommended in heavily sedated animals
- Always review and remember the cardiovascular and other side effects of the chosen drugs! Understand the normal response so you know when something needs or does not need to be treated (Example: expect hypertension and profound bradycardia seen when a high dose of α2-adrenergic is given)
References:


ANESTHESIA IN RUMINANTS
Andrea Sanchez, DVM, DVSc, ACVAA candidate

General considerations
Most domestic ruminants and trained camelids have a calm temperament and accept physical restrain without much effort. For this reason a combination of sedatives, physical restrain, and loco-regional anesthetic techniques is commonly used for most routine procedures. If necessary, more profound sedation and rope restrain techniques can be use to perform field procedures on a recumbent animal, higher doses of sedatives may be needed to maintain recumbency specially in more nervous or untrained animals. More invasive surgical procedures or grade of immobilization may require general anesthesia. Ruminants are at higher risk of complications related to recumbency and anesthesia than other species for their unique anatomy and physiology such as tympany, regurgitation, aspiration pneumonia, or myopathies in case of heavy cattle.

Anesthesia and sedation decreases or abolish motility and eructation, therefore gas produced in the rumen cannot be eliminated and results in progressive distension and tympany that may lead to decrease functional residual capacity and venous return, compromising both respiratory and cardiovascular function. Distension of the rumen and loss of oesophageal sphincter tone during deep planes of anesthesia often result in regurgitation and risk of aspiration of ruminal contents if the airway is not protected. Fasting and water withholding will decrease the volume of ruminant contents and the risk of regurgitation. Current recommendations for fasting adult cattle are 24 to 48 hours, and water withdrawal for 12 to 18 hours, depending on the size of the animal and the procedure to be performed. Small ruminants and camelids are generally fasted for 12-18 hours, and water is withheld for 8 to 12 hours (Valverde and Doherty 2008, Riebold 2015). Neonate and lactating animals should not be fasted to avoid hypoglycaemia and longer than recommended fasting times may result in a change in ruminal flora and predispose the animal to ketosis and should be avoided (Seddihi and Doherty 2016). Upper airway obstruction may also happen in anesthetized animals due to the combination of production of large volumes of saliva and the inability to swallow. Heavy adult cattle are at risk of developing myopathy and peripheral neuropathy associated with low muscle perfusion when recumbent, especially for long periods of time on inadequate padded surfaces.

All these considerations should be contemplated when planning general anesthesia in ruminants and benefits/detriments of standing sedation versus recumbent sedation or general anesthesia need to be weighed based on specific patient, procedure, physical status, associated risks, resources available and specific characteristics of every facility. Fasting, physical exam, assessment of haematological and chemistry values, weight estimation, venous catheterization, proper anesthetic and analgesic protocol, plan for positioning, and standard monitoring are basic considerations prior to general anesthesia in ruminants.

Premedication/Sedation:
The most commonly used drugs for sedation/tranquilization of ruminants are α2-agonists, benzodiazepines, opioids, and phenothiazines. Multiple anesthetic drugs are not licensed to use in food animals in Canada, in situations where off-label (ELDU) administration of drugs is considered necessary to ensure adequate welfare of animals and maintain standard of care, withdrawal periods must be carefully followed as recommended by the Food Animal Drug Residue Avoidance & Databank (FARAD). Specific information about use and policies for ELDU in Canada are available at Health Canada and CVMA websites.

**Acepromazine**: can be use alone for mild sedation in ruminants but is most commonly administered combined with an opioid such as butorphanol and/or an α2-agonist for moderate sedation or standing sedation. Common doses are 0.01-0.02 mg/kg IV or 0.03-0.05 mg/kg IM for cattle, 0.03-0.05 mg/kg IV or 0.05-0.1 mg/kg IM for sheep and goat. Acepromazine causes minimal cardiopulmonary effects and changes in oxygen delivery to the uterus in pregnant cows when compared with xylazine (Hodgson et al. 2002). It can cause penile prolapse in bulls and subsequent risk of damage during induction and recovery (Riebold et al. 2015)

**Benzodiazepines**: midazolam and diazepam are use to produce sedation without analgesia with minimal cardiovascular effects and are particularly effective as part of pre-medication in small ruminants, calves and debilitated animals. At high doses they will cause recumbency. Doses recommended for sedation in sheep and goats are 0.1-0.3 mg/kg IV or 0.3-0.6 mg/kg IM (for midazolam only). Benzodiazepine effects can be reverse with flumazenil.

