Update on Pain Management

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Rising number of publications indexed on Pubmed with keywords “analgesia” or “pain” and “laboratory animals.”
Tile of Talk: Special Topic Lecture: Update on Pain Management
Presenter: Jennifer Lofgren, DVM, MS, DACLAM

Objective Statement: The objective of this talk is to provide the participants with an overview of recent advancements in the prevention and treatment of pain in laboratory animal species. This talk will review different approaches to pain management, taking into account ease of delivery in a high throughput setting.

Abstract: Providing effective analgesia is an ever-present challenge to laboratory animal veterinary staff. Recent evaluations of novel analgesics, sustained release and oral formulations, multimodal analgesic combinations, and even non-pharmacological approaches to preventing, minimizing, and treating pain in lab animal species may provide new tools for the lab animal veterinarian’s toolbox.

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<td>0.3, 1.2, or 4.5 mg/kg SC BupSR (ZooPharm) (Rats)</td>
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Sustained Release Analgesia References:


Hot Topics in Analgesia

- Pain Assessment
- Non-pharmacologic Analgesia
- Oral Dosing of Analgesia
- Sustained Release Analgesia
- Tramadol
- Multimodal Analgesia
- Transdermal Analgesia
- Regional Analgesia
Pain Assessment

- Facial Coding Units:
  - Orbital Tightening: 2
  - Cheek Flattening: 1
  - Pointed Nose: 2
  - Whisker Change: 2
  - Total Pain Score: 2

- Heart Rate Comparison:
  - Normal: 1 day
  - Major Surgery: 1 day

- Feces Quality:
  - Score 0:
    - Fewer than 20-40 droppings.
    - Poorly formed feces, usually tiny and distorted in shape (oval).
    - Photo Ideal:
      - Image of undisturbed, normal-looking feces.
Identifying Pain

- Consumption behaviors / Body Weight
- Fecal or Serum Corticosterone
- Telemetry
- Pain Specific Behaviors
- Pain Faces
- Nesting
Consumption/Body Weight

- After OVH, rabbits demonstrated significantly depressed (Weaver 2010):
  - food consumption (days 1-7)
  - water consumption (days 1-4)
  - fecal output (days 1-2)
  - No significant differences were found between analgesic treatment groups (just pre and post-op)
- Fecal output scoring system facilitated rapid quantification of fecal output by all staff members.

- Mean fecal output did not return to baseline until day 4 after OVH.

- No difference was found between treatment groups.
  - Including transdermal fentanyl and SQ buprenorphine treated groups.

(Weaver 2010)
Fecal or Serum Corticosterone

- Not pain specific, often do not see effects of treatments:
  - Did not differ between analgesic groups treated after castration in mice. (Wright Williams 2013)
  - Was not correlated with postoperative pain and stress in vasectomized mice (Jacobsen, 2012)
  - Did not differ between sham and tattoo treatments in rabbits (Keating 2012)
Telemetry

• Benefits of remotely assessing free-moving animals
  - In mice, major surgery was followed by an increase in heart rate, particularly in the daylight phase, and depression of locomotor activity. (Cesarovic, 2011)
  - Tattoo in rabbits resulted in higher peak heart rate, as well as higher systolic and mean arterial blood pressure. EMLA prevented these changes. (Keating 2012)
Pain Specific Behaviors

- wound licking
- hind-leg stretching
- twitch
- flinch
- pressing of the abdomen into the substrate while stretching
- abdominal writhing
  - Wright-Williams, 2013
  - Jacobsen, 2012
  - Leach, 2012

www.ahwla.org.uk
Changes in Body Posture in Mice

• In response to *abdominal* pain, mice demonstrate abdominal contractions, often accompanied by extension of the hind limbs.

Changes in rat body posture with abdominal pain

• Assessing the Health and Welfare of Laboratory Animals organization
• http://www.ahwla.org.uk/site/tutorials/RP/RP08-arch480/RP08-arch1.html
NS: No surgery  S: Surgery  Ket: Ketoprofen (NSAID)
Pain Faces: Mice

• **Mouse Grimace Scale (MGS)**
  
  – score a image of a mouse in which eyes and ears are visible.
  
