

# Anesthesia Refresher & New Anesthesia/Analgesic Products



AMERICAN COLLEGE OF VETERINARY ANESTHESIA AND ANALGESIA

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## Acknowledgements



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## Objectives

- Sedation versus general anesthetic: what are the considerations?
- Be prepared: Who? What? Where? When? Why?
- Formulate a treatment plan appropriate for patient and type of pain involved
- Brief review of major classes of analgesic drugs
- Reassess and modify pain management plan PRN
- Understand basic monitoring parameter normal values in dogs and cats, perform surgical safety checklist, recognize patient vs monitor issues

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## General Anesthesia

- Reversible unconsciousness
- Amnesia
- Analgesia
- Muscle relaxation
- Perform a procedure
  - w/o suffering
  - Safely
    - Patient
    - Veterinary Care Provider(s)

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## General Anesthesia Definitions

- Multi-modal approach
  - DO NOT "mask down" (canine/feline) patients!
  - Patient & occupational safety concerns
- MAC (minimum alveolar concentration)
  - = amount of inhalant needed for 50% of patients non-responsive to supramaximal stimulus
  - Isoflurane: ≈ 1.3% canine, ≈ 1.6% feline
  - Sevoflurane: ≈ 2.3% canine, ≈ 3% feline
  - allows estimate the amount of inhalant required
    - factors: procedure, patient pre-med response, inhalant



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ASA CLASSIFICATION	DESCRIPTION	EXAMPLES
I	Normal, healthy patient	Healthy young patient presenting for spay/neuter
II	Patient with mild systemic disease	Cutaneous mass removal; uncomplicated orthopedic procedures, well-controlled diabetic or managed asthmatic requiring procedure that may or may not be related to disease
III	Patient with severe systemic disease	Cardiac dysfunction, early renal disease, poorly controlled diabetes mellitus (patient may require procedure possibly unrelated to disease itself), mild anemia
IV	Patient with severe disease that is a constant threat to life	Hemoabdomen, sepsis, intestinal foreign body with potential for bowel rupture, hypovolemic shock, anemia
V	Moribund patient who is not expected to survive	Massive trauma, hemoabdomen with cardiac abnormalities, multi-organ dysfunction, GI foreign body with large amounts of ischemic bowel

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## Anesthetic Risks

- ↑ risk of mortality seen with increasing ASA status
  - Importance of patient evaluation and stabilization PRIOR to commencement of procedure
  - Identify risk factors and monitor carefully
- Largest proportion of deaths in post-procedure period
  - Continued patient monitoring & support vital
- Main factor related to anesthetic death = poor health status!
  - Risk of anaesthetic mortality in dogs and cats: an observational cohort study of 3546 cases  
C Bille et al. Veterinary Anaesthesia and Analgesia, 2012, 39, 59-68
- ↑ anesthetic risk with ASA classification
  - > **ASA III: 4.77%**
    - ASA III: 2.9%
    - ASA IV: 7.58%
    - ASA V: 17.33%

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## Anesthesia-Related Mortality

- |   |  |
|---|--|
| <p><b>DOGS</b></p> <ul style="list-style-type: none"> <li>5/10 000 (0.05%)</li> <li>↑ age</li> <li>nonelective sx</li> <li>Pre-anes PE not performed/recorded</li> <li>Hct outside RR</li> <li>Underweight                             <ul style="list-style-type: none"> <li>15x &gt;</li> </ul> </li> </ul> | <p><b>CATS</b></p> <ul style="list-style-type: none"> <li>11/10 000 (0.11%)</li> <li>↑ age</li> <li>nonelective sx</li> <li>SpO2 not monitored/recorded</li> <li>↑ body weight                             <ul style="list-style-type: none"> <li>NOTE: not BCS</li> </ul> </li> </ul> |
|---|--|

from Mathews et al. JAVMA 2017

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## How can we make anesthesia safe(r)?

Bille et al., VAA (2012 & 2014)

- Emphasize pre-anesthetic medical mgt whenever possible
  - Improve patient's ASA status **BEFORE**
- Anesthetic Plan:
  - premedication
  - IV induction agent
  - inhalant maintenance
- Monitor & Record: pre, during, post!
- When? Recovery period

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## Preparing the Patient



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## Patient Prep: Fear Free Approach

- [www.fearfreepets.com](http://www.fearfreepets.com)
- Benefits:
  - Increased standard of patient care
  - Staff satisfaction
  - Business model



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## Pre-PreMeds: Fear Free Pets

Many methods ↓ Fear, Anxiety, Stress (FAS)

[www.fearfreepets.com](http://www.fearfreepets.com)

- Trazodone
  - 3-5 (up to 10) mg/kg q8h
- Gabapentin
  - 10-20 mg/kg q 8h
- Must be administered BEFORE FAS levels high
  - Recommend dosing night before, then morning of dropoff
- Melatonin, CHILL Protocol (melatonin, gabapentin, acepromazine) developed at Tufts University
  - 0.1 mg/kg
  - (0.5-3 mg/cat, 1-6 mg/dog)

\*caution when patients are already on other behavioral modifying meds!



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### Who Should Have Vascular Access?

