Anesthesia and Analgesia for Patients with Comorbidities

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Abstract: Our veterinary patient population has changed as our medical skills have progressed and we have become capable of supporting patients with advanced disease and/or advancing age. All tranquilizers, induction drugs and inhalant drugs cause CNS depression and most cause some degree of dose-dependent physiologic dysfunction. In healthy patients, many of the physiologic effects of anesthetic drugs are tolerated or can be counteracted by routine measures such as administration of oxygen or intravenous (IV) fluids. In compromised patients, these effects can be quite dangerous as they may magnify pre-existing disease-related physiologic dysfunction. Patient needs should be addressed in each of the 4 distinct and equally important periods: 1) preparation /premedication; 2) induction; 3) maintenance and 4) recovery. In healthy patients, many of the physiologic effects of anesthetic drugs are tolerated or can be counteracted by routine measures such as administration of oxygen or intravenous (IV) fluids. In compromised patients, these effects can be exacerbated, further contributing to the demise of the patient. Successful anesthesia in compromised patients is highly dependent on adequate patient stabilization, diligent patient support and monitoring, and the use of appropriate anesthetic drugs at appropriate **dosages.**

Key Words: anesthesia, analgesia, comorbidity, stabilization, monitoring, oxygen delivery

Preparation for Anesthesia & Premedications

Stabilization of critical or challenging patients prior to sedation and/or anesthesia is imperative. Both increasing American Society of Anesthesiologists (ASA) scores and increasing urgency of the procedure increase risk of anesthetic death (Brodbelt 2009).

Analgesia should be part of stabilization. Pain creates a tremendous sympatho-adrenal stress response and can contribute to **morbidity** and perhaps even **mortality**. Relief of pain can provide hemodynamic and respiratory stabilization, along with many other positive benefits. If relieving pain does **not** provide stabilization, the veterinarian will know to rapidly continue diagnostics as something other than pain is the main cause of the patient's condition. Safe, reversible drugs like the opioids are excellent choices for most challenging patients. When possible, decreased fear/anxiety/stress (FAS) should also be part of stabilization as FAS can often exacerbate the negative components of underlying disease through the FAS-induced stress response and can increase pain intensity. Drugs like gabapentin, trazodone and alfaxalone are generally safe and often administered to hospitalized patients if not administered before the patient left home.

Oxygen delivery. Most critical patients have disease or conditions that cause at least some degree of cardiovascular and/or respiratory compromise, potentially resulting in decreased tissue oxygen delivery. Many anesthetics also cause at least some degree of cardiovascular and respiratory compromise, also potentially resulting in decreased tissue oxygen delivery. One of the critical roles of the anesthetist is to support oxygen delivery by promoting normal function in both the cardiovascular and respiratory systems. Monitoring of those systems may need to start prior to induction in some patients.

Equipment. Both anesthesia delivery and anesthesia support/monitoring equipment should be checked and rechecked to insure they are working properly. The anesthesia machine and breathing system become part of the patient's airway when connected to the endotracheal tube. So any equipment malfunction = patient malfunction.

Sedatives / tranquilizers: Although not intuitive that critical patients need premedicants, the use of premedicants will decrease the dose of induction and maintenance anesthetic drugs. Since adverse effects are dose dependent, decreasing the dosages will improve anesthetic safety.