  – Assign a value of 0, 1, or 2 for each of the 5 facial action units (FAUs): orbital tightening, nose bulge, cheek bulge, ear position, and whisker change.
  
  – Matsumiya, 2012
  
  – Leach, 2012
Pain Faces in Mice

- 5 Facial Action Units
- Each unit scored on a basis of no pain (0), mild to moderate pain (1), severe pain (2).
- Correlated with traditional pain measures used in the laboratory.
MGS Detects Post-Operative Pain

Leach et al, 2012

1 hr post vasectomy
Pain Faces: Rats

• Rat Grimace Scale (RGS) (Sotocinal, 2011)
  – score image of face and shoulders
  – Scale is 0-2 on four facial action units (FAUs):
    • Orbital Tightening
    • Nose/Cheek Flattening
    • Ear Changes
    • Whisker Change.
Rat Pain Face

• Sotocinal, et al. 2011.

• **Orbital Tightening**: Rats in pain display a narrowing of the orbital area, manifesting either as (partial or complete) eye closure or eye “squeezing.”

• **Nose/Cheek Flattening**: Rats in pain display successively less bulging of the nose and cheek, with eventual absence of the crease between the cheek and whisker pads.

• **Ear Changes**: The ears of rats in pain tend to fold, curl and angle forwards or outwards, resulting in a pointed shape. The space between the ears may appear wider.

• **Whisker Change**: The whiskers of rats in pain move forward (away from the face) from the baseline position, and tend to bunch, giving the appearance of whiskers standing on end.
Using the rat grimace score
Pain Faces: Rabbits

- Rabbit Grimace Scale (RbtGS) (Keating, 2012)
  - Score image of face and shoulders
  - Scale of 0-2
  - Five facial action units (FAUs);
    - orbital tightening
    - cheek flattening
    - nose shape
    - whisker position
    - ear position
### Rabbit Pain Face

- **Keating et al, 2012.**

#### Orbital Tightening

<table>
<thead>
<tr>
<th>Not Present (0)</th>
<th>Moderately Present (1)</th>
<th>Obviously Present (2)</th>
</tr>
</thead>
</table>

The eyelid is partially or completely closed. The globes themselves may also be drawn in toward the head so that they protrude less. If the eye closure reduces the visibility of the eye by more than half, it would be scored as ‘2’ or ‘obviously present’.

#### Cheek Flattening

<table>
<thead>
<tr>
<th>Not Present (0)</th>
<th>Moderately Present (1)</th>
<th>Obviously Present (2)</th>
</tr>
</thead>
</table>

Contraction around the muzzle so that the whisker pads are pressed against the side of the face. The side contour of the face and nose is angular and the rounded appearance of the cheeks to either side of the nose is lost.

#### Nose Shape

- Not Present (0)
- Moderately Present (1)
- Obviously Present (2)

The nares (nasal slits) are drawn vertically creating a more pointed nose that resembles a ‘V’ more than a ‘U’. The tip of the nose may also be tucked under towards the chin exaggerating this appearance.

#### Whisker Position

- Not Present (0)
- Moderately Present (1)
- Obviously Present (2)

Whiskers are straightened and extended horizontally or pulled back toward the cheeks instead of the normal position where whiskers tend to have a gentle downward curve.

#### Ear Position

- Not Present (0)
- Moderately Present (1)
- Obviously Present (2)

Normally the ears are roughly perpendicular to the head, facing forward or to the side, held in an upright position away from the back and sides of the body with a more open and loosely curled shape. In pain the ears rotate away from normal position so face towards the headquarters, tend to move backward and be held closer to the back or sides of the body and have a more tightly folded or curled shape (i.e. more like a tube).
Rabbit grimace scale to detect pain

EMLA cream is a lidocaine cream that provides local anesthesia - in this case to the ear prior to ear tattoo application (clamp).
Challenges to observing pain:

• Rodents and rabbits are prey species
• Do NOT exhibit the familiar ‘fight or flight’ response, instead they exhibit ‘Conservation withdrawal’ response.
  