- ALL anesthetized patients
- Titrated-sedation patients
- “Choose your own adventure” patients
  - Top-ups likely or warranted
  - Difficult IV access patients
- GOAL – individualized plans! (pt mgt (type, size, location access), drugs, etc.)
  - prepare & anticipate possible complications
  - Ensure good outcomes



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### Intravenous Access

- Benefits**
- Increased patient comfort overall
  - Increased patient safety – emergency situations!
  - Ability to administer fluids, transfusions, medications
  - Access to draw blood samples (in some instances)
  - Hemodynamic monitoring – i.e. CVP (in some instances)
- Potential concerns:**
- Hemorrhage
  - Infection – systemic v phlebitis
  - Vascular trauma – scarring, phlebitis



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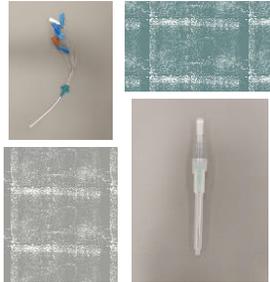
### Types of Vascular Access

More common:

- Intravenous catheter
  - Peripheral (most common)
  - Central line
  - Sampling line
- Intra-arterial catheter

Less common: (but certainly options to consider!)

- Vascular Access Ports
- Intra-osseous catheter (situation, species dependent)



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### Premed & Induction: Neuroleptanalgesia

- Recommended approach for pre-anesthetic medication

**= sedative + opioid**

- synergistic effects
  - use less of both drugs with greater effect
  - higher safety margin, lower side effects
  - ↓ stress and provides analgesia

1+1 > 2!

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### Premed: Opioid + Sedative

OPIOIDS

- Pure mu agonists
  - Morphine, hydromorphone, fentanyl!
- Others
  - Butorphanol
  - Buprenorphine



SEDATIVES

- Phenothiazines
  - Acepromazine
- Alpha-2 agonists
  - Dexmedetomidine
- Benzodiazepines
  - Midazolam
  - Diazepam

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### Induction: Propofol & Alfaxalone

- Amount of induction agent 1/∞ to level of sedation!
  - You can always add more, but can't take it away...
  - Hypotension, dose-related resp depression → apnea
  - Entire dose rarely needed in ASA ≥ III
- Propofol
  - 0.5-4 mg/kg IV SLOW
- Alfaxalone
  - 0.25-2m kg IV SLOW



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**Induction: How much to give?**

Signs to consider:

- Muscle relaxation
- Palpebral reflex
  - Negative LATERAL
  - Keep in mind (+) medial into surgical plane
- Eye position – rotated ventromedially
- Jaw tone – check it LAST!

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**Induction: ketamine + benzo**

- Ketamine + benzodiazepine
- Premed 1<sup>st</sup> : opioid + sedative
- Induce:
  - Ketamine 5 mg/kg
  - Diazepam or midazolam 0.25 mg/kg
- Give it all?
  - It depends...



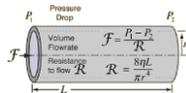
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**Induction: Endotracheal Tubes for GA!**

- Size: palpate the trachea
  - 3 tubes ready: 1 you need, 1 bigger, 1 smaller
- Diameter: BIGGER IS better!
  - Poiseuille's law
    - [resistance to flow, ↓work of breathing]
- Length: SHORTER is better!
- Cuff inflation: MINIMAL!
  - Inflate air as someone is bagging to 20 cmH2O
  - AVOID BLIND FILLING & SQUEEZING!
  - AFTER tube tied in
  - BEFORE turning on inhalant!
- Steps for proper cuff check:
  - Close APL (pop-off) valve
  - Fill reservoir bag to 20 cmH2O

Q	Flow rate
P	Pressure
r	Radius
ΔP	Fluid viscosity
L	Length of tubing

$$Q = \frac{\pi Pr^4}{8\eta l}$$



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**Induction: Use a Laryngoscope**



**Laryngoscope!**

- Placement
  - Base of tongue
  - IN FRONT of epiglottis
  - Why? Better visual, larger ETT
  - do NOT grab epiglottis & push down → fx hyoid apparatus
- Light bulb gets hot when left on – burns reported
  - Get LED if possible

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**GA: Vaporizer Settings**

- MAC = Minimum Alveolar Concentration
  - Amount of inhalant needed to render 50% of patients unresponsive to noxious stimulus
  - Studies done with just inhalant, no premed/ind agents
- 1.2-1.4x MAC for most procedures
  - Healthy, elective
  - LESS, MUCH LESS for patients with comorbidities, high risk anesthesia, other drugs (i.e. analgesic CRIs) coadministered
- Isoflurane
  - Dog: 1.2-1.3%, Cat: 1.4-1.6%
- Sevoflurane
  - Dog: 2.2-2.3%, Cat: 2.6-3.2%
- GOAL: to minimize inhalant use in high-risk cases
  - Multimodal drugs, analgesic CRIs, locoregional anesthesia
  - VENTILATION over increasing vaporizer settings!