**α2-agonists**: xylazine is probably the most commonly used drug from this class and is approved in Canada for use in dairy and beef cattle. Romifidine, detomidine, medetomidine and dexmedetomidine are alternative options with longer duration of action. α2-agonists cause moderate to profound sedation and have antinociceptive properties when given systemically or by the epidural route, at low doses can be used for standing procedures or sedation prior to general anesthesia, at higher doses produce recumbency. Ruminants are more sensitive to α2-agonists sedation than other species therefore doses are lower. Transient hypoxemia and hypercapnea are often seen in ruminants after xylazine administration, but sheep appear to be more sensitive to pulmonary effects of α2-agonists with hypoxemia, pulmonary edema, and pulmonary intravascular macrophage activation seen after administration (Cell 1997, Celly et al. 1999). Xylazine can increase uterine tone and has the potential to decrease fetal oxygen delivery (Hodgson et al. 2002). Other side effects of α2-agonists include peripheral vasoconstriction, bradycardia, decrease motility and hyperglycemia. In general doses of xylazine of 0.01 to 0.03 mg/kg IV or IM will provide sedation without recumbency in most species and doses of 0.05 to 0.1 mg/kg IV or 0.1 to 0.2 mg/kg IM may cause profound sedation and recumbency for up to 1 hour in sheep and cattle with goats being more sensitive.

**Opioids**: opioids generally produce mild sedation and mild to profound analgesia in ruminants depending on the drug selected. There are some reports of excitatory responses
after opioid administration so, if administered for sedative purposes or anesthetic premedication, they are usually administered in combinations with other drugs for a more reliable sedation. Probably the most widely used combination prior to general anesthesia in ruminants is butorphanol 0.01-0.02 mg/kg, IV with and α2-agonists or a benzodiazepine. Butorphanol provides only mild analgesia, for invasive procedures or moderate to severe pain more potent analgesics such as morphine, buprenorphine, and fentanyl can be used instead.

**Anesthetic induction:**
Ruminants generally do not require profound sedation in order to have a calm and smooth anesthetic induction, although aggressive or untrained large cattle or camels may be an exception. An injectable protocol is preferred over mask induction due to risk of regurgitation and aspiration, ideally a combination of drugs with ultra-short onset of action that provide smooth induction and adequate muscle relaxation are preferred. Most commonly used drugs for anesthetic induction are ketamine alone after α2-agonists premedication, or in combination with a benzodiazepine or guaifenesin to enhance muscle relaxation, propofol, alfaxalone, thiopental, or the combination tiletamine and zolazepam.

**Intubation:**
To minimize risk of regurgitation of ruminal and salivary contents ruminants should be kept in sternal position during anesthetic induction, until endotracheal intubation is achieved. Intubation is always recommended in anesthetized ruminants. Visualization of the laryngeal structures can be challenging in ruminants due to a narrow and long oral cavity, larynx positioned in a rostro-dorsal angle, and thick tongues specially at the base. In small ruminants and calves a long laryngoscope can be used to visualize the larynx with the neck completely extended but in cattle, blind intubation techniques usually by direct manual palpation of the epiglottis are more effective. Nasotracheal intubation is also possible in ruminants.