  – to many observers a very painful rodent appears to be “QAR, sleeping/resting comfortably”
Loss of Normal Behaviors

• Activity
  – Automated behavioral analysis of mouse behavior, specifically walk and jump, was significantly depressed after surgery (Leach 2012)
    • Unable to distinguish between analgesia vs. saline groups.

• Distance traveled
  – Mean travel distance and rearing in rabbits after OVH (Weaver 2010).

• Wheel running
  – CFA-induced decrease in voluntary wheel running in mice was dose-dependently reversed by subcutaneous administration of NSAIDs and opioids (Cobos 2012)
Table 1. The HomeCageScan scored behaviours that significantly decreased in frequency from pre to post vasectomy.

<table>
<thead>
<tr>
<th>Behaviour (P-value)</th>
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</thead>
<tbody>
<tr>
<td>Come down (P = 0.000)</td>
<td>Jump (P = 0.000)</td>
</tr>
<tr>
<td>Rear up (P = 0.000)</td>
<td>Come down to partial rear (P = 0.001)</td>
</tr>
<tr>
<td>Remain rear up (P = 0.000)</td>
<td>Rear up from partial rear (P = 0.003)</td>
</tr>
<tr>
<td>Stretch (P = 0.002)</td>
<td>Unknown (P = 0.008)</td>
</tr>
<tr>
<td>Land vertically (P = 0.000)</td>
<td>Remain hang vertically (P = 0.01)</td>
</tr>
<tr>
<td>Walk left (P = 0.000)</td>
<td>Hang vertically from rear up (P = 0.000)</td>
</tr>
<tr>
<td>Walk right (P = 0.000)</td>
<td>Turn (P = 0.048)</td>
</tr>
<tr>
<td>Walk slow (P = 0.002)</td>
<td>Rear up to partial rear (P = 0.052)</td>
</tr>
</tbody>
</table>

Leach, 2012
Nesting

• Time-to-integrate-to-nest test (TINT score) (Rock, 2014)
  – mice are acclimated to nesting for several days
  – small amount of nesting material added to cage
  – if it is integrated into the main nest site within 10 min a positive TINT is assigned
  – failure to interact with the nesting material within 10 min was a negative TINT score.
TINT Score

Probability of a Negative TINT (%)

Days from Carotid Injury Surgery

Rock, 2014
Nesting

• Nest complexity (Gaskill, 2013)
  – place nesting material in cage and return 7-9 hours after lights-on to score.
  – Score ranges from 0 (material untouched) to 5 (nest walls are taller than ½ the height of a dome).
Graph showing the relationship between Average Nest Score and Average Number of Wounded Mice (x/5). The data points are labeled A, B, and C. Gaskill, 2013.
Nesting

• Latency to nest building (Jirkof, 2013)
  – Time from provision of nestlet to manipulating or carrying the nestlet or nestlet material for more than 3 s.

Gaskill, 2013
Pain Assessment *Recommendations*

• Consumption/Body Weight/Fecal Production
  – Easy to measure
  – Reliable indicator of distress
  – Retrospective – can take 24 hours to observe.
  – Good practice as part of standard husbandry care.

• Corticosterone
  – Did not correlate to pain. Not recommended.
Pain Assessment *Recommendations*

- **Telemetry**
  - May not be pain specific.
  - Require surgery for implantation – not practical for high throughput or cage-side use.
Pain Assessment *Recommendations*

• Nesting:
  – Measuring latency to nesting or evaluating nest quality may not be pain specific.
  – However, it is an easy, first line cage-side assessment for identifying animals in need of veterinary attention.
  – If normals are established, can assess a large number of cages in matter of minutes.
Pain Assessment Recommendations

• Pain Faces and Pain Specific Behavior
  – Once identify animals in need of veterinary attention, use to evaluate presence and severity of unalleviated pain.
  – May take more time, but is pain specific.
Hot Topics in Analgesia