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### General Anesthesia: O<sub>2</sub> flow

- Rebreathing Systems
  - Circle/Universal F
    - Induction & Recovery: 50-100 mL/kg/min O<sub>2</sub>
    - Maintenance: 20-50 mL/kg/min O<sub>2</sub>
- Nonbreathing Systems
  - Mapleson F
  - Bain (Modified Mapleson D), Universal Arm
  - ≥ 200-300 mL/kg/min O<sub>2</sub>



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### Anesthesia Monitoring

VETERINARY PRACTICE GUIDELINES

#### 2020 AAHA Anesthesia and Monitoring Guidelines for Dogs and Cats\*

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**ABSTRACT**

Risk for complications and even death is inherent to anesthesia. However, the use of guidelines, checklists, and training can decrease the risk of anesthesia-related adverse events. These tools should be used not only during the time the patient is unconscious but also before and after this phase. The framework for safe anesthesia delivered as a continuum of care from home to hospital and back to home is presented in these guidelines. The critical importance of client communication and staff training have been highlighted. The role of perioperative analgesia, analgesics, and proper handling of fractious/feared/aggressive patients as components of anesthetic safety are stressed. Anesthesia equipment selection and care is detailed. The objective of these guidelines is to make the anesthesia period as safe as possible for dogs and

<https://www.aaha.org/aaha-guidelines/2020-aaha-anesthesia-and-monitoring-guidelines-for-dogs-and-cats/anesthesia-and-monitoring-home/>

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### Anesthesia Monitoring: AAHA Guidelines

- Patient preparation
- Individualized anesthetic plans
- Constant monitoring:
  - Cardiovascular
  - Respiratory
  - Central nervous system
- Adjustments based on patient status

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### Anesthesia Monitors

PARAMETER	MONITOR	INFORMATION
Oxygenation	Pulse Oximeter	SpO <sub>2</sub> , pulse rate (PR)
Ventilation/Respiration	Capnometer/Capnograph	Respiration rate, ETCO <sub>2</sub>
Blood Pressure	Doppler w/ sphygmomanometer, Oscillometric, Direct Arterial Line (invasive)	SAP (systolic arterial pressure), MAP (mean/weighted calculated SAP/DAP), SAP, MAP, DAP (diastolic), PR
Pulse rate	Pulse oximeter, Doppler, Oscillometric*, ECG	Pulse by pulse, audible info * not real time with ausculto Electrical impulses of heart
Temperature	Thermometer	Rectal or esophageal temperature

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### Anesthesia Monitoring

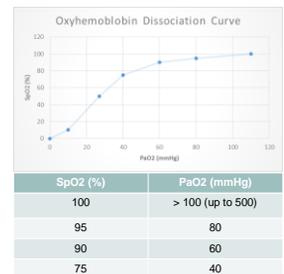
#### The Big 3

- SpO<sub>2</sub>
  - ETCO<sub>2</sub>
  - BP
- Then,
- ECG, T<sub>0</sub>, eye lube
- Anesthesia-dedicated RVT, record q5 min

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### Pulse Oximetry: Why is it important?

- Sigmoid shape
- FiO<sub>2</sub> 21% PaO<sub>2</sub>: 80-110 mmHg
- FiO<sub>2</sub> 100% PaO<sub>2</sub>: 400-500 mmHg
- SpO<sub>2</sub>: PaO<sub>2</sub> benchmarks



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## Pulse Oximeter

- From induction through recovery (GA)/ entire sedation procedure whenever possible!
- Oxygen desaturation events
  - SpO<sub>2</sub> < 95%
  - Please NEVER ignore!
  - Induction: esophageal intubation, endobronchial intubation, oxygen supply problem
  - Maintenance: hypoventilation
  - Recovery: hypoventilation, VQ mismatch



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## Capnography

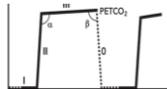
- Parameters:
  - Real-time respiratory rate (RR)
  - End-tidal CO<sub>2</sub> (ETCO<sub>2</sub>)
- Normal ranges:
  - ETCO<sub>2</sub> 35-45 mmHg
  - RR: Dogs (≈ 8-20 bpm), cats (≈10-30 bpm)
  - Recall, V<sub>m</sub> = V<sub>t</sub> \* RR
- Advantages:
  - Affordable, noninvasive, portable, valuable info



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## Capnography

- From induction (intubation) to recovery (extubation)
- Hypoventilation events
  - ETCO<sub>2</sub> > 45 mmHg
    - Common causes: too deep (inhalant), obese, opioid/sed
    - (-): respiratory acidosis
    - You have control!
- Hyperventilation events
  - ETCO<sub>2</sub> < 35 mmHg
    - Dilutional effects?
    - Is the patient: light, painful, hot/opioids, acidemic, hypoxemic?



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## Blood Pressure Monitoring

- Parameters:
  - Pulse rate (PR)
  - Arterial pressure (SAP, MAP, DAP in mmHg)
- Normal ranges:
  - MAP ≥ 60 mmHg: normal, healthy, young pts
  - Doppler BP ≥ 90 mmHg
  - MAP > 80 mmHg: geriatric, renal, hypertensive pts
  - Or ideally, within 20 mmHg of awake BP if possible
- Sedation
  - Acepromaine: ↓ SVR (vs) Dexmedetomidine: ↑ SVR, reflex bradycardia
- General Anesthesia
  - Inhalant: ↓ CO, ↓ SVR
- From start of procedure until ...?
  - Patient monitoring should end once the patient has vitals WNL!
    - TPR, BP, SpO<sub>2</sub>, +/- ETCO<sub>2</sub>



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## Blood Pressure Monitoring

### Oscillometric

- Popular, easy to apply, automated
- MAP measured
  - BP cuff ≈ 40% the circumference of the limb to machine attached to tubing
    - auto-inflate → system deflates slowly until oscillations in the arteries are detected when blood flow is first terminated, then when it returns
  - Oscillations terminate w/normal blood flow → MAP
  - SAP, DAP calculated using a computer algorithm
- (-) ↓ accuracy: hypotension, hypertension, tachycardia, bradycardia, very small patients

