The Joy of Analgesia

My favorite recipes

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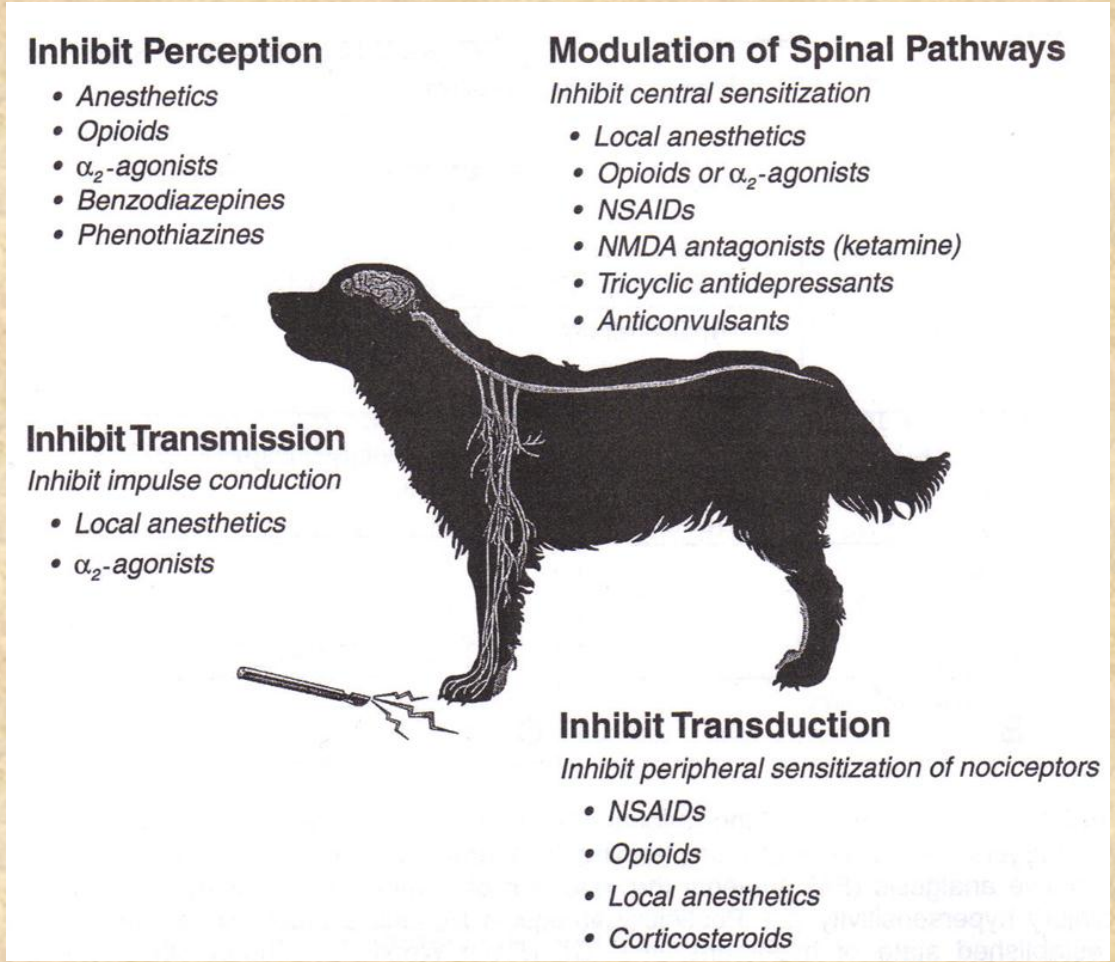
Sites of Action of Major Analgesic Classes

- Transduction
- Transmission
- Modulation
- Projection
- Perception



Lamont, VCNA, July 2000

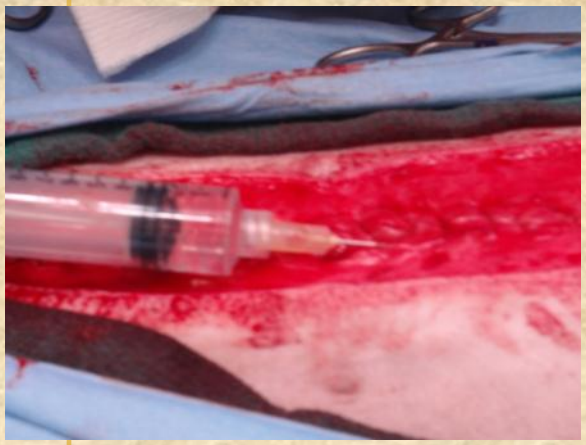
Pre-emptive Pain Scoring System

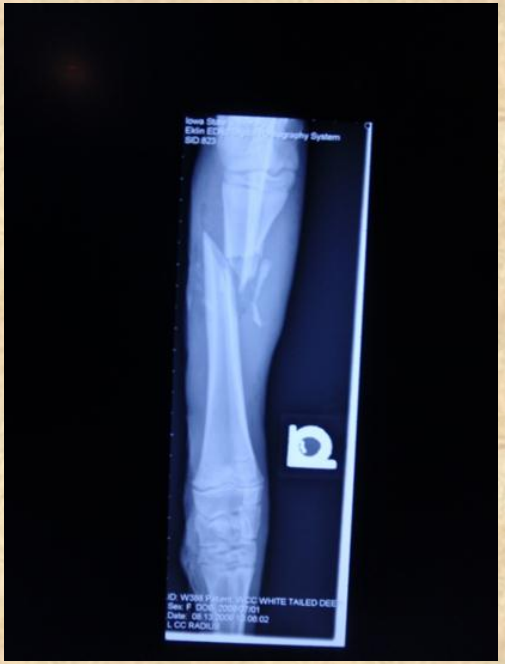
Simple Descriptive Scale

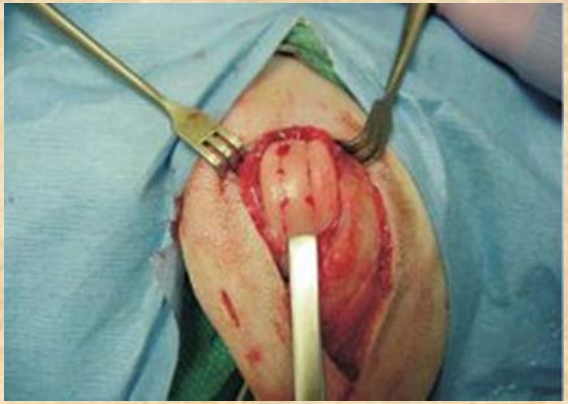
- Assign degree of pain based on the procedure performed and the amount of tissue trauma involved
  - No Pain
  - Mild pain
  - Moderate pain
  - Severe pain
- Allows preemptive/intra-op analgesia planning
- Not tailored to individual, not useful in assessing response to therapy
- Monitoring/assessment evaluate effectiveness/allow modification

Consider Types of Pain

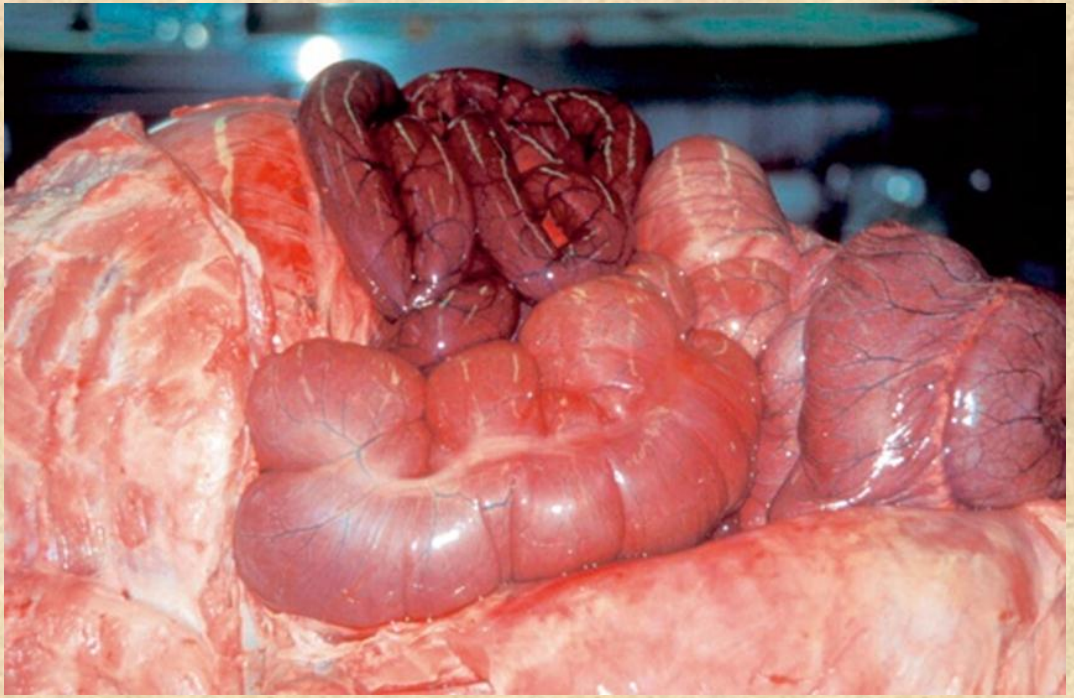
- **Somatic** – Originates from damage to bones, joints, muscle or skin; described as localized, constant, sharp



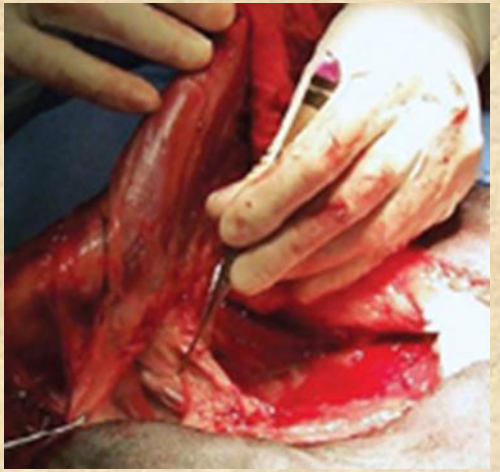


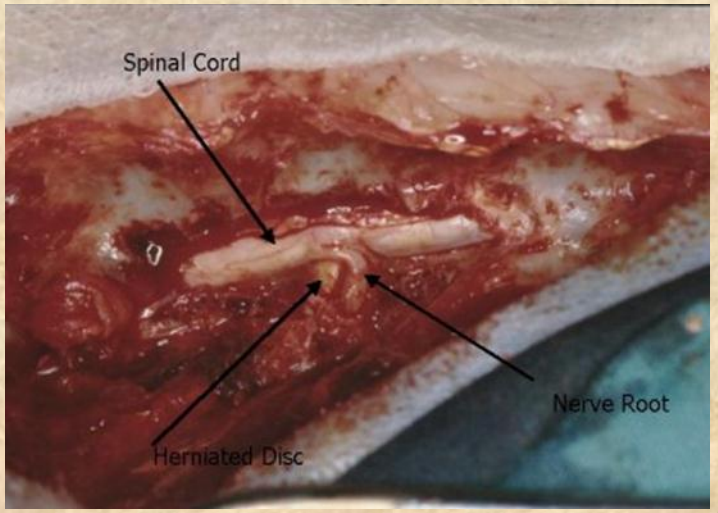


- **Visceral** – Arises from stretching, distention or inflammation of viscera; described as deep, aching, without good localization



- **Neuropathic** – Originates from injury or involvement of the PNS or CNS; described as burning or shooting; maybe associated with neurological deficits



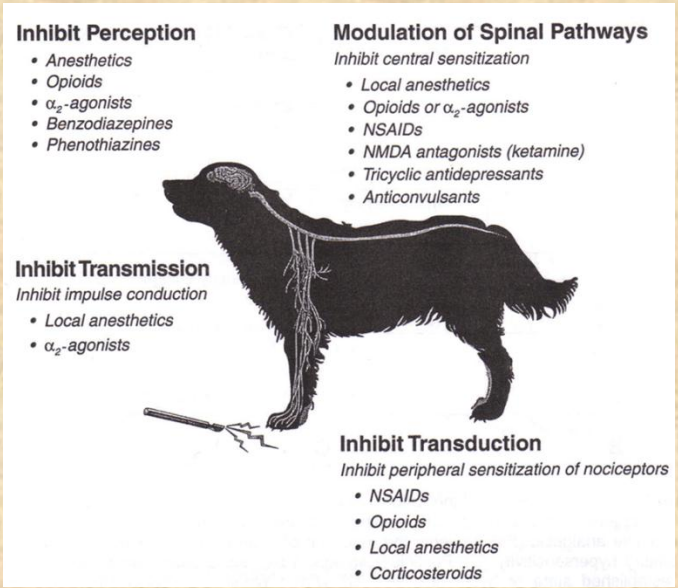


Recipes – Intra-op & Post-op

- MLK - Morphine, Lidocaine, Ketamine
- HLK- Hydromorphone, Lidocaine, Ketamine
- FLK - Fentanyl + Lidocaine, Ketamine
- Fentanyl
- Fentanyl + Ketamine
- Remifentanil
- Dexmedetomidine*
- Dexmedetomidine + MLK*

MLK – Multimodal Analgesia

- Morphine:
  - transduction, modulation, perception
    - Visceral pain, 'backbone' of most/all analgesic protocols



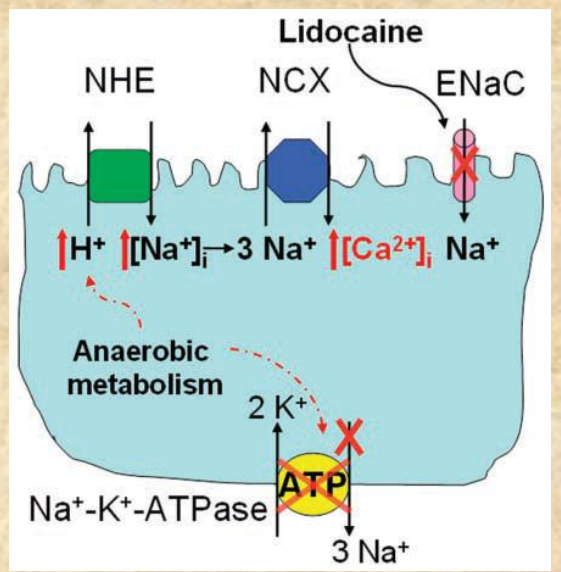
Lamont, VCNA, July 2000

MLK

- Lidocaine:
  - transduction*, transmission, modulation
    - Anti-inflammatory, central analgesic properties with CRI
    - 'Prokinetic' agent in horses due to anti-inflammatory properties (↓ TNF)
    - Neuroprotection (?)