• Pain Assessment
• Non-pharmacologic Analgesia
• Oral Dosing of Analgesia
• Sustained Release Analgesia
• Tramadol
• Multimodal Analgesia
• Transdermal Analgesia
• Regional Analgesia
Non-pharmacologic Analgesia Approaches

- Acupuncture
- Cryoanalgesia
- Social Housing
- Enrichment
Acupuncture

- Acupuncture treatments resulted in significant improvement in mobility in chimps with osteoarthritis pain. (Magden, 2014)
Acupuncture

• Electroacupuncture (EA) in rats:
  – Inhibited neuropathic pain after spinal ligation surgery. (Jiang, 2013)
  – Reduced thermal and mechanical nociception, as well as paw inflammation after intraplantar CFA injection. (Wang, 2013)
(Wang, 2013)
Cryoanalgesia

• Topical vapocoolant for local anesthesia for tail biopsies in preweanling mice:
  – Significant increase in tail pinch latency and had significantly lower increase in blood glucose. However, more licking and re-bleeding (Matthias, 2013).
  – Struggled more, had more bleeding, erythema, and swelling, which persisted for up to 12 h (Paluch 2014 ).

• Did not significantly improve behavioral response to tail biopsy in adult mice (Jones, 2012 ).
What did work for tail biopsies:

• In pre-weanling mice, immersion of tail after biopsy in bupivacaine for 30s decreased tail grooming for 30 min.
• Buprenorphine if provided 20-30 min before biopsy.
• Jones, 2012
Social Housing & Self-Administration

- Post-operatively, individual housing and barren caging resulted in greater post-operative self administration of ibuprofen water (Pham, 2010).
Social Housing

• Anesthesia and surgery resulted in clear changes in behavior, but differences between individual and pair housing conditions were minor.
  – Pair housed mice had a shorter latency to burrowing, possibly reflecting faster recovery
  – (Jirkof, 2012)
Social Housing & Enrichment

• In a model of chronic pain, rats housed socially with enrichment reduced alldynia from 4 to 3 weeks. (Gabriel 2010)

• Socially housed mice recovered quicker and showed less stress following telemetry implantation compared to both singly housed grid separated mice. (Van Loo, 2007)
**Recommendations for Non-Pharmacologic Analgesia Approaches**

- Acupuncture appears to be a promising therapy for both post-operative and chronic pain.
- Cryoanalgesia was not ideal for preventing pain associated with tail biopsies.
  - Dipping tail in bupivicaine or providing buprenorphine was effective.
- Social housing and enrichment sped recovery and reduced analgesic self administration.
Analgesics provided orally

- Acetaminophen
- NSAIDS
- Buprenorphine
Oral Acetaminophen

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<th>PRO</th>
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<tbody>
<tr>
<td>Increased voluntary home cage wheel running after CFA/IFA injection.</td>
</tr>
<tr>
<td>Longer latency to withdrawal on hot plate test than non-medicated water control.</td>
</tr>
<tr>
<td>Increased consumption of medicated water after surgery.</td>
</tr>
<tr>
<td>If provide both medicated gel and water, can reach targeted dose of 200 mg/kg.</td>
</tr>
</tbody>
</table>

Christy, 2014; Caro, 2014; Matsumiya, 2012; Kolstand, 2012; Mickley, 2006; Bauer, 2003; Speth, 2001; Cooper 1997
Acetaminophen failed to alleviate post-operative pain.
<table>
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<th>PRO</th>
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<tbody>
<tr>
<td><strong>Mice drinking water with liqui-gel ibuprofen consumed more food/water, showed less pruritic behavior, had greater healing of ulcer derm lesions and greater locomotor activity.</strong></td>
</tr>
<tr>
<td><strong>After surgery, individually housed and non-enriched mice increased ibuprofen water self-administration.</strong></td>
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</tbody>
</table>

| Meloxicam and carprofen were stable in aqueous solutions when held for 7 d in dark, light, and cold environmental conditions. |
| Mice readily consumed carprofen-medicated water. |
| No gross or microscopic evidence of toxicity was seen in mice provided carprofen or meloxicam in drinking water. |
Carprofen Medigel: post OVH in mice