- *Opioids - morphine, fentanyl, methadone, butorphanol, buprenorphine:* Advantages: Provide moderate to profound analgesia, minimal to no cardiovascular effects, minimal respiratory effects, allow a decrease in dosage of maintenance drugs, reversible, many are inexpensive, provide sedation, versatile (can be administered PO, IM, IV, SQ, in the epidural space, in the intra-articular space, etc...). Disadvantages*:* cause vomiting (administer maropitant), relatively short duration of action when compared to the duration of most pain (administer as an infusion).
- *Benzodiazepines – Diazepam, midazolam:* Advantages: Wide safety margin, minimal to no cardiovascular or respiratory effects, reversible. Excellent choice for critical patients – either as a premed or a part of induction. Disadvantages: Minimal to no sedation when used alone in healthy patients and can cause paradoxical excitement, especially in stressed or fractious patients, no analgesia.
- *Alfaxalone* – Advantages: Can provide dose-dependent light to moderate sedation and can be administered IM or IV. Disadvantages: Some dose-dependent cardiovascular & respiratory effects – VERY minor at the sedative dose, volume limited to small patients, can cause 'rough' recoveries – unlikely at the sedative dose, no analgesia.
- *Acepromazine* – not commonly used in compromised/challenging patients (the exception is patients with upper airway compromise that need long-term sedation and some patients with cardiovascular disease that would benefit from a reduction in afterload). Disadvantages: not reversible, causes vasodilation which could contribute to hypotension in compromised patients.
- *Alpha-2 agonists* – not commonly used in compromised patients because they rarely need profound sedation but appropriate in stable emergency patients that need sedation/analgesia.

Advantages: Provide both sedation and analgesia, effects are reversible. Disadvantages: Causes increased cardiac work.

Other drugs: Maropitant is recommended, both for its anti-emetic effects and its potential for contributing to analgesia. Vomiting itself, with the intense contraction of abdominal muscles, is painful. This can greatly exacerbate the pain level in patients with pre-existing abdominal pain. Disease-specific drugs might also be necessary, as an example, a lidocaine infusion could be necessary in patients with ventricular tachyarrhythmias.

Other tasks: As mentioned, monitoring prior to induction is recommended in patients with comorbidities, depending on which comorbidity and how severe. PREOXYGENATE! Takes only 3 minutes to fully saturate hemoglobin with oxygen, which decreases the time of patient desaturation from 1 minute (patient on room air) to 5 minutes. Great support of oxygen delivery!

Induction

- *Propofol:* Advantages: rapid induction and recovery, easy to titrate 'to effect', multiple routes of clearance from the body, good muscle relaxation. Disadvantages: Causes mild to moderate dose-dependent respiratory and cardiovascular depression
- *Alfaxalone:* Advantages: rapid induction and recovery, easy to titrate 'to effect'. Disadvantages: Causes mild to moderate dose-dependent respiratory and cardiovascular depression. Can cause rough recoveries, uncommon in appropriately sedated patients.
- *Ketamine:* Advantages: inexpensive, can be administered IM, mild respiratory depression, no cardiovascular depression in heart-healthy patients. Disadvantages: can cause cardiovascular depression in patients with cardiovascular compromise, can cause muscle rigidity.
- *Etomidate*: Advantages: no cardiovascular effects. Disadvantages*:* expensive, poor muscle relaxation, vocalization, maybe not appropriate in septic patients due to adrenocortical suppression.
- ***Inhalant induction is NOT appropriate*** *for almost all dogs and cats.* The dose of the inhalant is entirely too high when used alone (side effects of inhalants are dose-dependent) and the induction will be stressful and will be prolonged. Furthermore, use of inhalants alone for induction and maintenance increases the risk of anesthesia-related death (Brodbelt 2009).

REMINDER: All tranquilizers, induction drugs and inhalant drugs cause CNS depression and most cause some degree of **dose-dependent** respiratory and cardiovascular dysfunction. **All drugs should be dosed 'to effect'**. In many comorbidities, the circulation becomes centralized so a larger percentage of the drug dose gets to the brain, thus decreasing the dose the patient would need for induction when compared to a healthy patient. Also, in many comorbidities,

cardiac output is decreased so the time it takes for the induction drug to get to the brain is increased. So give a LOW dose and wait longer to see the effect than you would wait in a healthy patient. Repeat the mantra: “Low and slow”.