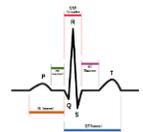
Other options: direct BP (IBP/art line), Doppler



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## ECG: Electrocardiogram

- Parameters:
  - Cardiac electrical activity
  - HR
    - Canine: 60-160 bpm
    - Feline: 120-220 bpm
- When to use?
  - Normal pts: after the "big 3": pulse oximeter, capnograph, BP monitor
  - Place in advance of anesthetic induction in patients where cardiac arrhythmia concern
    - i.e., hx cardiac dz, hemoabdomen, GDV, septic shock
- Why is it important?
  - Under abnormal circumstances, electrical activity does not result in appropriate cardiac contraction
    - ↓ CO, circulation, perfusion
    - i.e. AV block, VPCs, V tach, etc.



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### Temperature Support

- Temperature monitoring +/- heat support should be provided in all sedated/GA pts
- Hyperthermia
  - ↑ metabolism, ↑ ETCO<sub>2</sub>, ↑ anesthetic drug need
  - T > 108°F → multiple organ failure and death
- Hypothermia
  - T < 96°F: ↑ infection and bleeding risks
  - T < 94°F: prolonged and poor quality recovery
    - ↓ drug metabolism
    - shivering → discomfort, ↑ oxygen consumption

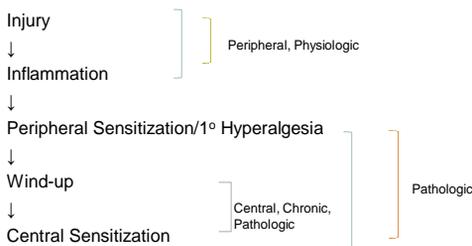
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### Why manage pain?

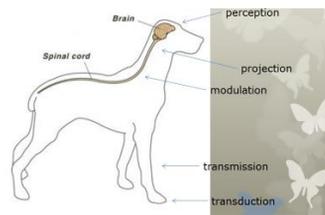
- Optimize patient well-being
  - Reduce stress
  - Optimize healing
  - Prevent unwanted behaviors
  - Allow rest – patient AND client
- Prevention of enhanced pain states
  - Peripheral Sensitization
  - Central Sensitization

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### Progression of Pain



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### Acute Pain

- **Transduction:** noxious stimulus at peripheral nociceptors
- **Transmission:** triggers A-δ and C fibers information from periphery to SC
- **Modulation:** → SC dorsal horn amplifies or inhibits ascending transmission from SC to CNS (brainstem)
- **Perception:** CNS (cortex)

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### Pain Sensitization

- Maladaptive pain
  - No biologic function (not protective)
  - Self-perpetuating and stressful
- Sustained sensory input modifies inhibitory descending (antinociceptive) processes
- Central & peripheral sensitization of nociceptive pathways
  - Brain, spinal cord, dorsal horn
  - Aka "wind-up"
  - Neuroplasticity → anatomic changes → exaggerated pain!

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### Pain Recognition and Evaluation

- Pain Behaviors
  - Posture and activity
- Vocalization
  - Nonspecific, species differences
- Appetite
- Appearance
- Response to Manipulation
- Urinary and Bowel Habits
- DIFFERENCES IN SPECIES AND TYPES OF PAIN!

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### Objective and Categorical Pain Assessment

- Difficulties:
  - Species differences
  - Validation of scale (species, type of pain)
  - Physiological factors not dependable
    - Fear, anxiety, anesthesia, etc
  - Behavioral assessment can be subjective
    - Subtle changes
    - Individual differences

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### Pain Scale Use

- Measure of patient's pain intensity at a specific time point
  - Objective, repeatable
  - Type, severity, duration → diagnose, treat, reassess!
- Ensure that pain is assessed and treated in EVERY patient (please reassess frequently!)
- PAIN = 5<sup>th</sup> vital sign
  - Use in conjunction with patient evaluation and complete PE
- ALL pain scales have limitations
  - Use appropriate scale for type of pain
- If in doubt, try analgesic trial based on individual needs
- GOAL = low pain score + comfortable patient!

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### What are our challenges in assessing pain?

- Species differences
- Validation of scale (species, type of pain)
- Physiological factors not dependable
  - Fear, anxiety, anesthesia, etc
- Behavioral assessment can be subjective
  - Subtle changes
  - Individual differences

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### Options for assessing ACUTE pain in DOGS

- Glasgow Composite Measure Pain Scale (CMPS) Canine
  - Morton CM, Reid J, Scott EM, Holton LL, Nolan AM. Application of a scaling model to establish and validate an interval level pain scale for assessment of acute pain in dogs. *Am J Vet Res.* 2005 Dec;66(12):2154-66. doi: 10.2460/ajvr.2005.66.2154. PMID: 16379662
- Glasgow Composite Measure Pain Scale –Short Form (CMPS-SF) Canine
  - Reid J, Nolan AM, Hughes JM, Lascelles D, Pawson P, Scott EM. Development of the short-form Glasgow Composite Measure Pain Scale (CMPS-SF) and derivation of an analgesic intervention score. *ANIMAL WELFARE-POTTERS BAR THEN WHEATHAMPSTEAD.* 2007 May 1;16:97
- Colorado State University (CSU) Pain Scale
  - not validated, but widely used