**Positioning and anesthetic maintenance:**
Same as in horses, positioning and adequate padding is extremely important in adult cattle. Inappropriate positioning or uneven or insufficient padding can lead to post-anesthetic myopathy and neuropathies. The head and neck should be always be positioned in a way that facilitates draining of saliva and ruminal contents out of the oral cavity so they do not accumulate in the laryngeal/pharyngeal area. Anesthesia maintenance for long procedures is usually performed with inhalant agents such as isoflurane, sevoflurane, halothane or desflurane but total intravenous protocols (TIVA) are available to use under field conditions or short procedures in hospital. Some options for TIVA protocols in ruminants are triple drip (50 mg xylazine and 1.0 to 1.5 g ketamine are added to 1 L of a 5% guaifenesin solution) titrated carefully to effect, or combinations of ketamine with xylazine and butorphanol. Continuous rate infusions of propofol or alfaxalone can also be used to maintain general anesthesia in goats and sheep (Moll et al. 2013, Ndawana et a. 2015, Ferreira et al. 2016, Deschk et al. 2016)
Monitoring:
Basic standard monitoring of respiratory, cardiovascular, and central nervous systems are crucial and mandatory to ensure a safe general anesthesia in all species. Contrary to horses, palpebral reflexes disappears quickly in all ruminants except in camelids and they do not display nistagmus when transitioning to a lighter plane of anesthesia, therefore they are not reliable signs for monitoring anesthetic depth in ruminants. In general, adequate muscle relaxation and ventral rotation of the eyeball indicate surgical plane in cattle. Minimal monitoring should include assessment of peripheral pulses, heart rate (SpO2, ECG, or direct count), respiratory rate and invasive or non-invasive blood pressure measurements. Capnography is a useful tool to confirm endotracheal intubation, and to monitor ventilatory function, especially during mechanical ventilation, small animal adaptors can be used in small ruminants and calves but adaptors are available for large animal anesthetic machines.

Recovery:
Ruminants have usually calm recoveries and additional sedation is not necessary except when dealing with aggressive or wild animals. Before recovery, careful inspection of the oral cavity to clean possible regurgitation contents is important to prevent aspiration during recovery and at extubation. Animal should be positioned in sternal recumbency and the tube left in place until laryngeal reflexes return, ruminants will keep regurgitating and salivating during the recovery period. With small ruminants and calm cattle the author prefers to remain in the recovery stall until active swallowing and eructation is consistent and the animal is able to keep the head up, at that moment extubation with the cuff partially inflated is recommended. Other clinicians prefer nasotracheal intubation in small ruminants and camelids for recovery, which allows them to fully recover and stand before extubation. All ruminants are mandatory nasal breathers; if nasal edema is suspected after a prolonged recumbency period, diluted phenylephrine 1:10 (total max dose of 0.02 mg/kg) can be topically applied to each nostril prior to extubation.

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Web resources:

Health Canada

Canadian Veterinary Medical Association
https://www.canadianveterinarians.net/documents/extra-label-drug-use-eldu
A vast number of emergency conditions commonly seen in general practice may require surgery and therefore general anesthesia. Multiple factors such as the out-of-hours nature of most procedures, or to have to deal with unstable patients that require fast intervention, make general anesthesia under these conditions challenging. Two things are crucial for a safe and successful anesthesia: first, to understand the pathophysiology behind the disease in order to identify, anticipate, and successfully treat potential complications. Second, to understand the pharmacology and beneficial and detrimental effects that anesthetic drugs are going to exert in the different body systems.

Safe anesthesia practices start with throughout but efficient physical examination and patient history to identify any other concomitant diseases that may increase anesthetic risk. Critical patients should always be evaluated and stabilized in a systematic fashion before surgery. Initial assessment should include hydration status, cardiovascular and respiratory stability, pain level, and basic laboratory tests. In life-threatening conditions benefits/detriment of rapid surgical intervention in unstable patients need to be balanced and considered. Cardiovascular stabilization is crucial and, if possible, fluid deficits, electrolyte abnormalities, and arrhythmias should always be detected and addressed before general anesthesia.

The use of a balance protocol that includes general and loco-regional anesthetic techniques individually designed that take in consideration the particularities of the disease process, surgical procedure, and physiological and cardiovascular status of the patient should always be chosen over pre-design anesthetic protocols.

The objectives of this session are to review some common emergency procedures that require general anesthesia, understand and treat the complications that can arise, and provide information and tools to clinically apply proper monitoring practices and pharmacological information available in the literature.

ANESTHETIC AND ANALGESIC CONSIDERATIONS FOR THE TRAUMA PATIENT

When receiving a trauma patient, the primary clinician should approach the animal in methodical manner, sometimes trauma happens without witnesses or the owners may not be able to provide accurate information. Evaluation of vital signs, including level of consciousness and adequacy of airway, breathing and circulation, should be the first step of triage in severe traumatic injury patient. Cardiovascular stabilization and optimization of oxygen delivery to vital organs is always essential and should the priority and main therapy goal followed by adequate pain management.
Complete physical, orthopaedic and neurological exam, wound management, and additional diagnostics such as imaging should be performed once the animal is stabilized. Animals suffering traumatic injuries may need general anesthesia for multiple reasons, in some occasions advanced diagnostic tests are necessary, in others trauma leads to injuries that need quick surgical resolution. Again, most procedures such as fracture repairs, lacerations repairs, diagnostics, or other surgical intervention for non life-threatening conditions are not anesthetic emergencies but in some situations more rapid and urgent interventions are necessary. Before anesthesia basic hemodynamic monitoring and minimum blood work should always be performed.