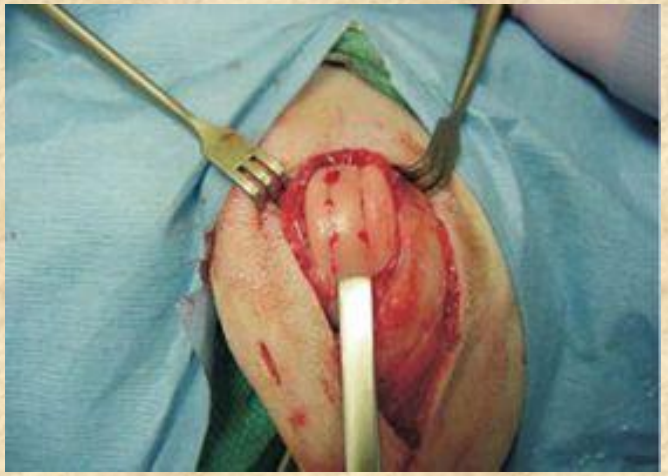
Lidocaine

- 50ug/kg/min ↓ MAC ISO & Sevo ~20%
  - Valverde et al. VAA 2004
  - Wilson et al. VAA 2008
- ↓cardiac/cerebral ischemia-reperfusion injury by preventing intracellular Na+ overload and through its anti-inflammatory properties
  - Cook & Blikslager, JAVMA 2008



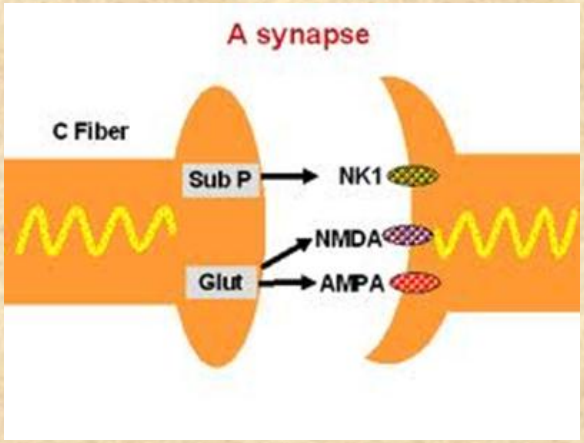
MLK

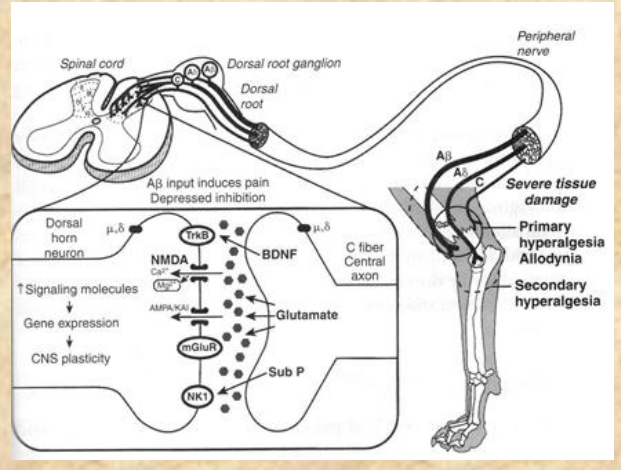
- Ketamine:
  - Modulation of spinal pathways
    - Somatic Pain => bones, joints, ligaments, skin
    - 10ug/kg/min ↓ MAC ISO ~ 10%



Ketamine – Central Sensitization

- Frequent/severe activation of Aδ and C nociceptors => excitatory neurotransmittors (glutamate, Substance P) => activates NMDA, NK, AMPA receptors => ↑ signal molecules, gene expression, neuroplasticity
- Aβ mechanoreceptors activated so that nonpainful stimuli contribute to pain response - 2^{o} hyperalgesia

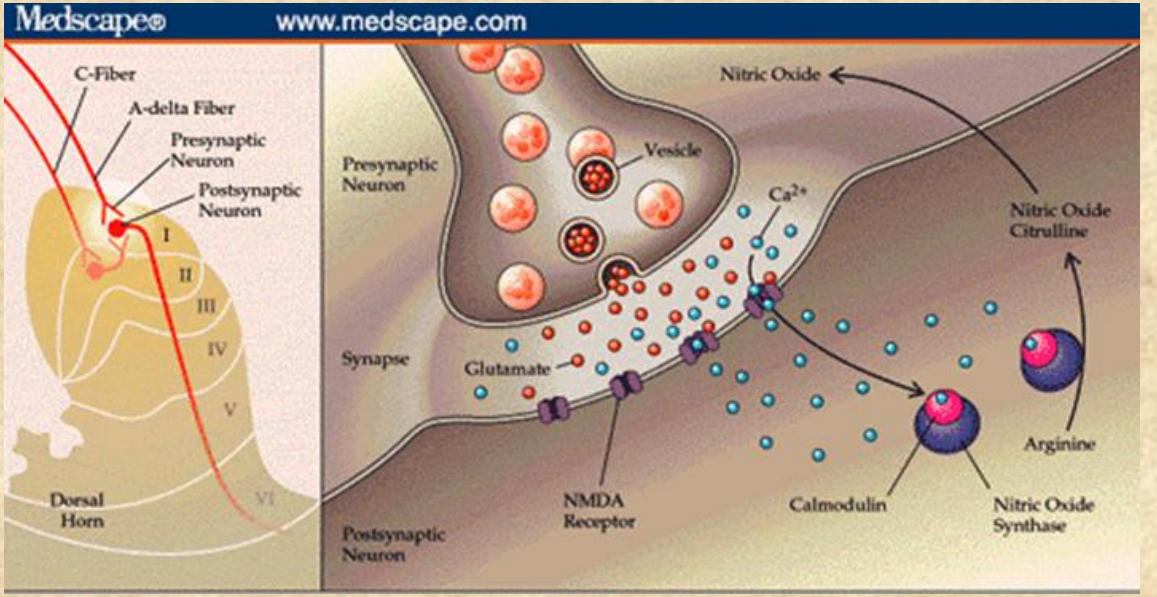




Gaynor & Muir, 2009

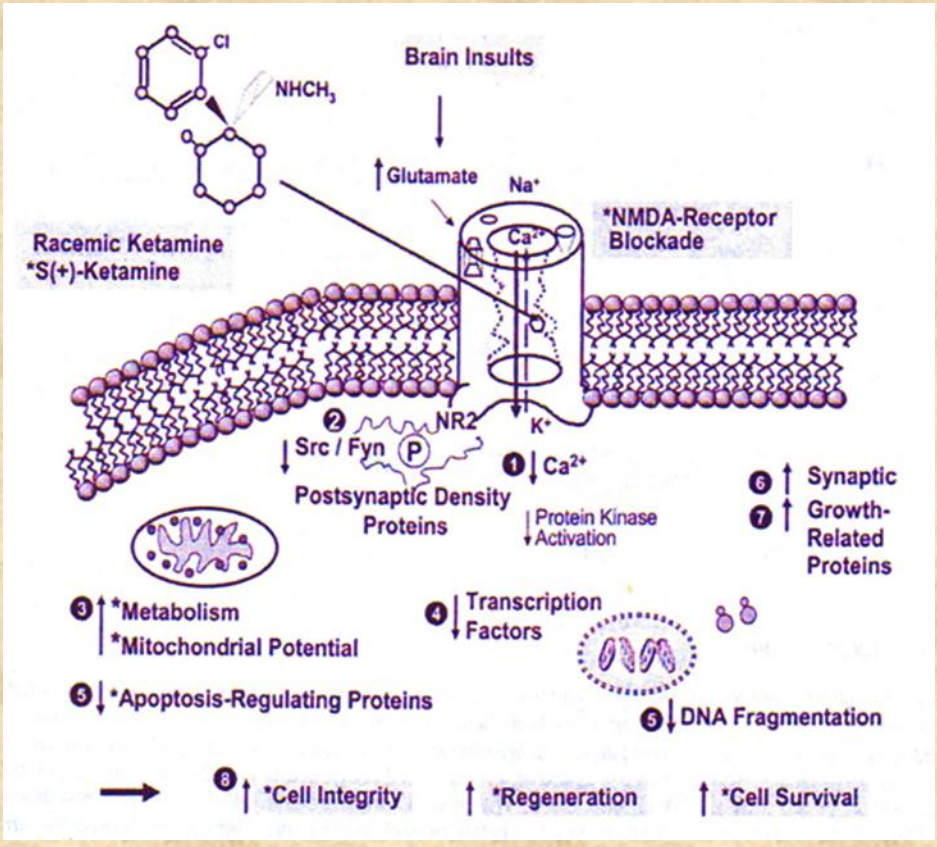
Ketamine – Central Sensitization

- Blocking NMDA receptors ↓ central sensitization, wind-up, 2^{o} hyperalgesia, chronic pain



Ketamine - Neuroprotection

- via NMDA blockade
- ↓Ca influx =>
  - ↑Cell integrity
  - ↑Cell survival
  - ↑Regeneration



MLK

Morphine, Lidocaine, Ketamine (MLK) – ISU modification of original recipe by W. Muir
Add to 500ml bag of crystalloid fluids:

Drug (conc.)	Volume to add (mg)	Infusion dose 1st hour	2nd hour & after
Morphine (10mg/ml)	3.0mls (30mg)	.3 mg/kg/hr	.15mg/kg/hr
Lidocaine (20mg/ml)	15 mls (300mg)	50 ug/kg/min	25ug/kg/hr
Ketamine (100mg/ml)	1.2 mls (120mg)	20 ug/kg/min	10ug/kg/hr

Infuse @ 5mls/kg/hour for the first hour then reduce to 2.5mls/kg/hr *

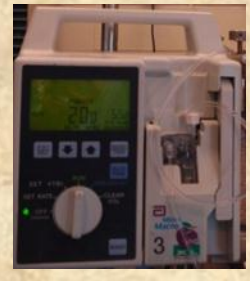
DO NOT BOLUS!!!

Intra-operative IV Fluid Rate

- Historically, 5-10 ml/kg/hr recommended
- Recent study indicates: @ 10mls/kg/hr for 4hrs
  - Median urine output only 0.46 mg/kg/hr
  - Total body fluid retention 1 -2 liters in 30kg dog/4hrs
  - Gain in body wt 1.1 +/- .6 kg
  - PCV ↓ to 29-33, TP ↓ 4.5 – 5.1
  - 30-45min after crystalloid, 30% in vascular space, 70% excreted by kidney or into ECF (fluid retention)
    - Boscan et al. AJVR 2010
  - ISU intra-op fluids 5ml/kg/hr for first hour, 2.5ml/kg/hr thereafter

MLK

- Decreases MAC of ISO by 45%
  - many patients <1% ISO
- Recommend:
  - monitoring EtCO2
  - IPPV available



- Supplemental opioid if ↑ pain or long procedure (Fentanyl advantage)
  - 0.75mg/kg over first 4 hrs
- Fluid pump recommended, but NOT necessary

HLK

- "HLK" Substitute Hydromorphone 10mg/ml
  - 0.2ml (2mg)
  - Gives infusion dose of 0.02mg/kg/hr =>
    - total dose of 0.02mg/kg for 1st hour, 0.01mg/kg/hr thereafter
    - 0.05mg/kg over 4 hrs

- Clinical impression:less sedation, more vocalization/dysphoria at recovery

Loading Doses?