Hofmeister EH, Barletta M, Shepard M, Brainard BM, Trim CM, Quandt J. Agreement among anesthesiologists regarding postoperative pain assessment in dogs. *Vet Anaesth Analg.* 2018 Sep;45(5):895-702. doi: 10.1016/j.vaa.2018.04.001. Epub 2018 May 22. PMID: 30078533

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SHORT FORM OF THE GLASGOW COMPOSITE PAIN SCALE

Dog's name: \_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_  
 Hospital Number: \_\_\_\_\_  
 Veterinary Practice: \_\_\_\_\_  
 Breed/sex or Condition: \_\_\_\_\_

A. In the abdomen (ventral) or in the abdomen (dorsal) (check one box for each pain focus in the last two in the dog's)

Rest	0	Resting or sitting or lying down	0
Staring	1	Looking for source of pain/area	1
Whining	2	Looking around or barking	2
Cowering	3	Whining or crying out	3

B. In the case of central neck or visible limb flexion, or when assessment is hindered by obstruction or fear only tick boxes B and D instead of C.  
 Please tick A/B in the case C has passed C:

B. The head on dog and back up of the torso. C. If the dog is unable to perform any of the following, tick the appropriate limb strength assessment 2

When the dog is unable to sit	0	Head up	0
Rest	1	On looking	1
Staring	2	On touch	2
Whining	3	On touch	3
Cowering	4	On touch	4
On touch	5	On touch	5

D. Overall

0	At the dog's	0	At the dog's
1	Rest or sitting or lying down	1	On looking
2	Staring	2	On touch
3	Whining	3	On touch
4	Cowering	4	On touch
5	On touch	5	On touch

E. Sum of all dog's Total Score (underlined) = \_\_\_\_\_

### Rescue for Dogs:

- Non-Ambulatory ≥ 5/20
- Ambulatory ≥ 6/24

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### Options for assessing ACUTE pain in CATS

- Glasgow Composite Measure Pain Scale (CMPS) Feline
  - Reid J, Scott EM, Calvo G, Nolan AM. Definitive Glasgow acute pain scale for cats: validation and intervention level. *Vet Rec.* 2017 May 6;180(18):443. doi: 10.1136/vr.104206. Epub 2017 Jan 27. PMID: 28130405
- UNESP-Botucatu
  - Brondani JT, Mares KR, Luna SP, Wright BD, Niyom S, Ambrosio J, Vogel PR, Padovani CR. Validation of the English version of the UNESP-Botucatu multidimensional composite pain scale for assessing postoperative pain in cats. *BMC Vet Res.* 2013 Jul 17;9:143. doi: 10.1186/1746-6148-9-143. PMID: 23867050. PMCID: PMC3722032
  - Belli M, de Oliveira AR, de Lima MT, Trindade PHE, Steagall PV, Luna SPL. Clinical validation of the short and long UNESP-Botucatu scales for feline pain assessment. *PeerJ.* 2021 Apr 12;9:e11225. doi: 10.7717/peerj.11225. PMID: 33954046. PMCID: PMC8046399
- Feline Grimace Scale
  - Evangelista, M.C., Watanabe, R., Leung, V.S.Y. et al. Facial expressions of pain in cats: the development and validation of a Feline Grimace Scale. *Sci Rep* 9, 19128 (2019). <https://doi.org/10.1038/s41598-019-55693-8>
- Colorado State University Feline Acute Pain Scale (CSU-FAPS)
  - Shipley H, Quevedo A, Graham L, Goudie-DeAngelis E, Wendt-Horrickle E. Preliminary appraisal of the reliability and validity of the Colorado State University Feline Acute Pain Scale. *J Feline Med Surg.* 2019 Apr;21(4):335-339. doi: 10.1177/1098612X1877506. Epub 2018 May 31. PMID: 29848148
  - **Conclusions & Relevance:** The CSU-FAPS showed moderate-to-good inter-rater reliability when used by veterinarians to assess pain level or need to reassess analgesic pain after ovariohysterectomy in cats. The validity, fit short of current guidelines for correlation coefficients and further refinement and testing are warranted to improve its performance

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### Sugar: 4 days post-op at referral



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### Sugar's Amputation Surgery

- Pre-op:
  - CBC/Chem/lytes: NSF
  - CXR (3v) no evidence of metastasis
- Premed?
- Induce?
- Maintenance? CRIs?
- Locoregional anesthesia?
- Recovery concerns?
- Post-operative pain management?
- TGH analgesia?

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### Sugar's Anesthesia Plan

- Pre-premed: maropitant 1 mg/kg IV
- Premed: hydro 0.1 mg/kg + dexmed 1 mcg/kg IV
- Induce: midazolam 0.2 mg/kg IV, followed by propofol up to 4 mg/kg IV slow
- Maint: iso + O2, fentanyl CRI, ampicillin-sulbactam IV q 90 min, LRS at 5 mL/kg/h
- Locoreg: intra-op nerve blocks (bupivacaine) + LE bupivacaine (Nocita)
- Post-op analgesia: fentanyl CRI, deracoxib once eating, fentanyl patch 50 mcg/h, gabapentin 300 mg PO q8h

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### Sugar's Evaluation



0730, October 18, 2022: 1d post-op

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### Sugar's Evaluation

- 0730 rounds
- Fentanyl CRI d/c, oral meds given (gabapentin, deracoxib)
- Nurse reports that patient has been demonstrating
  - Bruxism
  - Wakes from a sound sleep, jumps up & tries to bite at R flank
- Glasgow Composite Score: /24
  - 0+1+1+2+0+0
  - = 4!?! What to do?