Maintenance

Low-dose inhalant anesthesia is generally the most logical way to maintain anesthesia that will last 30 minutes or more since inhalants don’t have to be metabolized for the patient to regain consciousness. However, inhalant anesthetic drugs should never be used as the sole anesthetic drug since inhalants can cause significant hypotension and hypoventilation. Our goal should always be to keep the vaporizer setting as low as possible. Often, *analgesia* must be provided in order to minimize *anesthesia* drug doses. *Advantages*: easy to administer, relatively inexpensive, are eliminated with minimal metabolism. *Disadvantages*: DOSE DEPENDENT contribution to hypoventilation, hypotension and hypothermia. MONITOR, MONITOR, MONITOR. **NOTE:** The advantages and disadvantages of the inhalant drugs are class effects and apply to all inhalants. However, sevoflurane has an advantage in critical patients since it is more easily dosed ‘to effect’ because of its lower solubility coefficient.

Analgesic Drugs & Techniques

Maintenance of anesthesia is much easier and safer if analgesia is provided prior to the painful stimulus. Most anesthetic drugs, including the anesthetic gases, block the brain's perception that pain has occurred but don't actually block pain. If pain is severe enough, the brain can still respond and make the patient appear to be inadequately anesthetized. This usually leads to an increased inhalant dose and the brain ceases to respond, but the patient is now too deeply anesthetized and can be at a very dangerous physiologic plane. A more appropriate response would be to block the pain and maintain anesthesia at a light, safe depth. The advantage to all of the drugs and techniques listed below is that they are anesthetic-sparing, meaning that they allow a decrease in the anesthetic dose necessary to maintain unconsciousness.

- *Opioids:* Advantages: provide moderate to profound analgesia, cause minimal cardiovascular or respiratory effects, are reversible. Disadvantages: Previously discussed opioid-meditated adverse effects.
- *Local anesthetic drugs & locoregional techniques:* Advantages: Inexpensive, easy to administer, very effective. Drugs block the pain impulse from getting to the dorsal horn of the spinal cord and thus decrease the incidence of central sensitization. This results in pain that is much lower, not only during the block, but even beyond the expected duration of the drug itself. Local blockade also decreases the likelihood that chronic pain will develop secondary to the acute pain. Disadvantages: Relatively short duration of action when compared to the duration of pain, except for NOCITA®.

  NOTE: Local anesthetics are underutilized, yet they are easy to use, inexpensive and highly effective.

- *Constant rate infusions (CRIs):* Advantages: EASY, inexpensive, effective, many drug choices (opioids, lidocaine, ketamine, alpha-2 agonists and combinations). Disadvantages: Almost none because of the low dose delivered but side effects from any drug could always occur. There is a very useful open-access CRI calculator at IVAPM.org under the 'professionals' tab.

Monitoring & Support

Monitoring: Anesthesia causes changes in all organ systems but the changes in the CNS, cardiovascular and respiratory systems are the most immediately life-threatening so monitoring and support is focused on these systems. Also, support of these systems will provide support for other systems by providing adequate oxygen delivery to the organs/tissues of that system. Don't forget the basics: mucous color, capillary refill time, jaw tone, eye position, etc… Utilize SpO_2 (pulse oximeter) and end-tidal CO_2 to assess respiratory function. Utilize ECG and **blood pressure** to assess cardiovascular function. Measurement of blood pressure is IMPERATIVE in critical patients.

Cardiovascular support includes use of IV fluids & positive inotropic and antiarrhythmic drugs.

- *IV fluids* should be used, as needed, to rehydrate the patient and replace ongoing losses. Do not overhydrate – excessive administration of fluids can cause edema.
- Many critical patients would benefit from the use of *colloids* in addition to crystalloids. Voluven (Vetstarch) is commonly used and the total dose in the dog is $\leq$50 ml/kg in a 24-hour period. Cats should generally receive $\leq$30-40 ml/kg in a 24-hour period.
- If patients have hemorrhaged, if severe hemorrhage is expected intraoperatively or if the patient is anemic (PCV < 18-20%), collect blood for a *blood transfusion* prior to anesthesia.
- Oxygen bound to hemoglobin is the main source of oxygen delivered to the tissues. If the patient is hypoproteinemic (albumin <2 g/dl), administer *plasma* prior to anesthesia.
- If the patient is hypotensive:
    1. If anesthetized, TURN DOWN THE VAPORIZER.
    2. Give boluses of fluids (5-10 ml/kg rapidly) or colloids (5 ml/kg rapidly).
    3. Consider positive inotropes like dopamine or dobutamine. Dose of each is 1-10 microg/kg/min (up to 15 with dopamine). Patients with conditions that cause decreased cardiac contractility (eg, sepsis, etc…) are likely to need positive inotropes for effective blood pressure support.
    4. If these measures are not effective or if the patient is severely vasodilated, vasopressors (eg, norepinephrine, vasopressin) may be necessary.