As a clinician, either if you are dealing with an apparent stable case or a more deteriorated patient that needs intensive monitoring and cardiovascular support during anesthesia is always important to consider acute and delayed complications that can arise in trauma patients. These patients can present with a single mild injury or endless combinations of orthopedic lesions, ocular traumatic lesions, neurologic traumatic injury, different grades of soft tissue trauma and inflammation, shock, abdominal trauma, or thoracic trauma among others depending of the severity of the event. Probably the most challenging consequences during general anesthesia are the ones associated with thoracic, abdominal and brain traumatic injury but the first two require surgery and general anesthesia more often.

**Thoracic trauma:** some examples are pulmonary and cardiac contusions, pneumothorax, hemothorax, pleural effusion, or diaphragmatic hernia. Some of these complications are going to be life threatening or easily diagnosed at presentation during physical exam or thoracic radiographs, but pulmonary and cardiac contusions may evolve over time and be missed during initial evaluation and can show during anesthesia. Traumatic damage results in parenchyma damage that can lead to hemorrhage, bronchospasm, increase mucus production, decrease surfactant production and edema. Clinical signs on presentation are going to depend on severity and extension of the contusion but can go from normal respiratory patterns and auscultation, to dyspnea, tachypnea, hypoxemia, or abnormal lung sounds with crackles. Clinical signs can peak at about 4 to 72 h after injury and include respiratory distress with hypoxemia and hypercarbia. These animals may need conservative mechanical ventilation during general anesthesia to counteract ventilation-perfusion mismatch, may be more prone to barotrauma and need oxygen therapy or even ventilatory support in the post-operative period. Cardiac contusions happen more often in lateral chest traumas and may result in arrhythmias and conduction defects such as ventricular tachycardia, multifocal ventricular premature contractions, ventricular arrest, and complete heart block and sinus tachycardia. Pre-operative cardiac rhythm evaluation and continuous ECG monitoring during anesthesia is crucial to detect and correct arrhythmias as soon as possible.

**Abdominal trauma:** most common complications seen are hemoperitoneum, hemo- or retroperitoneum, bladder rupture, uroperitoneum, and gallbladder or biliary ducts rupture, peritonitis or traumatic body wall herniation. Blood products should be available in cases of severe bleeding and electrolyte and acid-base corrected ideally before anesthesia.
Anesthetic for the unstable thoracic/abdominal trauma case:

Anesthetic goals:
- Adequate analgesia management
- Balanced anesthesia technique: combine drugs with synergic effect to minimize the dose and the adverse effects
- Goal directed fluid therapy: Maintenance of adequate perfusion and cardiac output without administration of excessive quantities that may exacerbate hemorrhage and edema
- Ventilatory goals: Improve oxygenation always balancing risk of barotrauma and cardiovascular effects of IPPV

Drugs:
- Opioids and benzodiazepines are good choices due to minimal cardiovascular effects
- Ketamine is a good option as induction agent, sympathetic stimulation, analgesic properties. Careful in patients with tachyarrhythmias
- Propofol and alfaxalone are good and rapid induction agents but cause some degree of cardiovascular depression that can be significant in hypovolemic patients. Titrate to effect, use strategies to decrease induction doses
- Inhalants cause dose-dependent cardiovascular depression, should be kept and the minimum effective % concentration. Consider the use of a balance protocol using intravenous agents to decrease inhalant requirements
- Lidocaine can be very useful as part of a balance anesthetic protocol in trauma patients due to analgesic, anti-inflammatory, MAC sparing and anti-arrhythmogenic properties