Presented at AALAS. N = 3 per group. Needs to be assessed in peer-reviewed publication

https://clearh2o.com/images/Nutritionals/MediGel%20CPF%20Sheet%20for%20AALAS%20Show-7.pdf
Caveats to NSAIDs

• Combining Paracetamol with either ibuprofen, meloxicam, or celecoxib (via gavage) augmented analgesia and exacerbated gastrotoxicity and nephrotoxicity. (Kumar 2010)

• A single 5-mg/kg dose of ketoprofen caused acute mucosal damage to the rat small intestine (Shientag 2012).
## Oral Buprenorphine

<table>
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<tbody>
<tr>
<td>Buprenorphine extruded diet pellets increased thermal latency on hot-plate test (equianalgesic to SC).</td>
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<tr>
<td>Better food &amp; water intake, less post-op weight loss, and reduced corticosterone levels.</td>
</tr>
<tr>
<td>Voluntary ingestion or gavage resulted in a plasma concentrations above 1 ng/ml for 14 hrs compared to only 2 hrs when administered IV or SC.</td>
</tr>
<tr>
<td>A single injection of buprenorphine followed by buprenorphine in the drinking water induced an earlier onset of analgesia than buprenorphine in drinking water alone.</td>
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</table>
Oral Dose Analgesia Recommendations

- Acetaminophen:
  - Limited evidence for analgesic efficacy
  - Must overcome significant neophobia

- Carprofen and Ibuprofen:
  - Some evidence for analgesic efficacy
  - Alleviated discomfort associated with ulcerative dermatitis.

- Buprenorphine:
  - Provided in water, food pellet or Nutella promising.
    - Some analgesic efficacy and appropriate seurm concentrations.
  - Can still have side effects of opiates – sedation, decreased food intake, hyperthermia.
Sustained Release Analgesia

• BupSR (ZooPharm)
Buprenorphine SR

• **Mice:** (Carbone, 2011)
  – increased thermal latency up to 12 hours
  – Majority of mice developed scabs at site of injection

• **Rats:** (Chum, 2014; Foley, 2011)
  – Marked sedation at high doses but evidence of analgesia at lower doses for up to 48-72 hours.
  – Some skin irritation and scabbing noted
  – Plasma concentrations remained over 1 ng/mL for 72 h after a single dose

  • In humans, the minimal effective analgesic concentration is 0.1 ng/mL, target plasma concentration is 0.5 to 0.7 ng/mL
BupSR in Rats

Foley, 2011
Buprenorphine SR

Nunamaker, 2013

0.01 mg/kg IM Bup HCl

0.2-mg/kg SC BupSR
Recommendations for Sustained Release Buprenorphine

• Appears to be efficacious in rats.
• More efficacy studies to verify plasma levels correlate to adequate pain relief in veterinary patients.
• Need to consider:
  – frequency of adverse reactions
  – inability to reverse
  – subsequent pain assessment following injection (i.e. not a “1 and done” analgesic)
Tramadol

• Not federally controlled
  – DEA has proposal to change to schedule IV.

• Some states currently list as schedule IV.
  – Arkansas, Illinois, Kentucky, Mississippi, New Mexico, New York, North Dakota, Oklahoma, Tennessee, and Wyoming.