A. Look at Rg to Raster	
In the dog?	
HR	100
RR	20
Temp	38.5
SpO2	98
MAP	65
UO	0.5
UO2	0.5
UO3	0.5
UO4	0.5
UO5	0.5
UO6	0.5
UO7	0.5
UO8	0.5
UO9	0.5
UO10	0.5
UO11	0.5
UO12	0.5
UO13	0.5
UO14	0.5
UO15	0.5
UO16	0.5
UO17	0.5
UO18	0.5
UO19	0.5
UO20	0.5
UO21	0.5
UO22	0.5
UO23	0.5
UO24	0.5
UO25	0.5
UO26	0.5
UO27	0.5
UO28	0.5
UO29	0.5
UO30	0.5
UO31	0.5
UO32	0.5
UO33	0.5
UO34	0.5
UO35	0.5
UO36	0.5
UO37	0.5
UO38	0.5
UO39	0.5
UO40	0.5
UO41	0.5
UO42	0.5
UO43	0.5
UO44	0.5
UO45	0.5
UO46	0.5
UO47	0.5
UO48	0.5
UO49	0.5
UO50	0.5

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### Sugar's Plan?

- Remain in hospital for an additional day
- Ketamine load 0.5 to 1 mg/kg IV, followed by CRI at 2-5 mcg/kg/min (dilute to 5 mg/mL)
  - Run CRI 12-24h
- Hydromorphone 0.05 mg/kg IV q 4-6h PRN
- TGH, add: amantadine 3-5 mg/kg PO q 12-24h x 21d

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## Considerations for New Product Integration?

- Efficacy
- Safety
  - Patient
  - Staff
  - Clients
- Supporting data
  - How many studies? Peer reviewed? Sample size? Sample population?
- Cost
- Availability
- Caseload?

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## Zenalpa® (medetomidine + vatinoxan HCl)

- Company: Dechra USA
- Formulation: medetomidine 0.5 mg/mL + vatinoxan 10 mg/mL
- Availability: 10 mL vial, multi-dose glass vials
- Label use: canine intramuscular injection
- Indication: sedation (and analgesia) for dogs
  - Clinical examinations
  - Clinical procedures
  - Minor surgery
- Recommended use: ASA I-II
  - Healthy, low risk



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## Zenalpa® (medetomidine + vatinoxan HCl)

- Pharmacology
  - Medetomidine = alpha-2 agonist
  - Vatinoxan = alpha-2 antagonist
- Why consider Zenalpa?
  - HR & BP closer to normal range
  - Minimal vomiting
  - Shorter onset and duration than dexmedetomidine
- Dosage and Administration
  - IM only, DOGS only
  - Chart = m<sup>2</sup>: single agent; young, healthy dogs → reduction for clinical use in most cases



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## Zenalpa® (medetomidine + vatinoxan HCl)

- Medetomidine
- α-2 agonist
  - Previous formulation Domitor
  - Racemic mixture of 2 optical stereoisomers
    - dexmedetomidine + levomedetomidine (50/50)
  - Profound sedation, mild analgesia
  - Same patient concerns as dexmedetomidine
    - i.e. avoid in patients: renal disease, hepatic disease, cardiac disease, DM



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## Zenalpa® (medetomidine + vatinoxan HCl)

- Vatinoxan
- α-2 antagonist
  - Unable to cross BBB
    - Permits sedative effects
  - Peripheral side effects minimized
    - BP, HR
  - (-) effect on analgesia?!?



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**Zenalpha® (medetomidine + vatinoxan HCl)**

- Onset time: 5-15 minutes\*
- Duration of action: ≈ 45 minutes\*
- \*sedation
- Monitor during sedation: HR, BP, RR, T<sup>o</sup> (and record!)
  - Tachycardia may be seen during recovery
- Flow by O<sub>2</sub>
- Side effects: pronounced cardiovascular effects (alpha-2 agonist)
  - Hypertension, reflex bradycardia
  - Less severe than with traditional α-2s

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**Zenalpha® (medetomidine + vatinoxan HCl)**

- Manufacturer recommends to AVOID in patients with:
  - Cardiac disease
  - Respiratory disorders
  - Shock
  - Hypoglycemia
  - Heat or cold stress, fatigue
  - Preexisting hypotension, hypoxemia, bradycardia
- Adverse effects:
  - Diarrhea, muscle tremors



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**Zenalpha® (medetomidine + vatinoxan HCl)**

IM dose volume based on body weight:

Dog body weight		Dose volume
lbs	kg	mL
4.4 to 7	2 to 3	0.3
7.1 to 9	3.1 to 4	0.4
9.1 to 11	4.1 to 5	0.6
11.1 to 22	5.1 to 10	0.8
22.1 to 29	10.1 to 13	1.0
29.1 to 33	13.1 to 15	1.2
33.1 to 44	15.1 to 20	1.4
44.1 to 55	20.1 to 25	1.6
55.1 to 66	25.1 to 30	1.8
66.1 to 72	30.1 to 33	2.0
73.1 to 81	33.1 to 37	2.2
81.1 to 99	37.1 to 45	2.4
99.1 to 110	45.1 to 50	2.6
110.1 to 121	50.1 to 55	2.8
121.1 to 132	55.1 to 60	3.0
132.1 to 143	60.1 to 65	3.2
143.1 to 154	65.1 to 70	3.4
154.1 to 176	70.1 to 80	3.6
>176	>80	3.8