Example protocol for unstable and depressed patient:
- Pre-oxygenation for 5 minutes: specially important if thoracic trauma suspected or confirmed
- ECG pre-anesthetic and connected during induction to detect possible arrhythmias or sudden changes in heart rate
- Inductions with fentanyl 5 mcg/kg, lidocaine 2 mg/kg, midazolam 0.2 mg/kg
- Maintenance with inhalant
- Continuous monitoring of ECG, SpO2, blood pressure (consider an arterial catheter if possible), and ETCO2
- For intra-operative analgesia and MAC reduction (combinations depending of the case, 1 or more of):
  - Fentanyl 5-10 mcg/kg/hr OR hydromorphone 0.01-0.02 mg/kg/hr
  - Lidocaine 100-200 mcg/kg/min (turn off 20 minutes before end of surgery if no arrhythmias, lower it to 25-50 mcg/kg/min if necessary to control ventricular arrhythmias post-operatively)
  - Ketamine 0.5-2.4 mg/kg/hr
Pregnant animals have higher anesthetic risk due to physiological changes and pharmacological alterations, in cases of emergency dystocia stabilization of the parturient prior to procedure becomes a priority. In cases of fetal stress minimize anesthetic times is crucial to improve fetal survival rates. Anesthetic and analgesic protocols are going to vary depending on cardiovascular status of the mother and fetus viability.

**Physiological changes during pregnancy**

**Cardiovascular system:** During pregnancy maternal blood volume increases by 40%, which results in decreased packed cell volume and hemoglobin concentrations. Cardiac output increases by 30-50% due to higher heart rate and stroke volume. These changes cause an increase in cardiac workload and can lead to blunted compensatory responses to hemodynamic challenges such as acute hypotensive events. This lack of reserve becomes aggravated by sympathetic depression caused by most anesthetics, animals with concomitant cardiac disease or hypovolemic. Despite higher cardiac output pregnant dogs and cats have lower blood pressure values due to decrease afterload probably by decrease peripheral vascular resistance cause by high plasma levels of relaxin and estrogens. Decrease maternal stress, proper pain control, avoid excessive doses of agents that may cause cardiovascular depression and close monitoring of blood pressure during anesthesia are highly recommended.

**Respiratory changes:** As a result of increase metabolic demands oxygen consumption increases 20-25 % with pregnancy and up to 70 % during parturition. Abdominal distension decreases functional residual capacity and this combine with the increase in oxygen requirements makes pregnant patients more susceptible to develop hypoxemia during situation of hypoventilation or apnea. For this reason pre-oxygenation with 100% oxygen prior to induction and ventilatory support are recommended practices. Progesterone enhances respiratory center sensitivity to PaCO₂ resulting in hypocapnea that can be exacerbated by hyperventilation during partum.

**Gastrointestinal system:** Pregnant animals are very prone to active and passive regurgitation and GER during anesthesia for a combination of factors. First, the large gravid uterus displaces the stomach cranially and the intragastric pressure is increased. Second, hormonal changes cause decrease gastrointestinal motility, increased gastric secretion, decreased lower esophageal sphincter tone and high progesterone levels cause delay in gastric emptying. Therefore this patients are at high risk of aspiration pneumonia, prophylactic administration of antiemetic, and/or prokinetic, keep the head elevated during anesthetic induction, secure the airway with auffed endotracheal tube quickly, have a suction unit available and avoid mask induction are measures to decrease associated risks.

**Renal:** During pregnancy renal blood flow and glomerular filtration rate increase resulting in lower levels of BUN and creatinine.
Uterine blood flow: One of the most important goals during anesthesia specially for fetal survival is to maintain blood flow to the uterus and therefore to the placenta. Systemic perfusion pressure and myometrial vascular resistance determine uterine blood flow. Placental hypoperfusion may happen during severe hypovolemia, maternal hypotension or anesthesia; but also during enhanced maternal sympathetic tone, increase catecholamine release, and subsequent vasoconstriction in response to tracheal intubation, stress, pain or surgical stimulation.

Pharmacological considerations

For the mother: Anesthetic requirements are decreased. Careful titration of injectable drugs and constant monitoring of anesthetic depth to adjust inhalant concentrations minimize the risk of drug overdose,

Crossing the placenta blood barrier: Ideal anesthetics have the ability to cross the blood brain barrier fast to exert desire effects in the CNS. The same physic-chemical characteristics make these agents to quickly cross the placenta. It is safe to assume than most drugs administered to the parturient are going to be present in some degree in the fetal circulation and are going to have effects in the fetus.