Tramadol

• **Mice:**  (Koutroli, 2014; Rätsep, 2013; Hugunin, 2010)
  - Meloxicam out-performed in efficacy studies.
  - No clear evidence for Tramadol’s analgesic efficacy.
  - Disrupted circadian rhythm, food consumption, activity and, increased weight loss.
  - Increased deaths in high dose group after CLP surgery.
Tramadol

- **Rats:** (Ciuffreda, 2014; Kimura, 2012; McKeon, 2011; Zegre Cannon, 2011)
  - All doses and routes (IP, intrathecal) produced analgesic effect in a dose-dependent manner.
  - Post-op wheel running returned to baseline levels one day earlier.
  - Compared to carprofen:
    - No significant differences in fecal corticosterone, body weight, consumption, or clinical observations.
    - More sedating.
  - Compared to buprenorphine:
    - Provided insufficient analgesia for incisional pain.
  - Some improved efficacy when co-administered with gabapentin or carprofen.
*Significant (P < 0.05) difference compared with baseline value for group.

McKeon, 2011
Recommendations for Tramadol

• Mice:
  – No clear evidence of efficacy
  – Multiple side effects shown

• Rats:
  – Some analgesic efficacy evidence
  – Given alone, provides inferior analgesia compared to other choices (Carprofen, Buprenorphine, co-administered with Carprofen or Gabapentin)
Hot Topics in Analgesia

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- Multimodal Analgesia
- Transdermal Analgesia
- Regional Analgesia
Multimodal Analgesia

- Tramadol & Carprofen
- Buprenorphine & Carprofen
- Buprenorphine & Meloxicam
- Tramadol & Gabapentin
Rats:  (Ciuffreda, 2014; Zegre Cannon, 2011)

- 80% rats treated with multimodal determined to be less stressed after surgery compared to 15-20% of rats treated with only one of the analgesics.
- Locomotor activity was similar before and after surgery in rats treated with carprofen or multimodal combination.
Tramadol & Carprofen

Figure 5. Example of stress behavior. (A) Carprofen treated rat exhibiting distress reactions 1 h after surgery. (B) Carprofen+Tramadol treated rat showing normal behavior 1 h after surgery.

doi:10.1371/journal.pone.0095913.g005

Ciuffreda, 2014
Buprenorphine & Carprofen

Mice: (Parker, 2011; Adamson, 2010)

• Multimodal analgesia had no significant positive or negative effect on the success of blastocyst transfer.

• The parameters used did not indicate either agent alone or combined improved recovery as compared with that of saline-treated mice.
Buprenorphine & Meloxicam

- **Rats:** (Schaap, 2012)
  - No significant differences in body weight or food intake between TID and BID Buprenorphine groups.
  - TID group did exhibit increased gnawing behavior however, no clinical sequelae reported.
Rabbit (Goldschlager, 2013) – Efficiently mitigated the fecal corticosterone increase after surgery – Resulted in better weight gain than the analgesics given alone or bupivacaine local block.
Tramadol and Gabapentin

- **Rats** (McKeon 2011; Narai 2012)
  - Ameliorated thermal hyperalgesia and weight-bearing deficits less effectively than did buprenorphine alone.
  - Intrathecal Gabapentin (alone) attenuated postoperative mechanical hyperalgesia for 7 days
Multimodal Analgesia Recommendations

• Tramadol & Carprofen
  – Evidence for analgesic efficacy in rats

• Buprenorphine & Carprofen
  – Questionable analgesic efficacy reported in mice but neutral impact on embryo transfer success.
  – Need more peer reviewed studies to support efficacy.

• Buprenorphine & Meloxicam
  – Neutral to positive evidence for analgesic efficacy in rats and rabbits.

• Gabapentin & Tramadol
  – Some evidence of efficacy in rats
  – Did not outperform other analgesic options such as buprenorphine.
Transdermal Analgesia

- Buprenorphine
- Fentanyl
Buprenorphine patch

• **Dogs:** (Moll, 2011, Piepera, 2011)
  – Equianalgesic to SC Buprenorphine for controlling clinical post-spay pain.
  – Thermal antinociception achieved beyond 36 h.
  – Peak concentration was 1.54 ng/mL 60 h after application.
  – Patch failed to work at all in 30% of the dogs.
Saline

Buprenorphine given SC (BSC) or sustained release (BP)

Pain Score consisted composite of categories: Physiologic, Response to Palpation, Activity, Mentation, Posture, Vocalization