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**Zenalpha® (medetomidine + vatinoxan HCl)**

Field Study:

- N = 208, 6 vet clinics, IM Zenalpha v dexmedetomidine
  - Zenalpha – shorter onset, shorter duration
    - 14 m v 18 m
    - 38 m v 90 m



Tip & Tricks for use:

- SIGNIFICANT dose-reduction from label dose PRN!
- Even more significant dose reduction when opioid co-administered!
- Use of additional reversal agents not likely needed
  - Goal = save time in your day, save clients \$

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**Zorbium™ (buprenorphine transdermal solution)**

- Company: Elanco USA
- Formulation: buprenorphine 20 mg/mL, 2 sizes:
  - 0.4 mL: 2.6-6.6# (1.3-3 kg)
  - 1 mL: > 6.6-16.5# (> 3-7.5 kg)
  - Solvent, permeation enhancer, buprenorphine
- Label use: transdermal application onto cervical area
- Indication: post-operative analgesia in cats
- Onset time: apply 1-2h prior to surgery
- Duration of action: up to 4 days
- Recommended use: management of post-operative pain in cats



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**Zorbium™ (buprenorphine transdermal solution)**

- Pharmacology of buprenorphine
  - PARTIAL  $\mu$  ( $\mu$ ) agonist
  - Effective for mild to moderate pain in cats
  - Duration of action: 6-8h, onset =30 m
  - Dose range: 10-30 mcg/kg (0.01 - 0.03 mg/kg)
  - Route(s) of administration: IV > IM > PO > SQ
    - \*Stegall et al., *Pharmacokinetic and pharmacodynamic modelling of intravenous, intramuscular and subcutaneous buprenorphine in conscious cats.* *Vet Anaesth Analg.* 2013 Jan;40(1):83-95.
  - Naloxone may be inadequate for reversal!
- Other formulations
  - Injectable 0.3 mg/mL
  - Simbadol

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**Zorbium™ (buprenorphine transdermal solution)**

FIELD STUDY



- N = 222 (113 tx, 109 control)
- Multi-center, randomized, blinded study
- Cats, age 4 mo-5y, 1.1-5.7 kg, elective surgical sterilization + thoracic limb orchiectomy
- Monitor regularly during anesthesia, continue to monitor temperature post-operatively
- Common adverse effects (1<sup>st</sup> 96h)<sup>2</sup> see insert for full details
  - During anesthesia: † hypoxemia (SpO<sub>2</sub> < 90%), bradycardia, hypotension
  - Post-operative: † hyperthermia (day 0-4), sedation (day 1)

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**Zorbium™ (buprenorphine transdermal solution)**

- Side effects (most common):
  - Hyperthermia
  - Sedation (< 1h)
  - Dysphoria (< 3h)
  - Mydriasis, euphoria 10-12h
- Manufacturer recommends to AVOID in patients with:
  - Debilitation, renal, hepatic, cardiac, or respiratory disease
  - Pregnant/lactating, < 4 months old, outside of weight ranges
  - Opioid hypersensitivity, intolerance to vehicle; abN skin at application site



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**Zorbium™ (buprenorphine transdermal solution)**

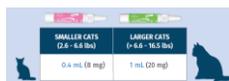
A note on hot cats... (aka FELINE DRUG-RELATED HYPERTHERMIA)

- Multi-factorial, moderate, self-limiting hyperthermia (106F, 5h)
  - Hydromorphone, morphine, butorphanol, buprenorphine, ketamine
  - Maximum temperature seems to be inversely proportional to cat temperature at extubation
  - NO morbidity resulting from the hyperthermia has been reported (Posner, 2007 & 2010)

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**Zorbium™ (buprenorphine transdermal solution)**

- Why consider Zorbium?
  - Difficult to administer oral meds to some cats
  - mild-to-moderate analgesia needs for up to 4d
- Dosage and Administration
  - PPE: gown, gloves, goggles
  - Schedule III opioid



Pounds of Body Weight	Kilograms of Body Weight	Dose of ZORBIUM
2.6 to 6.6	1.2 to 3	0.4 mL (8 mg) pink tube
>6.6 to 16.5	>3 to 7.5	1 mL (20 mg) green tube

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**Zorbium™ (buprenorphine transdermal solution)**

Tip & Tricks for use:

- Buprenorphine comfort - historically, test dose IV or IM 1<sup>st</sup>
  - i.e. Kitty magic, then Zorbium either immediately or 6h post
- Aggression seen more in repeated dosing
  - Likely compound plasma effect 4d w/o analgesia w/residual plasma levels
  - Reapply 5-6d – palliative, reassess based on individual
- Off label use for nonsurgical pain, may see more side effects
  - Prep owners! Day of application. Perhaps round down dose
  - 2 small cat doses 0.4 vs 1 mL (20 mg) - so can play with dosing