- Loading doses can be administered prior to CRI in order to more quickly achieve adequate plasma levels:
  - Premedication
    - Hydromorphone (0.1mg/kg)or Morphine (1.0mg/kg) IM

  - Induction adjunct
    - Lidocaine 2mg/kg IV over 2 minutes
  - Induction
    - Ketamine 4mg/kg + Midazolam .2mg/kg IV
    - Propofol 4mg/kg => .5mg/kg Ketamine IV

Post-op MLK

POST-OP MLK: add to 500ml bag of crystalloid fluid

Drug (conc.)	Volume to add (mg)	Infusion dose
Morphine (10mg/ml)	12.5 mls (125mg)	.25 mg/kg/hr
Lidocaine (20mg/ml)	37.5 mls (750mg)	25 ug/kg/min
Ketamine (100mg/ml)	.6 mls (60mg)	2 ug/kg/min

Infuse @ 1 ml/kg/hr

Fentanyl – Intra-op

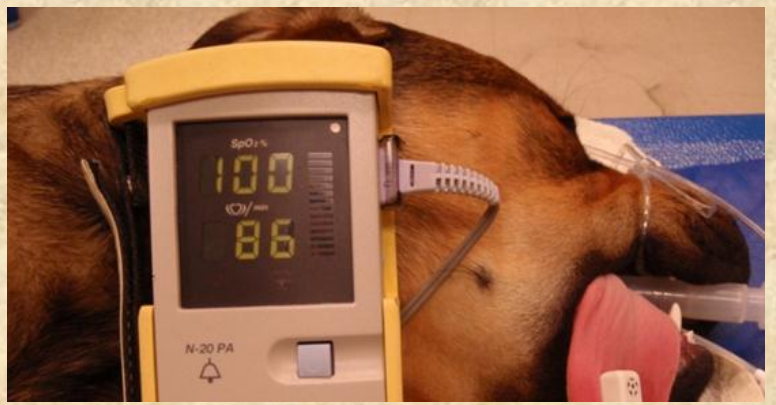
- .3 - .7ug/kg/min
  - Dogs & cats
  - Bradycardia
    - Glycopyrrolate, Atropine if also hypotensive
  - Monitor EtCO2, IPPV
  - 'one' dimensional analgesia

Calculate:

__ug/kg/min x __kg x 60min/hr ÷ 50ug/ml = __ml/hr

Fentanyl CRI & Recovery

- Wean from IPPV
- 10 minutes O2
- Continue to monitor EtCO2
- Flow-by O2 available

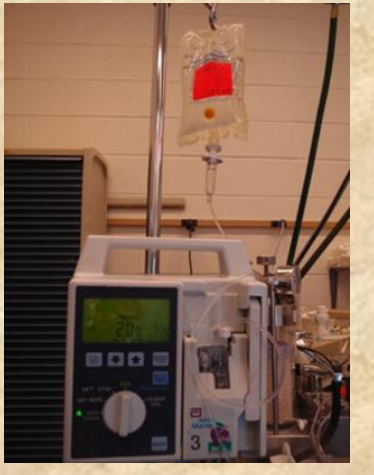


Fentanyl & Recovery

- Monitor SpO2 @ post-discontinuing O2
- Partial reversal if prolonged O2 dependence
  - .1ml (1mg) Butorphanol + .9ml NaCl
    - Give in .2ml (.2mg) increments

F + LK - Dogs

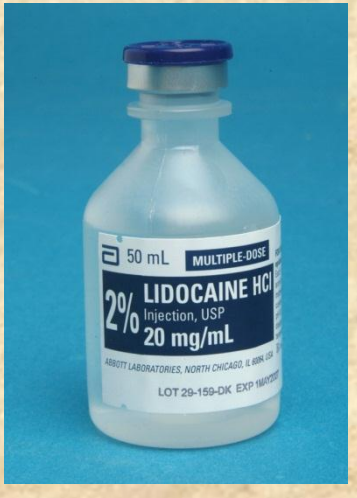
- More control/titration of opioid dosage
- Retain multi-modal, neuroprotective and/or anti-inflammatory effects of L and K.
- Use Fentanyl in syringe pump, add LK to IV fluids



FLK - Dogs

- Fentanyl
  - .3-.7ug/kg/min
  - Adjust independent of LK
  - Syringe pump

- Lidocaine/Ketamine
  - 500ml bag LRS
  - Lidocaine 15ml (300mg)
  - Ketamine 1.2ml (120mg)
  - Run @ 5ml/kg/hr 1st hr
  - Run @ 2.5mg/kg/hr thereafter



FK – Fentanyl/Ketamine - Cats

- Fentanyl .3 or .6 ug/kg/min
- Ketamine 10 or 20 ug/kg/min
  - (0.6 – 1.2mg/kg/hr)
- Somatic/neuropathic pain

FK – Fentanyl/Ketamine - Cats

- Do the math:
  - 5.0 kg cat, Fentanyl 0.3ug/kg/min, Ketamine 0.6mg/kg/hr, 3 hr sx => can double mls/hr

Fentanyl: .3ug/kg/min x 5kg = 1.5ug/min x 60min/hr = 90ug/hr ÷ 50ug/ml = 1.8mls/hr

Ketamine: .6mg/kg/hr x 5kg = 3mg/hr ÷100mg/ml = 0.03ml/hr

Set syringe pump for 1.8mls + .03mls = 1.83mls/hr

Multiply both volumes by the # of hours:

Fentanyl: 1.8mls x 3hours = 5.4mls
Ketamine: .03ml x 3hours = .09mls
Total in syringe 5.49 mls

Fentanyl – Post-op

- Fentanyl
  - 1- 10 ug/kg/hr, typical range 2 – 6 ug/kg/hr
  - Dogs & cats
    - Monitor cats for hyperthermia

Remifentanil

- Mu-receptor agonist
- Fast onset of action (~1minute)
- Metabolized by plasma esterases
  - Non-dependent on liver for metabolism
- Does not accumulate
  - Blood conc. ↓ 50% by 3-6 minutes even after prolonged infusion (6-8hrs)
- Cost: $120/2mg vial ($1.20/ml vs $.40 Fentanyl)

Remifentanil

- Side Effects => similar to Fentanyl
  - Dose dependent respiratory depression
    - IPPV available
  - Bradycardia due to ↑ vagal tone
    - Glycopyrrolate/Atropine IF hypotensive

- Dose dependent ↓MAC ISO in dogs, NOT cats
  - 0.1ug/kg/min => 1.3% ISO
  - 0.25ug/kg/min => .6% ISO

Remifentanil - Reconstitution

Preparation for Administration

To reconstitute solution, add 1 mL of diluent per mg of remifentanil. Shake well to dissolve. When reconstituted as directed, the solution contains approximately 1 mg of remifentanil activity per 1 mL. **ULTIVA should be diluted to a recommended final concentration of 20, 25, 50, or 250 mcg/mL prior to administration (see Table 14). ULTIVA should not be administered without dilution.**

Table 14: Reconstitution and Dilution of ULTIVA

Final Concentration	Amount of ULTIVA in Each Vial	Final Volume After Reconstitution and Dilution
20 mcg/mL	1 mg	50 mL
	2 mg	100 mL
	5 mg	250 mL

Can be diluted with:
Sterile water, 5% Dextrose, LRS,
0.9% NaCl, 0.45% NaCl

Does NOT contain antimicrobial preservatives
Care must be taken to assure sterility

Remifentanil Dose

- Induction
  - Humans: high incidence of apnea, muscle rigidity, tachycardia
  - Dogs 3ug/kg IV (Anagnostou JAAHA 2011)

Remifentanil Dose – Intra-op

- 5 dogs with Liver disease
  - .3ug/kg/min
  - Et_{iso} 0.6 - 1.5% , MAP > 60
  - $EtCO_2$ 45 – 52mmHg (w/o IPPV)
    - Anagnostou et al. JAAHA 2011

- Case Report: PDA correction
  - 0.2 – 0.6 ug/kg/min TCI with Propofol, IPPV
    - Musk et al. VAA 2007

Table 1 Mean cardiovascular variables and end-tidal isoflurane concentrations during 120 minutes of isoflurane anaesthesia for dogs undergoing orthopaedic surgery

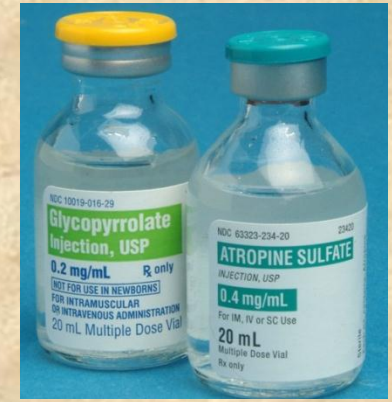
	Control group (C)	Low-dose remifentanil group (L)	High-dose remifentanil group (H)	*p*-value	*Post-hoc* test
Heart rate (beats minute^{-1})	92 ± 14	72 ± 16	78 ± 18	0.003	
Mean arterial blood pressure (mmHg)	75 ± 9	81 ± 11	84 ± 9	0.071	
End-tidal isoflurane (ɛ′ISO%)	1.28 ± 0.13	0.78 ± 0.17	0.65 ± 0.16	<0.001	C *versus* L ($p < 0.001$) C *versus* H ($p < 0.001$) L *versus* H ($p = 0.44$)

Low dose 0.1ug/kg/min
High dose 0.25ug/kg/min
Most frequent side effect => bradycardia => txt Glycopyrrolate
All dog IPPV

Allweiler et al. VAA 2007

Remifentanil – Intra-op

- 0.1 – 0.3 ug/kg/min up to 0.6 ug/kg/min
- Monitor HR
  - Treat bradycardia if hypotensive => anti-cholinergic
- Monitor EtCO2
  - IPPV available if > 60 mmHg
- Potent ISO sparing in Dogs
  - Maybe not cats



Remifentanil - Recovery

- Recovery
  - Return to spontaneous ventilation very quickly
  - Complete recovery 5-10 minutes
  - Less likely:
    - Prolonged recovery/oxygen dependency
    - Need for partial reversal
  - VERY short duration of action
    - **D/C CRI after alternate post-op analgesia established

Remifentanil – Post-op??

- 0.05 ug/kg/hr – 2.0 ug/kg/hr
- Based on Intra-op dose at lower end of Fentanyl dose => PO dose also at low end of Fentanyl dose

Ketamine CRI

- Somatic Pain => Bones, joints, ligaments, skin
- Neuroprotection via NMDA blockade,
  - ↓Ca influx =>↑Cell integrity, ↑Cell survival, ↑Regeneration
- Central sensitization/wind-up, chronic pain

- Use intermittent opioid dose + Ketamine CRI

Ketamine CRI

Dose: 10ug/kg/min (.6mg/kg/hr)

Dilute:

For cats/small dogs:

0.1ml (10mg) ketamine in 3mls D5W or saline = 3.33mg/ml

For large dogs:

0.5ml (50mg) ketamine in 10mls D5W or saline = 5mg/ml

Do the Math:

5kg cat => .6mg/kg/hr x 5kg = 3mg/kg/hr ÷ 3.33mg/ml = .9mls/hr

20kg dog => .6mg/kg/hr x 20kg = 12mg/kg/hr ÷ 5mg/ml = 2.4mls/hr

Intra-op CRI - Dogs

Changes in the minimum alveolar concentration of isoflurane and some cardiopulmonary measurements during three continuous infusion rates of dexmedetomidine in dogs

Pascoe et al. VAA 2006

Loading dose: 0.5 ug/kg & 3.0 ug/kg
CRI: 0.5ug/kg/hr & 3.0 ug/kg/hr

↓ MAC ~20 & 60%
HR lower => 93 vs 52 bpm
MAP higher => 84 vs 109 mmHg with higher dose

Dexmedetomidine continuous rate infusion during isoflurane anaesthesia in canine surgical patients

Uilenreef et al. VAA 2008

PreMed: Dex 5 ug/kg => 1, 2, 3 ug/kg/hr

High incidence 2^{o} AV block @ 3ug/kg/hr
Several dogs had 'sudden arousal' after acoustic stimulation

Recommended dose: 1ug/kg/hr

ISU Dexmedetomidine Intra-op CRI

Dose: 1.25ug/kg/hr

Recipe:
.5ml (.25mg) in 1 liter crystalloid fluids
Run @ 5ml/kg/hr = 1.25ug/kg/hr

Remember to empty bladder @ end of sx
Use additional analgesics => opioids
Have post-op sedation available/ready

Post-op CRI - Dogs

- Dose: 0.5 – 2 ug/kg/hr, typical dose is 1ug/kg/hr
  - Use with along with opioid