Respiratory support includes oxygen delivery and maintenance of ventilation.

- Oxygen is inexpensive and profoundly beneficial in many critical patients. When in doubt, administer oxygen!

- If the patient is having any trouble ventilating (head trauma, thoracic trauma, profound CNS depression, impingement on thorax by GI contents, etc…) ADMINISTER OXYGEN.
- If the ventilatory depression is moderate, consider intubation. If severe, INTUBATE.
- Obviously most anesthetized patients would be intubated. Intubate rapidly and quickly inflate the endotracheal tube cuff to an appropriate pressure.
- Many compromised patients will require assisted ventilation because the respiratory drive in-response to hypoxemia and/or hypercarbia may be impaired and/or the patient may not physically be able to ventilate normally (muscle weakness, thoracic trauma, electrolyte imbalance, GI distension, etc…). Assisted ventilation: 2 breaths/min to 15-20 cmH_2O on the manometer. Controlled ventilation: 6-10 breaths/min to 15-20 cm H_2O on the manometer. If a ventilator is available, set tidal volume to 15-20 ml/kg. MONITOR End-tidal CO_2 – normal is 35-55 mmHg in the anesthetized patient (35-45 mmHg in conscious patients); Do not over ventilate.

Hypothermia

Adverse effects of hypothermia

- Decreased need for anesthetic drugs
- PROLONGED RECOVERY from anesthesia
- Impaired metabolism (adds to prolonged recovery)
- Immune system depression
- Coagulation dysfunction, sludging of blood
- Decreased cardiac contractility, arrhythmias
- Respiratory impairment
- Increased oxygen consumption (shivering)
- Etc…

- **START WARMING AT INDUCTION, MINIMIZE ANESTHESIA TIME**

Recovery

Unfortunately, most anesthetic deaths occur in recovery and the majority of those occur within the first 3 hours of recovery (Brodbelt 2009). The cause is likely a decrease in anesthetist vigilance in recovery. Support and monitoring should be continued into the recovery phase, especially for challenging patients. Analgesia should also be re-addressed. If effective analgesia is utilized pre- and intra-operatively, the analgesic needs of the patient may be minimal. Opioid boluses and constant rate infusions are excellent choices during the recovery period. NSAIDs may be appropriate depending on the disease. The drugs diminish pain at its source (inflammation) making them very powerful. Administer NSAIDS if not contra-indicated.

Specific examples

Patient with cardiovascular disease/dysfunction

The cardiovascular system includes the heart, blood vessels and blood/plasma. Thus, cardiovascular disease or dysfunction encompasses `conditions ranging from decreased cardiac contractility to arrhythmias to anemia. Diseases that are not necessarily cardiovascular diseases but which affect the cardiovascular system (eg, hyperthyroidism, sepsis, etc…) should also be considered in this category when making anesthetic plans for patients with those diseases. In addition, anesthetic drugs (e.g. inhalants), perioperative manipulations (e.g. recumbency, positive pressure ventilation) and surgical complications (e.g. uncontrolled pain, hemorrhage) can exacerbate cardiovascular dysfunction – and can even cause cardiovascular changes that mimic cardiovascular disease. Thus, a fair number of anesthetized patients may need cardiovascular support, even in the absence of cardiovascular disease. Because of the vast number of diseases/conditions that affect the cardiovascular system, one anesthetic protocol may not be appropriate for all patients in this category, but an understanding of cardiovascular physiology and the cardiovascular effects of the anesthetic drugs will promote appropriate anesthetic/analgesic protocol selection. In addition to appropriate dose/drug selection, diligent patient monitoring and support are crucial.