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**Synovetin [Homogeneous Tin (<sup>117m</sup>Sn) Colloid]**

- Company: Exubriion Therapeutics USA
- Formulation: Tin (<sup>117m</sup>Sn) stannic colloid in ammonium salt
- Label use: 2–4 mCi (74–148 MBq)/mL suspension for intra-articular (IA) injection
- Indication: radioisotope → long-lasting reduction of inflammation & pain associated with elbow arthritis
  - Medical radiotherapy
- Duration of action: up to one year
- Repeated treatments: ok after 12+ months



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**Synovetin [Homogeneous Tin (<sup>117m</sup>Sn) Colloid]**

- Side effects: joint soreness post-injection (up to 3d)
- Sedation: required for intra-articular injection by DVM
- Day-patient case



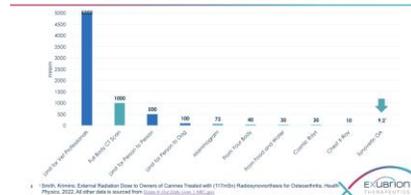
Radiation concerns MINIMAL:

- Facility requirements: federal or state license to use internal radiation-based medical therapies
- Home care: avoid co-sleeping for 2-6 weeks
- Additional note: 1 dog/household/yr

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**Synovetin [Homogeneous Tin (<sup>117m</sup>Sn) Colloid]**

Radiation limits and exposure from common sources



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**Synovetin [Homogeneous Tin (<sup>117m</sup>Sn) Colloid]**

Startup costs:

- Equipment, radiation (RAM) license, safety officer: approximately \$13k

Startup needs:

- Authorized veterinarian
- Online modules (6-8h)



Synovetin cost to vet office:

- 2 Injections = \$1,541
- Vials are NOT to be shared between patients!

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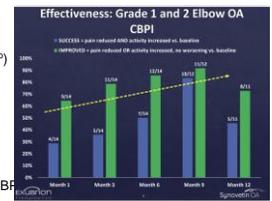
**Synovetin [Homogeneous Tin (<sup>117m</sup>Sn) Colloid]**

Pilot Study

- Grade I and II elbow OA
- N = 23
- Force plate (1°); CBPI, elbow goniometry (2°)
  - Pretx, 1, 3, 6, 9, 12 mo
- No adverse effects, improved scores

Additional study

- Grade III elbow OA
- Clinical (2)
- N = 14
- Pain assess @ baseline, then q90d for 1y CBPI
- Significant reduction in pain and lameness



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**Synovetin [Homogeneous Tin (<sup>117m</sup>Sn) Colloid]**

- Tip & Tricks for use:
- Patient selection = earlier OA is better
    - grade 1&2 elbow dysplasia
    - See chart (next slide) re: improvement and timing
    - Later tx still helpful, but need to set reasonable treatment goals and set expectations

- Questions being investigated:
- Repeated dosing
  - Joints other than elbows

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**Solensia™(frunevetmab injection)**



- Company: Zoetis USA
- Formulation: frunevetmab SQ injection
  - 7 mg / mL solution, single-use 4 mL glass vial
- Availability: EU since May 2021, now also in US – correct pkg 2023
- Label use: monoclonal antibody therapy administered control feline osteoarthritis (OA) pain
- Indication: feline OA
- Duration of action: month (q28d)

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**Solensia™(frunevetmab injection)**

- Pharmacology: binds nerve growth factor (NGF) to block effects
  - such mAbs = anti-NGF mAbs
- Field effectiveness studies
  1. N = 126, 14 US Vet Clinics, 56d
  2. N = 275, 21 US Vet Clinics, 112d
    - Outcomes: Client Specific Outcome Measures, Owner Global Assessments, Orthopedic Score

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**Solensia™(frunevetmab injection)**

- Use: feline pain osteoarthritis
- Dosage: 1 (to 2.8 mg/kg)



▪ Dosing Chart

Weight of Cat (lb.)	Weight of Cat (kg)	Volume	Number of Vials*
5.5-15.4	2.5-7 kg	1 mL	1
15.5-30.8	7.1-14 kg	2 mL	2

\*1 mL frunevetmab injection per vial

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**Solensia™(frunevetmab injection)**

- Adverse effects:
  - Immunogenicity (therapeutic protein)
  - Dermatitis or alopecia
  - GI (V&D)



- Cost: \$\$\$
- Tip & Tricks for use: ?

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Thank you!



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**NAVAS 2023 Symposium  
Program - May 6<sup>th</sup> and 7<sup>th</sup>**  
[mynavas.org](http://mynavas.org)



**Saturday: Advanced Stream**

- Management of the Difficult Airway Rachel Reed
- Fluid Therapy: Lydia Love
- CPR and Anesthesia: Veronica Salazar
- Anesthesia for Advanced Cardiac Procedures: Khurshheed Mama
- Capnography: Waveform Interpretation & Troubleshooting Abnormalities - Alyssa Ann Stair
- ECG Interpretation & Common Dysrhythmias - Tracey Lawrence

**Sunday: General Stream**

- Pain Physiology & Pathophysiology: Tami Grubb
- Regional Anesthesia for the Abdomen: Diego Portela
- Alternative Analgesic Modalities: Cornelia Mosley
- New & Updated Drugs: Odette O
- Pulse Oximetry: Claire Woolford
- Blood Pressure Monitoring & Hypotension: Bonnie Lockridge

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