Recipe:

1ml (.5mg) in one liter crystalloid fluids =>

run @ 1ml/kg/hr = .5ug/kg/hr

run @ 2ml/kg/hr = 1ug/kg/hr

2ml (1.0mg) in one liter crystalloid fluids =>

run @ 1ml/kg/hr = 1ug/kg/hr

run @ 2ml/kg/hr = 2ug/kg/hr

Post-op CRI Dogs

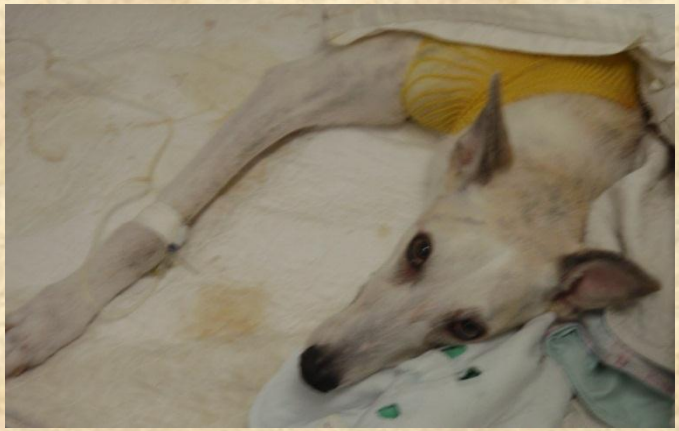
- Multi-trauma cases, high anxiety, dysphoria, aggressive

Reassess analgesic Plan:

Dexmedetomidine
2 ug/kg/hr + HLK

Post-op:
Hydromorphone 0.08mg/kg IV q 4hrs

CSUAPS: 3.5 – 4



MLK or HLK + Dexmedetomidine CRI in Dogs – Multi-trauma Cases

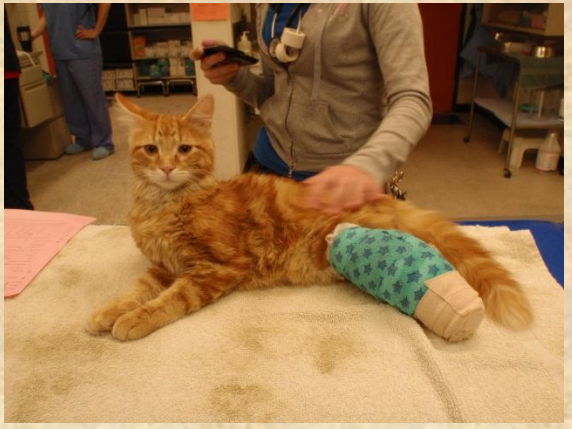
- Only after CV stable
- One-dimensional analgesia inadequate
- Stress/fear/anxiety as pain associated with all human contact => biting/aggression
- Opioid tolerance???

“Lady” 7 yr old SF Lab
Lt CCR => TPLO

- Premedication:
  - Hydromorphone 0.1mg/kg IM
  - Acepromazine 0.01mg/kg IM
- Induction adjunct
  - Lidocaine 2.0 mg/kg IV
- Induction
  - Ketamine 4.0 mg/kg IV
  - Midazolam 0.2 mg/kg IV
- Intra-op:
  - MLK
- Post-op: Hydromorphone 0.05 mg/kg IV q 4 hrs

“Arlo” – 5 mo CM Feline –
Tarsal Physeal fx

- Premedication IM:
  - Dexmedetomidine 7ug/kg
  - Butorphanol 0.2mg/kg
- Intra-op:
  - Ketamine CRI 10ug/kg/min
  - Buprenorphine 0.01mg/kg IV
- Post-op:
  - Buprenorphine 0.01mg/kg q 6 hrs
- Options if more painful:
  - Fentanyl + Ketamine

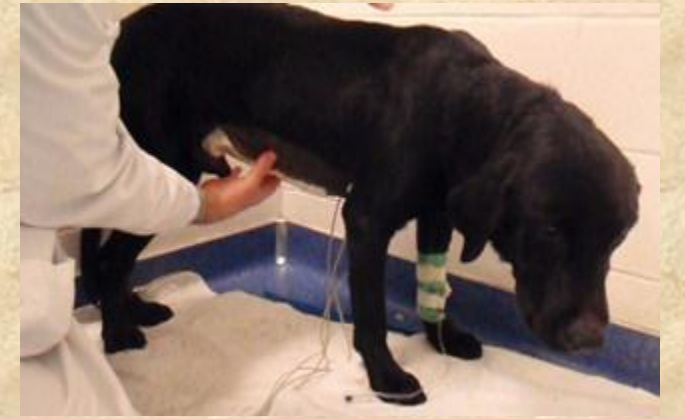


Dog Neurosurgical

- "Goldie", 5yr old SF Dshd, IVDD
- Pre-med:
  - Hydromorphone .1 mg/kg IM
- Intra-op:
  - MLK CRI
- Post-op:
  - Hydro .08mg/kg IV q 4 hrs
- Other PO options:
  - MLK, HLK, Fentanyl, FLK, Dexmed.

“Jake” 5yr CM Lab 2nd abd explore FB

- Pre-med/induction IV:
  - Fentanyl 5 – 10ug/kg
  - Midazolam 0.2mg/kg
- Intra-op:
  - Fentanyl .3-.7ug/kg/min
  - Nitrous oxide
  - LK???
- Post-op:
  - Hydromorphone .08mg/kg q 4hrs
  - CSU-APS => 3.5, reassess analgesia
  - Changed to Fentanyl CRI 4ug/kg/hr



!!Precaution!!

- Pain evaluation/assessment of analgesic plan
- Monitor level of sedation/consciousness
- Attention to bladder function/care
- Monitor HR, rhythm

Unarousable

- Assess for level of consciousness
- Best done after expected onset of action of analgesic drug(s)
- Risk of hypoventilation/hypoxemia, GER/aspiration

Treatment:

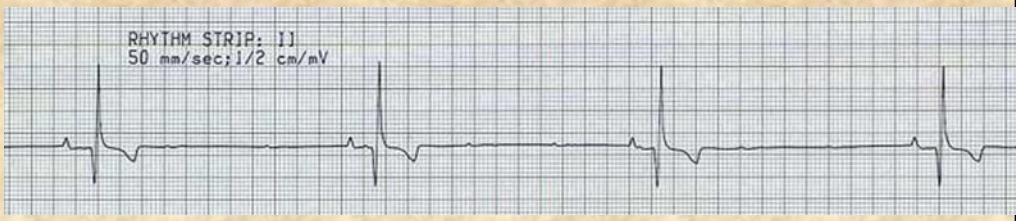
Full/partial reversal
Lower dose/increase interval

Bladder Care/Attention

- Express bladder at end of surgery
  - Dexmedetomidine ↑ urine production
  - Opioids ↓ urine production, ↑ sphincter tone
- Assess bladder size q 6 hrs
- Walk outside with assistance (sling), express, intermittent catheterization
  - ? ? Partial/full opioid reversal for enlarged bladders that cannot be expressed

Bradycardia

- Most commonly seen with
  - Fentanyl - ↑ vagal tone
  - Dexmedetomidine – reflex bradycardia
- Asssess MAP
- Treat if hypotensive:



  - Fentanyl (or other opioid) => Glycopyrrolate, Atropine
  - Dexmedetomidine => partial reversal

Take Home

- Be familiar with sites of action of drug classes
- Consider types/severity of pain
- Consider additional attributes
  - Neuroprotection, anti-inflammatory etc.
- Assess the individual
- Prepare for side effects
- Post-op monitoring: arousability, bladder, HR

Understanding and Managing Drug Shortages

Drug shortages on the rise

- 5 in 1996,↑ to 20/year by 1997 – 2000
- Human organizations devote .5 – 3 FTE to managing drug shortages
  - Investigate reason for shortage
  - Find alternative agents
  - Find alternative suppliers
  - Compound replacement product

- Manufacturers only required to provide advance notice of plans to discontinue a medication if the manufacturer is the sole producer of a medication

- Stockpiling drugs prolongs the shortage

Drug Shortages

- Human labeled drug shortage list:

  http://www.ashp.org/DrugShortages**

  http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm

  **sign up for e-mail alert service – receive info about drug shortages, get contact info for manufacturers, copies of letters sent to physicians regarding shortages.

- Veterinary labeled drug shortage list:

  http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm267669.htm

Reasons often multifactorial

- Natural disasters
- Voluntary Recall
- Raw material shortage
- Manufacturer rationing/restricted distribution
- Market shifts
  - Addition of generic product, ↓ brand name
- Unexpected demand

Reasons***

- Non-compliance with Regulatory Standards
  - Shortages can occur when the primary/ sole manufacturer of a product has its production halted by the FDA for reasons such as not adhering to Good Manufacturing Practices (GMPs).
- Industry Consolidations
  - Company mergers result in decisions to discontinue products/narrow the focus of the product line. ↓ in suppliers makes product vulnerable to shortages
- Manufacturer Discontinuation
  - A manufacturer may stop production of a drug product because of lack of financial return (generic drugs), poor demand (veterinary use) or potential safety concerns. FDA performs a medical necessity evaluation

Reasons for drug shortages

Am J Health-Syst Pharm. 2003

- Regulatory issues (7%)
- Raw materials issues (8%)
- Supply and demand problems (10%)
- Product discontinuation (20%)
- Manufacturing problems (28%)
- Unexplained (27%)

- http://www.ashp.org/DrugShortages
- Drug Shortages Resource Center
  - Current shortages
  - Resolved shortages
  - Drugs no longer available

Fentanyl Injection

Products Affected - Description

- Fentanyl Injection 50 mcg/mL, Hospira, 10 mL ampules (NDC 00409-9093-36) - *discontinued*
  Fentanyl Injection 50 mcg/mL, West-Ward (formerly Baxter products),10 mL ampule (NDC 10019-0034-73) - *discontinued*
  30 mL single-dose vial (NDC 10019-0036-82) - *discontinued*
  50 mL vial (NDC 10019-0037-83)
- 20 mL vial (NDC 10019-0037-25)

Reason for the Shortage

- West-Ward acquired Baxter's fentanyl injection products in May, 2011. The company cannot provide a reason for the shortage
- Hospira states the shortage is due to increased demand and manufacturing delays including quality improvement activities. Hospira is increasing production of the ampules to help meet the demand
- Akorn launched Sublimaze injection in late-March, 2012

Available Products

- Sublimaze Injection 50 mcg/mL, Akorn, 10 mL ampules (NDC 17478-0030-20)
  Fentanyl Injection 50 mcg/mL, Hospira, 2 mL Carpuject syringe (NDC 00409-1276-32)
  Fentanyl Injection 50 mcg/mL, West-Ward (formerly Baxter products),20 mL ampule (NDC 10019-0035-74)

Estimated Resupply Dates

- Hospira has fentanyl 50 mcg/mL 2 mL, 5 mL, 10 mL, 20 mL, and 50 mL vials on back order and the company estimates a release date of May, 2012. The 2 mL and 5 mL ampules are on intermittent back order and the company is releasing product as it becomes available.[3]
- West-Ward has most fentanyl 50 mcg/mL injections on intermittent back order and the company is releasing product as it becomes available except the 5 mL vials have an estimated release date of early-May, 2012 and the 20 mL vials do not have an estimated release date. **The 20 mL ampules are available**.

Implications for Patient Care

- Fentanyl is labeled for use in analgesia for short duration or as a narcotic supplement in general and regional analgesia. Fentanyl is also labeled for use with a neuroleptic for premedication of induction of anesthesia and as an adjunct for general anesthesia maintenance. Fentanyl is also labeled for use with oxygen as an anesthetic agent in high risk patients, including those undergoing complicated procedures.

Safety

- Remifentanil, alfentanil, fentanyl and sufentanil may sound alike/look alike. However, dosage recommendations vary significantly between the agents. Patient harm can occur if these agents are used erroneously. Use extra caution not to confuse these agents.

Alternative Agents & Management

- Alternative opiate agonists vary in onset time and duration of action, see Table 1.[5-15]
- No single agent can be substituted for fentanyl. The choice of an alternative agent must be patient-specific and based on the clinical situation, venous access, renal and hepatic function, and other comorbid conditions. Utilize stakeholder clinicians to help make specific plans for individual patient populations. Table 2 provides some alternatives to fentanyl for specific clinical situations.
- Some presentations of alternative agents including sufentanil and butorphanol are in short supply.[16]
- Drawing up individual doses in syringes may help conserve product. Ensure USP 797 requirements are met.
- Consider reserving fentanyl for high risk populations such as newborn and obstetrics.