Physiology of the Cardiovascular System & Anesthesia Goals

The ultimate goal of the cardiovascular system is to work in concert with the respiratory system to provide adequate oxygen delivery (DO_2) to the working cells. The cardiovascular system's role in this goal is achieved through support of cardiac output, which is a product of heart rate (HR) and stroke volume (SV). Stroke volume is determined by preload, afterload and myocardial contractility (inotropy). In all patients, the focus should be on support of normal physiologic processes in order to optimize tissue oxygen delivery.

Preanesthetic preparation

STABILIZE the patient! Long term if possible (eg, send home on drugs that improve cardiac function) or short term in not possible (eg, administer fast-acting anti-arrhythmic drugs to treat arrhythmias). However, drugs that may decrease blood pressure (eg, beta-blockers, calcium channel blockers) should be withheld on the morning of anesthesia. Once ready for anesthesia, preoxygenate to decrease the likelihood of decreased oxygen delivery. Start on JUDICIOUS rate of IV fluids if the patient is hypovolemic at a suggested rate of 2-5 ml/kg/hr depending on the disease and patient. Monitors should be connected to the patient prior to induction. Numerous physiologic changes can happen at induction. Warming should start now since body temperature starts to drop at induction. Hypothermia causes adverse cardiovascular effects like decreased myocardial contractility, arrhythmias and bradycardia.

Excitement, struggling and fear cause tachycardia and increased peripheral resistance, arterial blood pressure, cardiac work and cardiac oxygen consumption. These changes are generally well-tolerated in patients with a healthy cardiovascular system but are extremely dangerous in a patient with cardiovascular disease, possibly resulting in decompensation and cardiac failure. Pain causes the same sympathetic response as excitement, struggling and fear. Therefore, all of

these stressors must be avoided in patients with cardiovascular disease and calm handling, along with the administration of a low-dose of a tranquilizer and preemptive analgesic drug, are crucial. **Opioids** have minimal adverse impact on the cardiovascular system and are the drug class of choice for patients with cardiovascular disease.

Disease-specific comments

Hypertrophic cardiomyopathy (mostly cats) and dilatative cardiomyopathy/regurgitant valvular disease (mostly dogs) have different physiologic impacts and, thus, different anesthetic concerns.

- Hypertrophic cardiomyopathy: In this disease the cardiac muscle is overworked so avoid drugs that further increase cardiac work (through increased rate or contractility). Increased work will increase myocardial oxygen need - but the hypertrophic cardiac muscle is generally not matched by increased vasculature, thus oxygen delivery can be decreased. This could include ketamine (no concern at CRI dose), anticholinergics, etc… Inotropes are somewhat controversial as some clinicians feel that they are contraindicated but research shows they are safe and effective when used at low dosages. Both dopamine and phenylephrine improved blood pressure but only dopamine improved cardiac output. (Wiese et al 2012). Slower heart rates (allow time for ventricles to fill) and vasoconstriction (increased afterload which can decrease left ventricular outflow obstruction) is often beneficial in these patients, thus alpha-2 agonists may be considered (Lamont et al. 2002) if needed to adequately control the cat (Lamont et al. 2002).
- Dilatative cardiomyopathy/regurgitant valvular disease: In this disease the cardiac muscle is inefficient for appropriate ejection of adequate blood volume or the dysfunctional valve promotes inadequate ejection blood volume. In these patients, the goal is myocardial contractility support and decreased ejection resistance (ie, vasodilation). Low-dose acepromazine may be beneficial. Ketamine can be very useful as it increases both rate and contractility through SNS stimulation. Increased heart rate may be necessary so anticholinergics may be indicated. Inotropes are beneficial.