For the fetus/neonate: The hepatic ability to metabolize drugs is incompletely developed or absent the fetus/neonate so drugs that undergo hepatic metabolism have a longer duration of effect, especially when administered as a continuous rate infusion. Luckily physiology of fetal circulation has a relative protective effect by diminishing exposure of the fetal brain and heart to circulating drugs. Approximately 85 % of the umbilical venous blood passes through the fetal liver first and extensive shunting of the fetal circulation exists via the ductus venous, foramen ovale and ductus arteriosus so roughly 57% of fetal cardiac output returns to the placenta without perfusing fetal tissues. That means that fetal plasma concentrations of short acting drugs like propofol decrease quickly after a single bolus.

General recommendations

• Analgesia, sedation and muscle relaxation for the mother
• Maintenance of maternal airway, oxygen delivery, maternal blood pressure, and support of uterine blood flow
• Preventive treatment of regurgitation/vomiting, pre-oxygenation
• Minimize times from induction to delivery of all neonates
• Use drugs with minimal negative effect in neonatal outcome, short-acting and reversible. Have equipment, drugs, and team for neonatal resuscitation ready
• Use a balance anesthetic protocol depending on the individual case but in general:
  - Propofol, alfaxalone inhalants and epidural/local anesthesia are related with good neonatal outcome and low mortality
  - Ketamine, xylazine, thiopental and methoxyflurane are associated with high neonatal mortality or more severe neurological and respiratory depression of puppies/kittens
### Anesthetic plan for stable patient (example)

**Pre-op period:**
- Assessment of the mother (physical exam, PCV, TS, electrolytes…)
- Assessment of fetal status and viability
- Premedication:
  - Fentanyl 3-5 mcg/kg, IM,SQ or
  - Meperidine 3-5 mg/kg IM or
  - Hydromorphone/oxydormine 0.05-0.2 mg/kg IM,SQ or
  - Morphine 0.1-0.4 mg/kg IM,SQ
  - +/- Midazolam 0.2 mg/kg IM, SQ if additional sedation needed
- IV catheter placement
- Preventive administration of metoclopramide 0.3 mg/kg IV,SQ and/or maropitant 1 mg/kg IV, SQ and/or famotidine 0.5 mg/kg IV
- Pre-oxygenation for 5 minutes

**Induction:**
- Propofol 1-4 mg/kg to effect IV or
- Alfaxalone 1-2 mg/kg to effect IV

**Maintenance:**
- Inhalant to effect, lowest % necessary to keep a good anesthetic plane
- Isotonic fluid therapy at surgical rate 5-10 ml/kg/hr
- Use standard monitoring: ECG, $SpO_2$, BP, ETCO2
- Support ventilation as needed
- Keep MAP > 60 mmHg. Dopamine or dobutamine infusions to effect 1-10 mcg/kg/min IV
- Glycopyrrolate 0.01 mg/kg IV if bradycardia
- If additional analgesia is needed fentanyl bolus 1-5 mcg/kg, better when puppies/kittens are out

**Local/Regional anesthesia techniques:**
- Epidural with lidocaine/bupivacaine 0.1-0.15 ml/kg
- Incisional line block with bupivacaine

**Post-op analgesia**
- Opioid/NSAID (considerate drug transfer to milk)

### Different recommendations for the unstable patient:

- Place IV catheter at admission and correct fluid and electrolyte deficits prior to anesthesia
- If depressed, clipping surgical area while pre-oxygenating decreases anesthetic time
- Emergency drugs and reversal agents should be ready for both mother and neonates before procedure
- If physical status of the patient is very deteriorated propofol and alfaxalone may cause significant cardiovascular depression, co-induction with a combination of fentanyl 5 mcg/kg and midazolam 0.2 mg/kg IV will reduce the induction dose requirements
- Inhaled % should be kept as low as possible, if foetuses are not alive CRIs of drugs with MAC sparing effects such as fentanyl, lidocaine or ketamine can be added to minimize inhalant cardiovascular depression
- Hypotension should be treated aggressively with fluid therapy, or inotropes/vasopressors when necessary.
- Placement of an arterial catheter for monitoring IBP may be considered
REFERENCES

Blanco PG, Tórtora M, Rodríguez R et al. (2011) Ultrasonographic assessment of maternal cardiac function and peripheral circulation during normal gestation in dogs Vet J 190: 154-159