Related Shortages

- Hydromorphone Hydrochloride Injection
- Oxycodone Immediate Release Solution — Resolved
- Oxymorphone Hydrochloride
- Sufentanil Injection

Managing Drug Shortages

- Ration what we have or use it until it's gone?
- Assess potential impact of a shortage
  - Reason for shortage, resupply dates
- Find alternatives, prioritize patients
  - Stay current with literature, CE
- Educate staff about differences between unavailable product and alternative
- Contract compounding

Contract Compounding

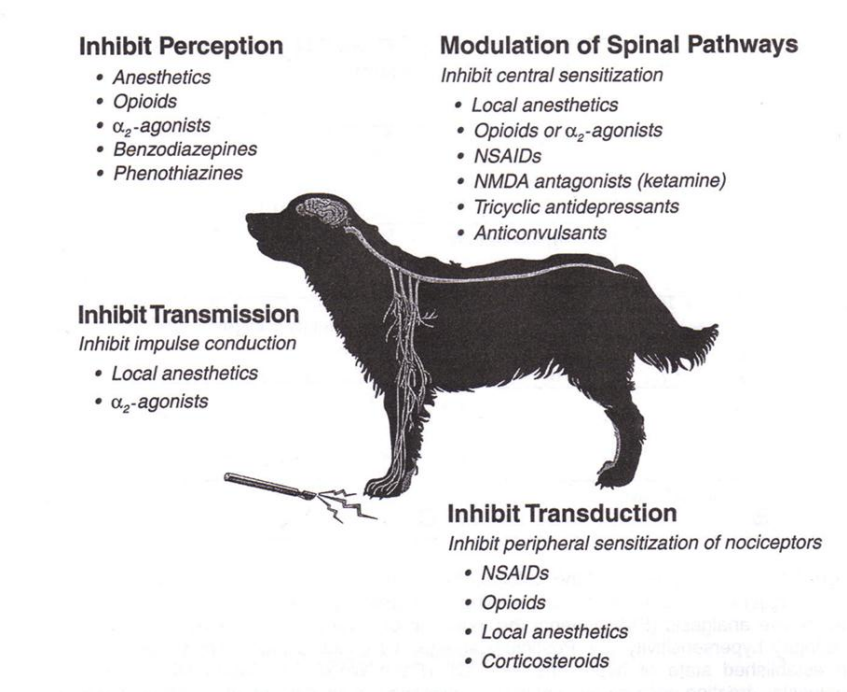
- Formulations for compounding not reviewed by FDA
  - FDA no control over quality/consistency of preparation process used
- Pharmacies registered in their state**
  - device manufacturers (FDA) or drug manufacturers (DEA)
- Compounding pharmacy MUST:
  - follow current compounding guidelines
  - have the appropriate facility and equipment
  - compounding pharmacist has the training/ability to do it

Wound Infusion Catheters

Local Anesthesia & Analgesia

Sites of Action of Local Anesthetics

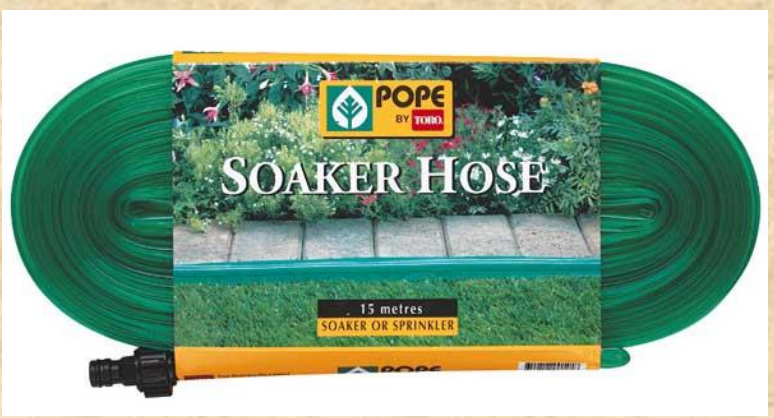
- Inhibit Transduction
- Inhibit Transmission
- Modulate Spinal Pathways
  - Central analgesic properties with CRI



Lamont 2001

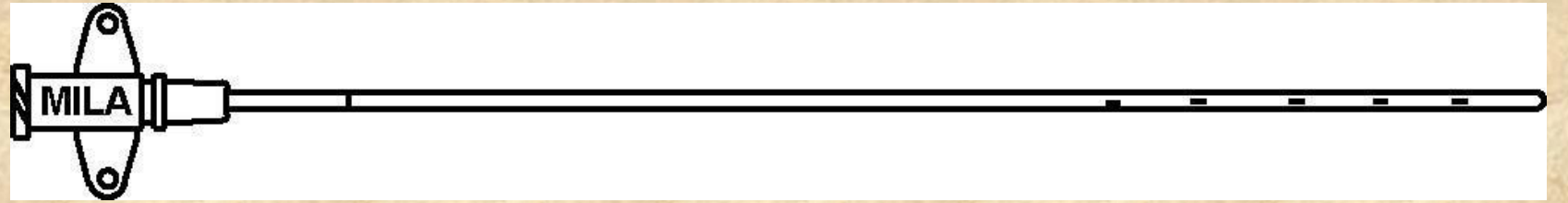
Wound Infusion Catheters

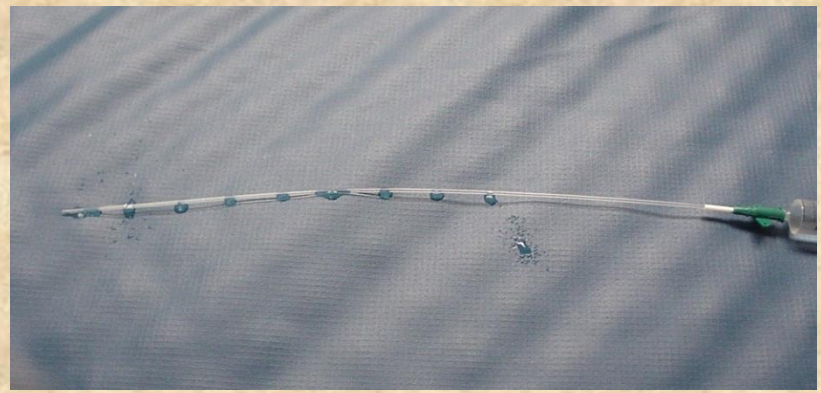
Modeled after the ‘garden’ variety

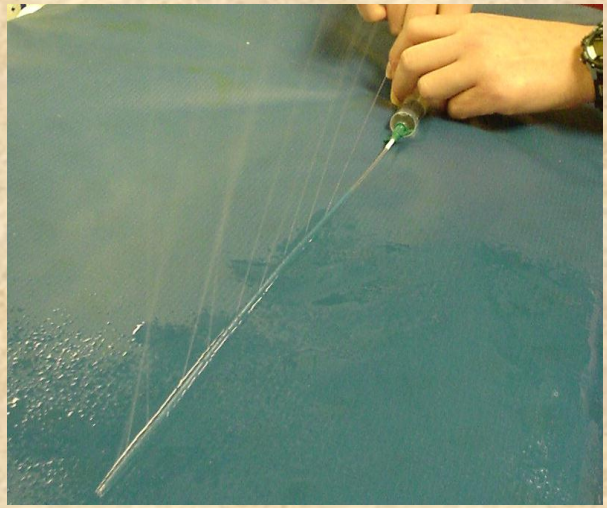


Wound Infusion Catheters/'Soakers' for People

Wound Infusion Catheters for Animals

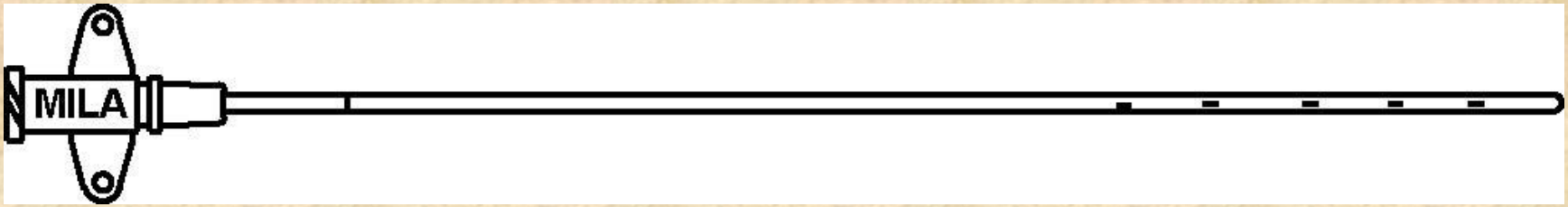






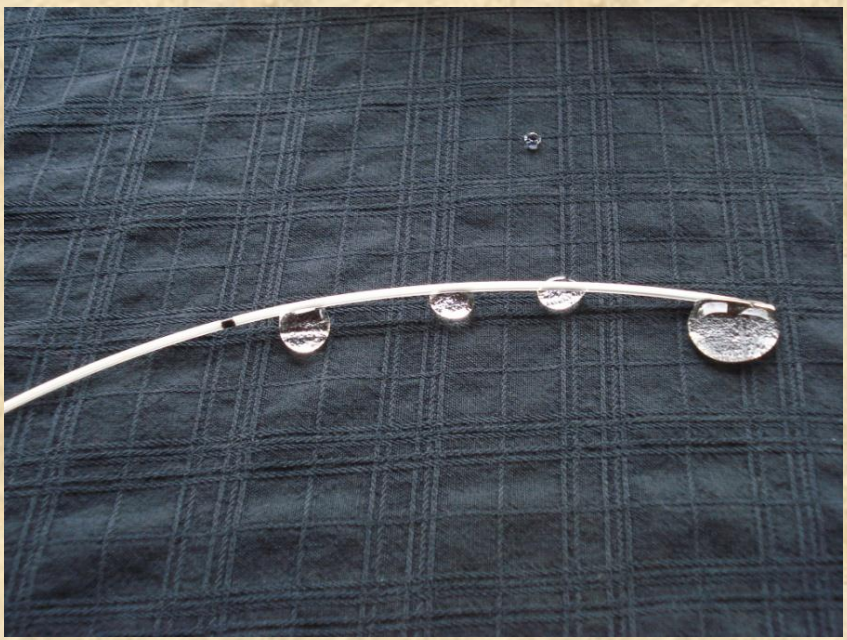
MILA INTERNATIONAL, INC.
Medical Instrumentation for Animals

www.Milainternational.com



- Distal tip of the catheter is sealed so that liquid exits only from the micropores
- Black depth indicator marks a point 1/2 inch (1.25 cm) from the first micropore
- Cost ~ $20.00 each

- Different lengths of micropores:
  - 2 inches
  - 4 inches
  - 6 inches
  - 7.5 inches
  - 9 inches



Where to use them?

- Limb Amputations
- Lateral thoracotomy
- Median sternotomy
- Hemi-pelvectomy
- Large wound
- Tumor removal
- TECA

WHY use a infusion catheter?

- Locally infused analgesia/anesthesia
- Fewer systemic drugs needed:
  - Less sedation, respiratory depression
  - Faster return of appetite
  - Less risk of aspiration/pneumonia
  - Less chance of urinary retention
  - Earlier mobilization
  - Less nursing care needs

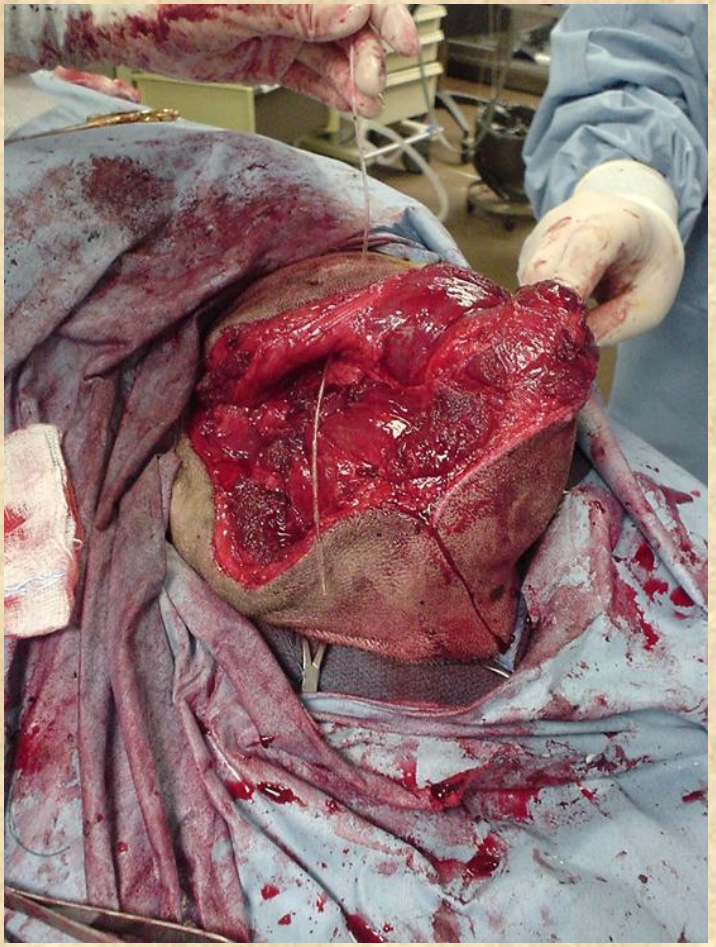
What about Cats?