Preanesthetic drugs: Specific cardiovascular (CV) effects/concerns

Opioids	Minimal CV effects – no change in contractility, some vagally-mediated bradycardia; 'cardio sparing'
Alpha-2 Agonists	Increased cardiac work from vasoconstriction. Generally contraindicated, but may be beneficial in some diseases[2]
Acepromazine	Low dose = decreased afterload but high dose = hypotension
Benzodiazepines	No CV effects; Cardio sparing; Not very sedating – combine with an opioid

Preoxygenate: Decreases the likelihood of decreased oxygen delivery. Preoxygenation for only 3 minutes increases the time do desaturation (SpO2<90%) approximately 1 minute to 6 minutes.

Induction drugs: Specific cardiovascular effects/concerns

Propofol	Mild to moderate dose-dependent cardiovascular (CV) depression.[3] Administer premeds to decrease the dose of induction drug required to produce anesthesia.
Alfaxalone	Mild to moderate dose-dependent CV depression.[3] Administer premeds to decrease the dose of induction drug required to produce anesthesia.
Ketamine	Increased HR & contractility through SNS in healthy hearts but direct myocardial depression in uncompensated heart failure; MAY exacerbate tachyarrhythmias? CRI dose is not concerning.
Telazol	Probably same effects as ketamine.
Etomidate	Minimal to no impact on CV system. Drug of choice for profound disease.
Inhalants	Moderate to profound dose-dependent CV depression. Don't induce with inhalants!

TIP: Administer a low-dose benzodiazepine or fentanyl bolus just before induction to decrease the dose of induction drug.

Maintenance

Inhalants can cause hypotension since they cause both dose-dependent decreased cardiac contractility and vasodilation. KEEP THE DOSE LOW. Add **analgesia**! Opioid boluses, local blocks and infusions of opioids, lidocaine and/or ketamine are all good options. Ketamine at the infusion dose used for infusions is unlikely to cause adverse effects and is commonly used for patients with cardiac disease.

Monitoring: Blood pressure, ECG, SpO_2 and $ETCO_2$. Need to monitor both the respiratory and cardiovascular systems to insure oxygen delivery.

Support: Maintain MAP >8 kPa (>60 mmHg). The steps to promote normotension are:

- DECREASE the INHALANT DOSE
- **Support cardiovascular function with inotropes**
    - Dopamine, dobutamine
    - In a patient with myocardial disease/dysfunction, decreased contractility is the most likely cause of hypotension so start inotropes early.
- Check the heart rate – fix if necessary
- JUDICIOUS use of IV fluids if hypovolemia is present
    - 2-10 ml/kg/hr intra-op
    - Balanced electrolyte solution
    - Blood or plasma if necessary
- USE COLLOIDS – eg, hetastarch
- Treat arrhythmias appropriately
    - Arrhythmias can affect cardiac output

Recovery
DON'T STOP MONITORING and SUPPORT
The more compromised the patient, the longer monitoring and support should continue.
Keep warm. Shivering can increase oxygen consumption by up to 200%, which may not be met by oxygen delivery in patients with cardiovascular disease.
Readdress analgesia; USE TRANQUILIZERS if necessary – DON'T allow a rough recovery! The stress physiologic stress can exacerbate cardiac dysfunction. NSAIDs if appropriate: No negative CV effects, Anti-inflammatory

Sample Protocol
Preanesthesia: Physical exam, complete blood work, thoracic radiographs, ECG. Consider maropitant.
Premedication: Opioid IM (unless catheter already placed); preoxygenate if possible
If the patient is really sick, skip the IM premed and use fentanyl IV at induction.
Induction: 0.2 mg/kg midazolam or diazepam IV followed by propofol, alfaxalone or etomidate SLOWLY to effect. Fentanyl (2-5 microg/kg) can be substituted for or added to the benzodiazepine.
Maintenance: LOW DOSE inhalant; use CRIs (especially fentanyl or other opioid) & local blocks. Monitor ECG and blood pressure; use dopamine CRI for hypotension; use active warming.
Recovery: Keep monitoring until patient is fully awake; Provide analgesia with opioids
Administer NSAIDs if there are no contraindications.

Resources
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