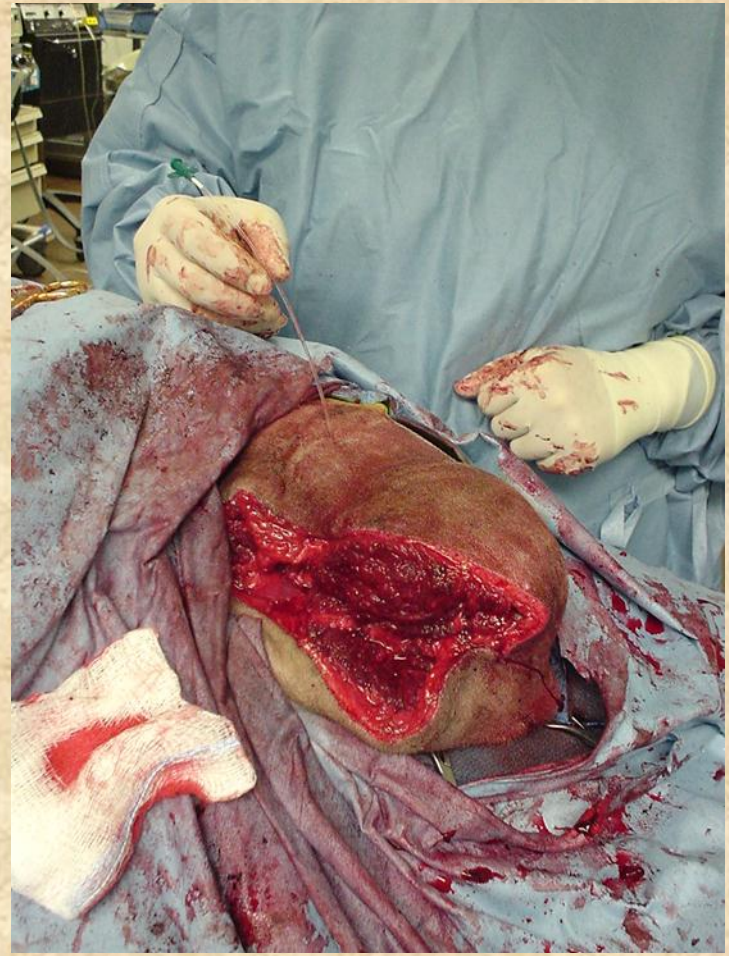
- More sensitive to toxic effects of local anesthetics
- OK to use but be careful with dosing
- Intermittent injection may be preferable to CRI

Placing the catheter

- Make a stab incision in the skin, insert the catheter tip, and pull the catheter into the wound bed.
- Insert the catheter with the distal tip in the deepest layer of the closure and then suture in place so it can't be accidentally pulled out.
- It is essential that all perforations are below the skin.

Distal tip in deepest part of wound

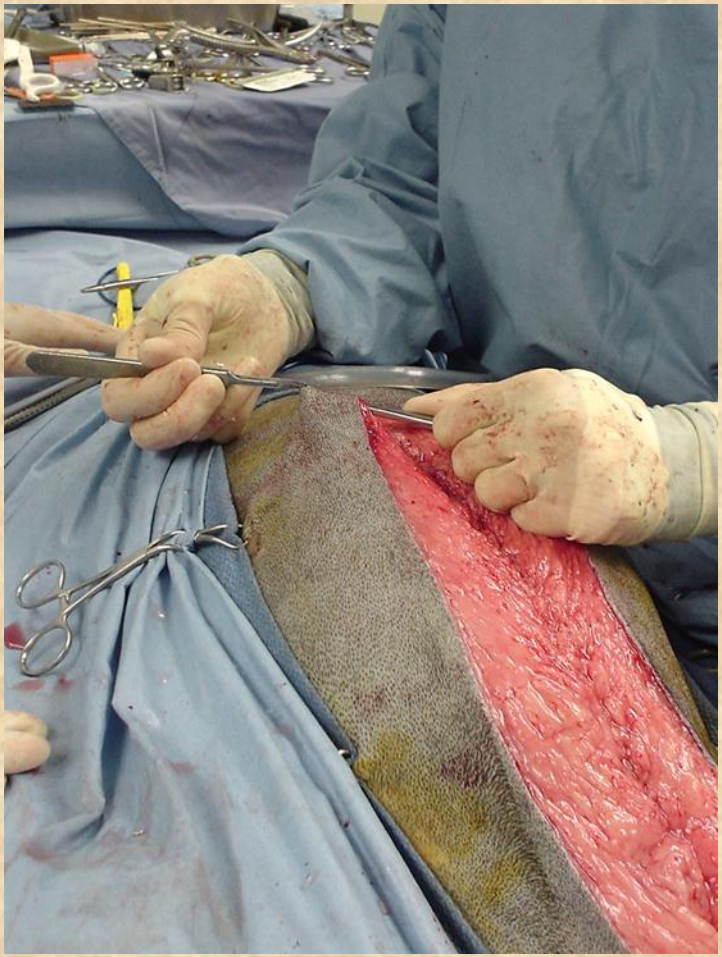


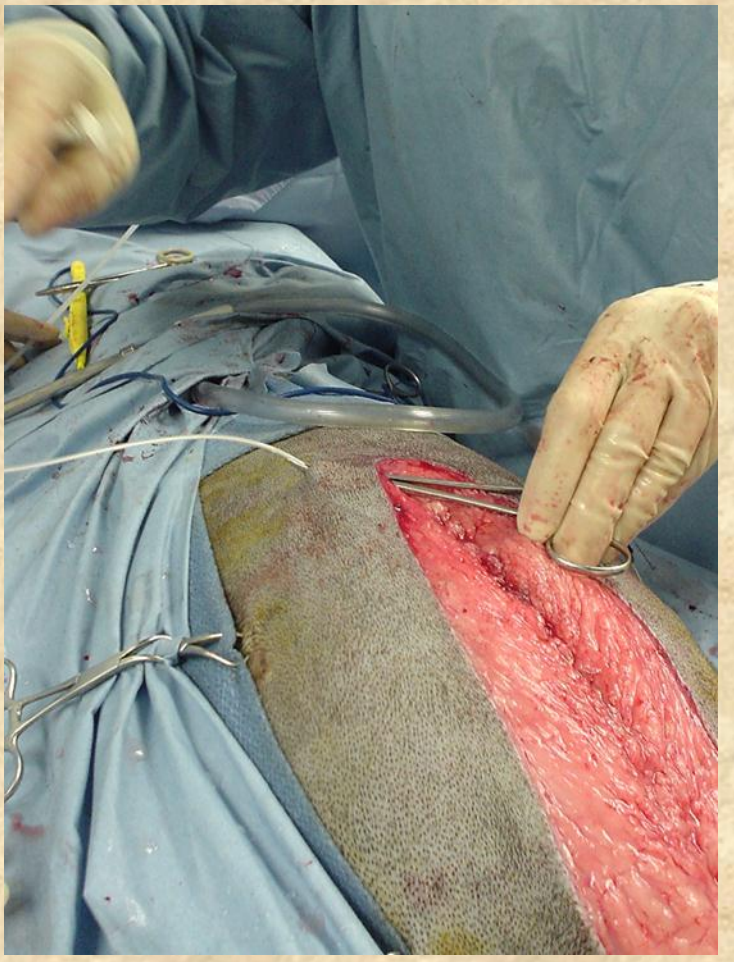


Median Sternotomy

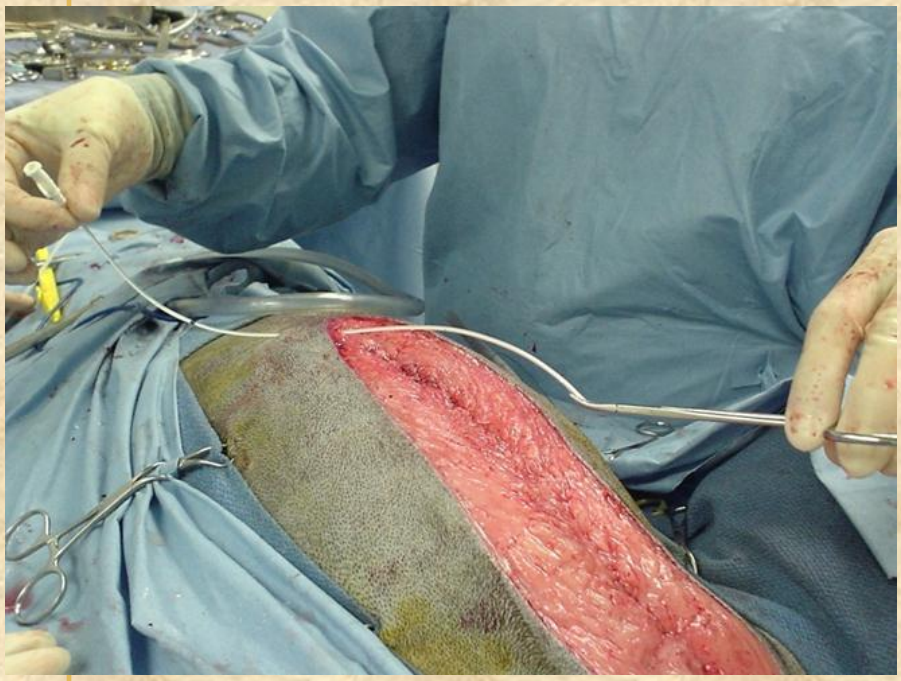
- Long painful incision
- Difficult for dog to lie sternal
- Impaired ventilation

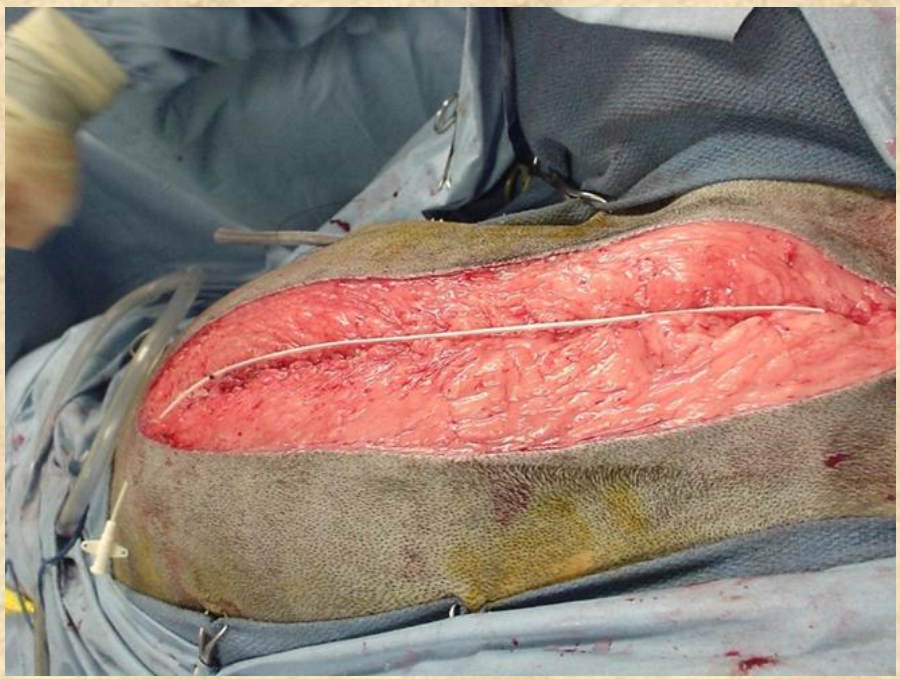
Stab incision, pull catheter thru



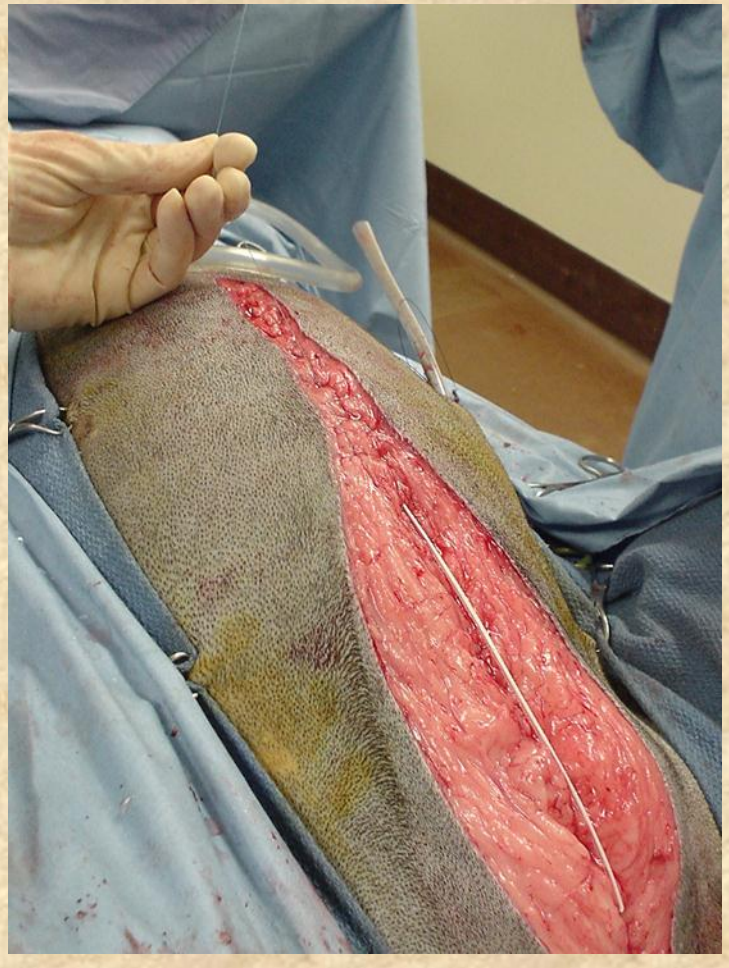


Catheter in place
All micropores below skin surface



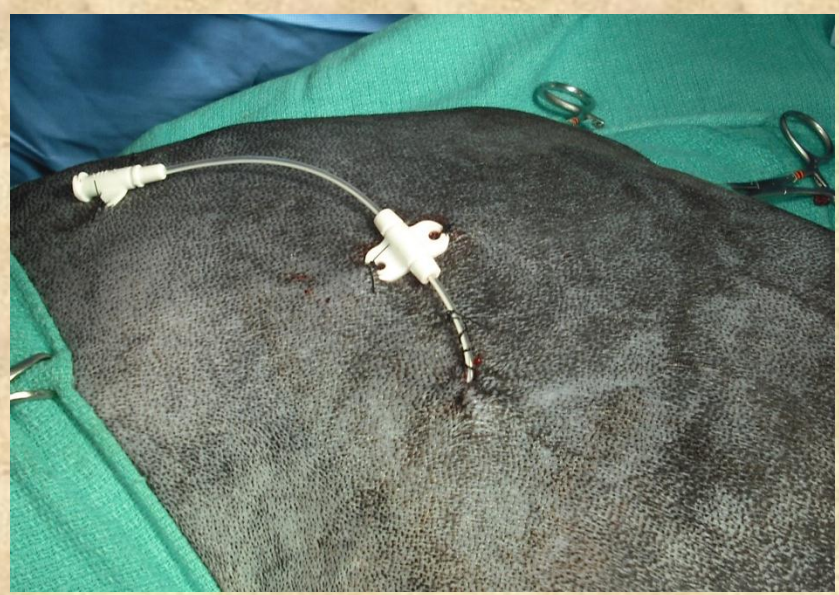


Routine Closure over catheter

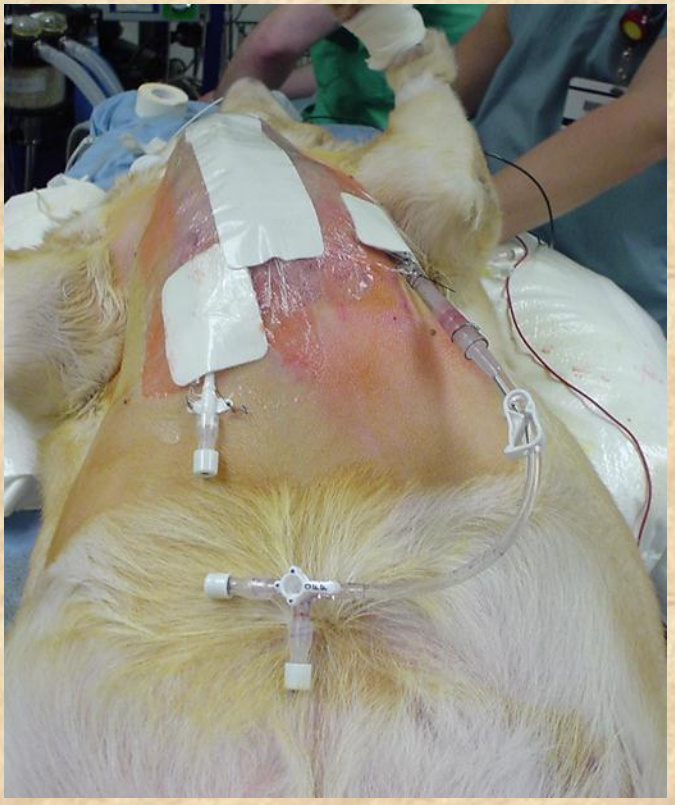


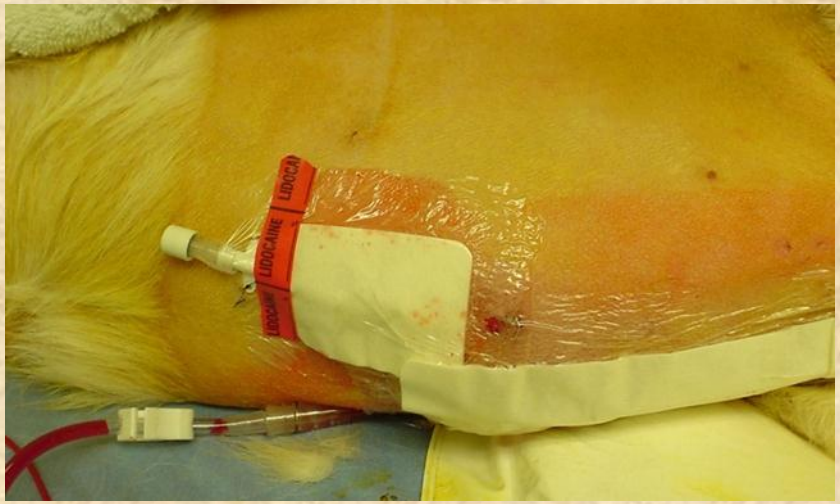
Securing catheter in place

- Place a purse string suture and Chinese finger trap to secure the catheter



Label well to avoid confusion with IV or chest tube





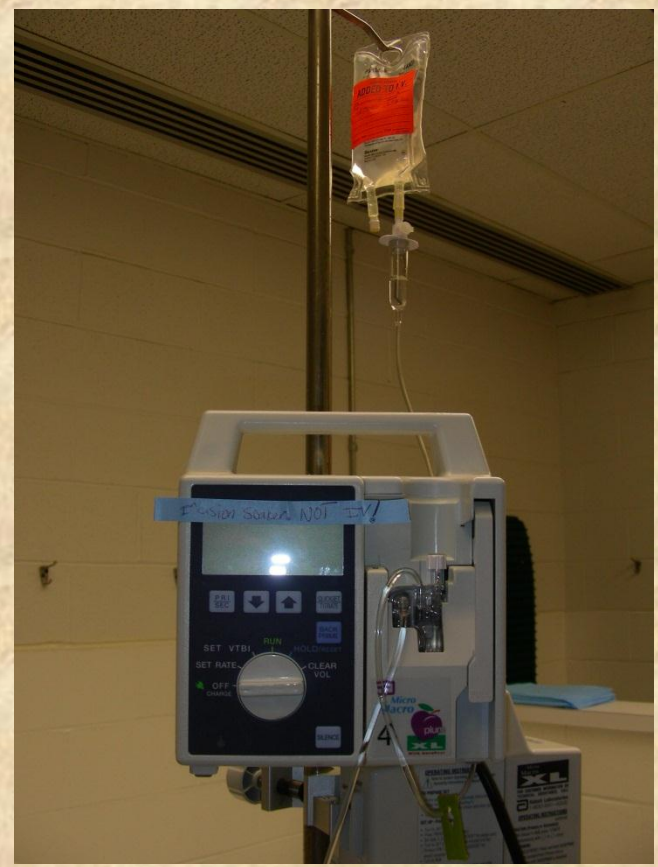
Filters?

Millex Syringe filter
by Millipore
.22 microns
~$3.00 each

Mila International
~$5.00 each
.2 Microns

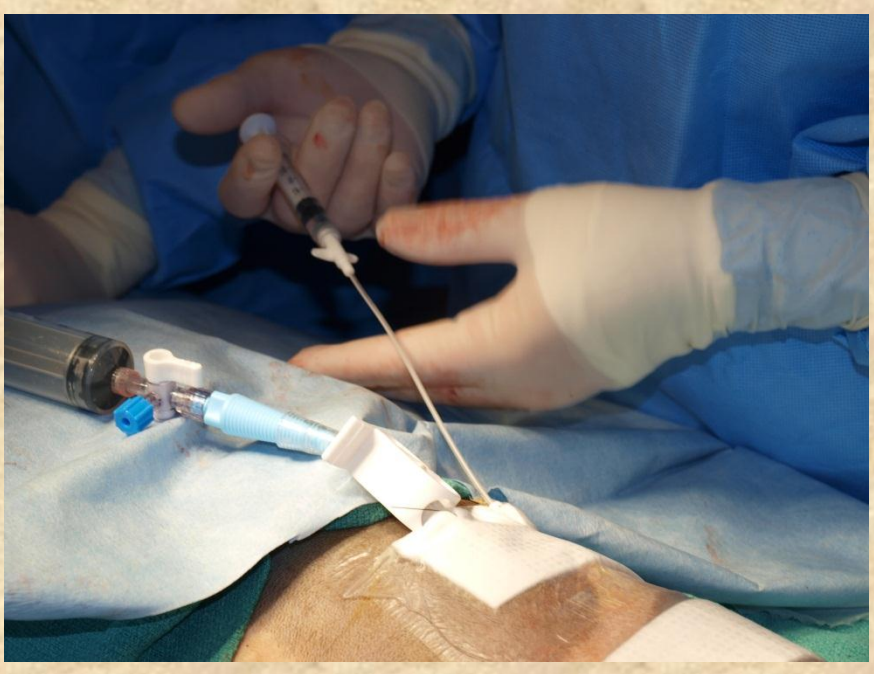
Drug Protocols
Intermittent Injection or CRI

- Intermittent injection
  - Cats & small dogs
  - Equipment & personnel
- CRI
  - Fluid pump
  - Patient observation



Intra-operative ‘loading’ of catheter

- Intermittent injection
  - Lidocaine 2mg/kg + Bupivacaine 1.5mg/kg
    - Immediate onset + long duration
- CRI
  - Lidocaine 2mg/kg



Drug Protocol(s)

- Intermittent injection:
  - Bupivacaine 1.5mg/kg q 4-6 hours
  - Bupivacaine comes in 5mg/ml & 7.5mg/ml
  - Low volume/high conc. may be more effective
- For small dogs/cats can dilute drug to make sufficient volume to reach entire tissue bed

CRI of Lidocaine

- Lidocaine 2mg/kg/hour
- First calculate dog's hourly requirement
- Then figure out if you need to dilute the drug

Flow rate = 3-5 ml/hour

Enough flow to 'bathe' tissue

Not enough to cause edema/seroma

- Five ml/hour of straight lidocaine at 2% provides 100 mg/hour
- Five ml/hour of lidocaine diluted to 1.5% provides 75 mg/hour
- Five ml/hour of lidocaine diluted to 1% provides 50 mg/hour

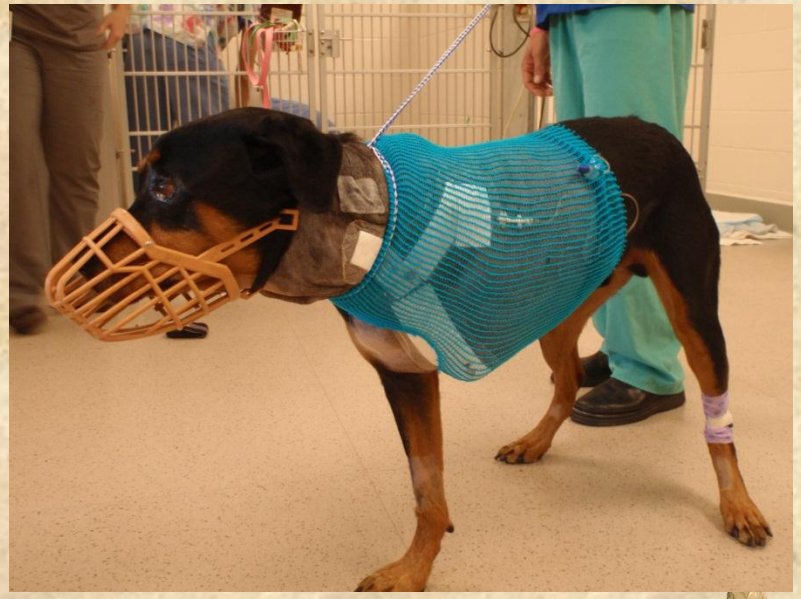
Greyhound ‘no infusion catheter’

Lt Forelimb amputation
Pre-med: Hydromorphone 0.1mg/kg
Intra-op: MLK, Lidocaine/bupivacaine block
Post-op: Hydromorphone 0.8mg/kg IV q 4hrs
CSUAPS: 3.5 – 4
Reassess analgesic Plan:
Dexmedetomidine 2ug/kg/hr + HLK

‘Kalil’ 8yr old Rottweiller
Lt Forelimb Amputation, 36kg

Post-op: Fentanyl 2 ug/kg/hr
Fentanyl Patch placed PO
WI catheter => Lidocaine CRI
5ml/hr of 15mg/ml 1.5% Lidocaine

CSU-APS 5 hrs PO = 1.5
Urinated & Ate well @8pm (5hrs PO)



D/C Fentanyl 24hrs PO
Tramadol, Deramaxx, Fentanyl patch in place

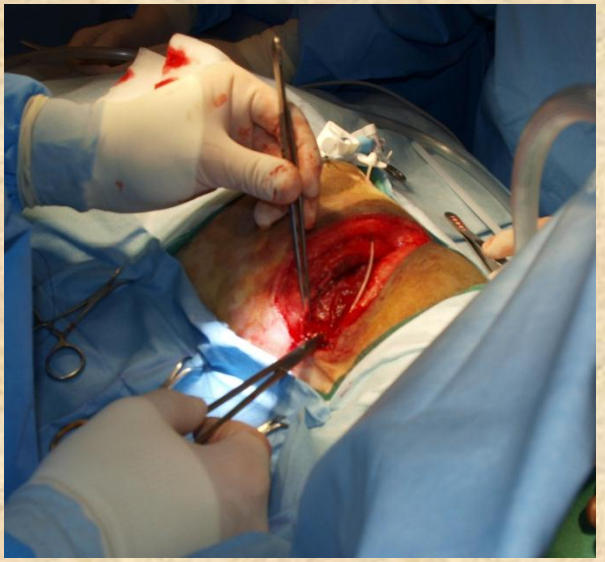
WI catheter removed 41hrs PO, infused with Bupivacaine 1.5mg/kg prior to removal

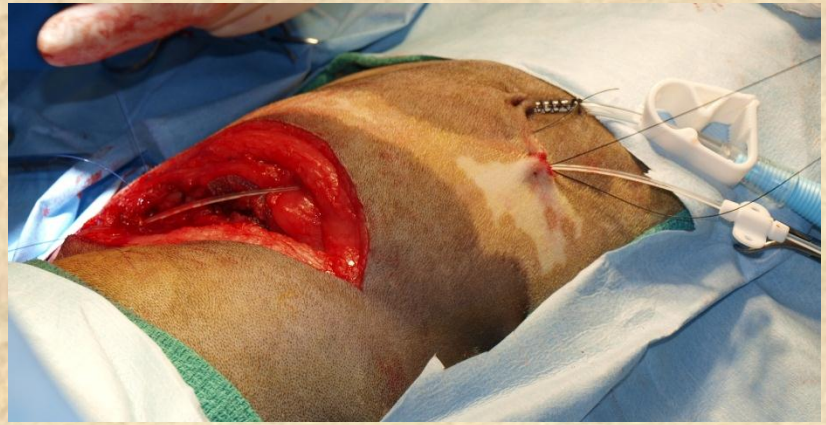
10 days PO

5 weeks PO

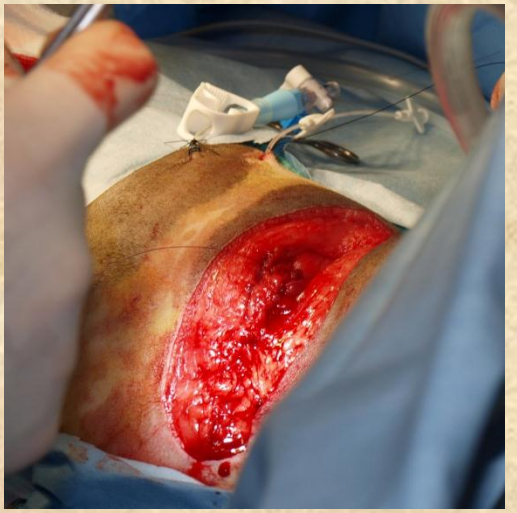
‘Sprout’ 8yr old, Chihuahua,

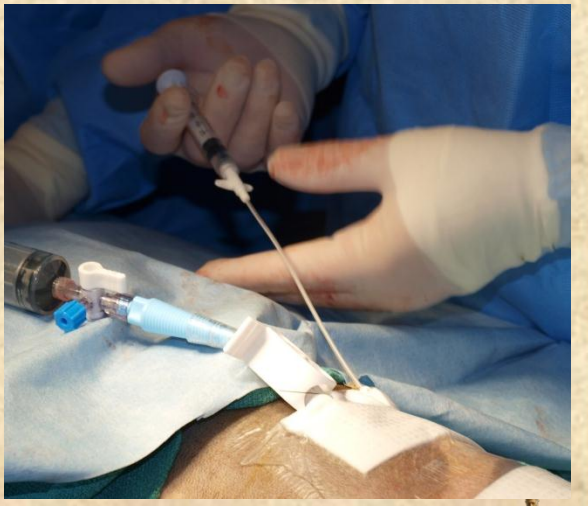
Lateral Thoracotomy for lung lobe resection





Load WI catheter with Lidocaine 2mg/kg





‘Sprout’ Lidocaine CRI in small dog

1% Lidocaine in .9%NaCl for infusion of WI catheter

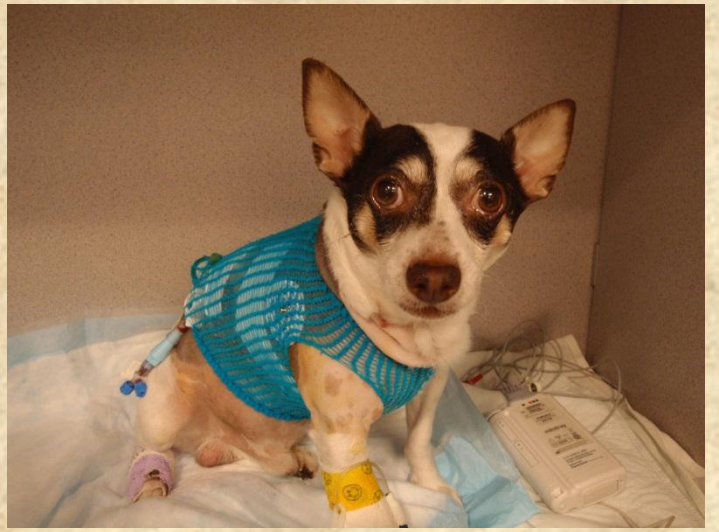
Take 100ml bag .9%NaCl, remove 50ml, add 50ml Lidocaine for 1000mg/100ml => 10mg/ml => 1%

2mg/kg x 6.5kg = 13mg/hr ÷ 10mg/ml = 1.3ml/hr

Run @ 1.5ml/hr => 15mg/hr => 2.3mg/kg/hr

100ml bag would last 66 hours

Important points: LOWER INFUSION RATE in SMALL DOGs for Lateral Thoracotomy



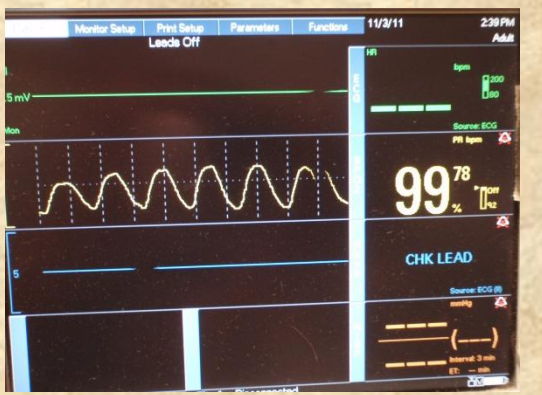
2 hours PO

Fentanyl CRI @ 2ug/kg/hr

CSUAPS: .5 – 1

SpO2 99%, HR 78 bpm

sitting sternal, ambulating

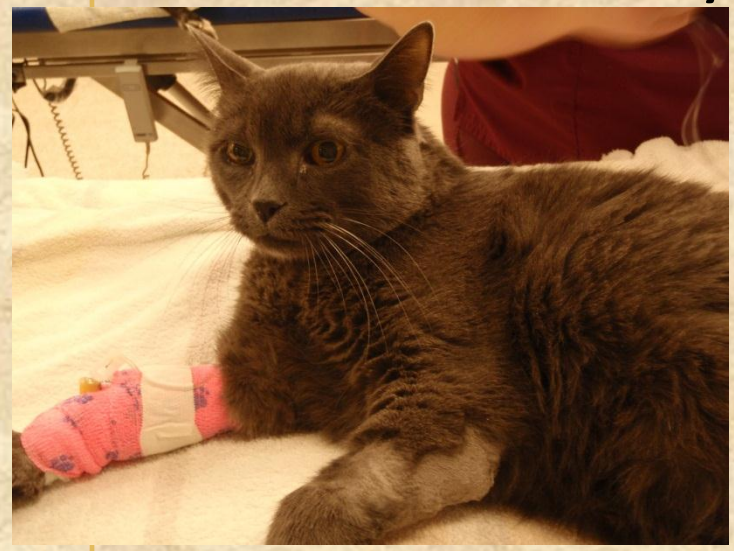


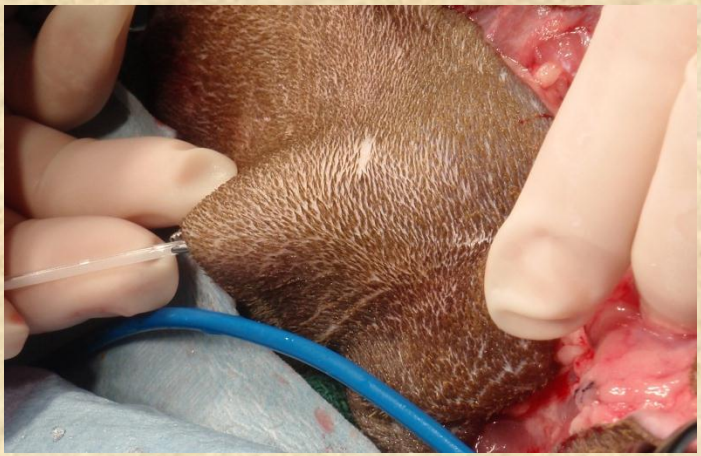
‘Sprout’ Next morning – 20 hrs PO

D/C Fentanyl, started oral Tramadol
Pain Scores: CSU: 0 Glasgow short form: 0-.5
Non-painful to palpation of thoracotomy site and chest tube site.
Walks freely, able to go outside to urinate/defecate
Ate normal amount of food readily
WI catheter removed following am ~ 44hrs PO
Injected Bupivacaine 1.5mg/kg before removal

‘Moe’ 14yr Russian Blue

LF rhabdomyosarcoma; LF amputation





Pre-op: Dexmedetomidine 2ug/kg IV
Intra-op: Fentanyl .3ug/kg/min + Ketamine 10ug/kg/min
Loaded 4” WI catheter intra-op:
Lidocaine 2mg/kg + Bupivacaine 1.5mg/kg

‘Moe’ 1hr PO

Intermittent injection of WI catheter:
Bupivacaine 1.5mg/kg q 4 hrs

6kg x 1.5mg/kg = 9mg ÷ 5mg/ml = 1.8ml

Priming volume = .8ml so added .8ml Saline to 1.8ml bupivacaine = 2.6ml total for first 24hrs then straight Bupivacaine 1.8mls q 4hrs

Initial Opioid Plan: Buprenorphine .02mg/kg IV q 6 hrs

Recommend ↓ dose to .01mg/kg

‘Moe’ day 1 & 2 PO

CSUAPS ~ .5 but still very sedate
Recommend ↑ dose interval for Buprenorphine to q 8 – 10hrs

WI catheter removed 40hrs PO
Eating, more alert, positive interaction, purring, non-painful to palpation

Points to Remember

- Bury in deepest part of wound/incision
- All micropores below skin
- Purse string + chinese finger trap, plastic tabs
- Intermittant vs CRI
  - Lidocaine @ 2mg/kg/hr
  - Bupivacaine 1.5mg/kg q 4-6 hrs
- Priming volume for all WI catheters = .8ml

Points to Remember

- Maintain for 24 – 72 hrs
  - Infuse w Bupivacaine 1.5mg/kg prior to removal
- Assess individual for:
  - Fluid accumulation => lower infusion rate/volume
  - Tenderness to palpation => ↑rate, conc.
- Lower Opioid doses!!

Questions?