Moll, 2011
Fentanyl Patch

- **Dogs** (Linton 2012)
  - Investigational formulation
  - administered 2–4 h prior to surgery
  - provides analgesia that is non-inferior to repeated injections of buprenorphine over 4 days

- **Pigs** (Malavasi, 2006)
  - In combination with epidural resulted in earlier return to normal activity levels and an immediate weight gain after surgery.
Table 5. Adverse event rate for TFS- and buprenorphine-treated dogs from the time of first treatment on Day 0 through Day 4 with an incidence of event rate of ≥1% in either treatment group

<table>
<thead>
<tr>
<th>Category</th>
<th>TFS (N = 223)</th>
<th>Buprenorphine (N = 222)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Emesis</td>
<td>12 (5.4)</td>
<td>11 (5.0)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9 (4)</td>
<td>9 (4.1)</td>
</tr>
<tr>
<td>Sedation</td>
<td>8 (3.6)</td>
<td>3 (4.1)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>7 (3.1)</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td>Hypersalivation</td>
<td>4 (1.8)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Ataxia</td>
<td>4 (1.8)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>3 (1.3)</td>
<td>5 (2.3)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3 (1.3)</td>
<td>4 (1.8)</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>3 (1.3)</td>
<td>4 (1.8)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>1 (0.4)</td>
<td>3 (1.4)</td>
</tr>
</tbody>
</table>

TFS, transdermal fentanyl solution.

Linton 2012

Buprenorphine – 0.02 mg/kg IM, every 6 hrs
Fentanyl Patch

- Rabbits (Foley, 2001)
  - Plasma concentration reached 1.11 ng/ml by 24 h and remained high until 72 hours.
  - Hair should be clipped and not removed with depilatory cream.
    - Use of cream resulted in increased rate of absorption leading to sedation and lack of sustained plasma concentrations.
Hair clipped prior to patch application  
Depilatory cream used to remove hair

If hair follicles are in anagen phase at the time of patch application, rapid hair regrowth poses a problem with drug absorption.

Foley, 2001
Transdermal Analgesia Recommendations

• Buprenorphine:
  – Analgesic for at least 1.5 days, possibly as long as 5 days in dogs.
  – High failure rate (30%)

• Fentanyl
  – Analgesic in dogs, pigs and rabbits
  – Careful prep of skin prior to placement
How to make a soaker-type catheter

Jan 1, 2009
By: Christine Egger, DVM, MVSc, DACVA, Lydia Love, DVM

The following materials are needed:

- 3.5-, 5-, or 8-F red rubber catheter
- Sterile scissors (Mayo/regular or Mayo/long
- Sterile Halsted mosquito forceps
- Heat source, such as a cigarette lighter
- Sterile 3-ml syringe
- 27-ga needle (found in insulin syringes)
- Sterile infusion plug
- Sterile gloves
- Sterile drape
Regional Analgesia

- **Sheep:** (Wagner, 2014; Carney, 2009; Lofgren 2014- clinical obs.)
  - Soaker catheter: sheep post thoracotomy improved, require less rescue analgesia (not published)
  - Multi-modal analgesia, including a diffusion catheter, contributed significantly to sheep recovery from ventricular assist device placement
  - Single Block: Aside from improved movement 2 h after the procedure, there were no significant differences between sheep that received blocks from controls
Regional Analgesia

• Pigs: ultrasound guided placement of infusion catheter at time of surgery – femoral fracture (Royal, 2013)
  – Lower subjective pain scores than did control animals
  – Shorter latency to return to eating after surgery and required less rescue analgesia than controls.
Time to first feed after femoral fracture surgery in pigs

Time to needing rescue analgesia

Royal 2013
Regional Analgesia

• Dogs, Cats, Goats (Abelson, 2009)
  – Wound soaker catheters remained in place for 1.6 days
  – Cat and goats received intermittent bupivacaine boluses every 6 hours
  – Dogs received continuous lidocaine infusions.
  – Complication and infection rates equivalent to historical control cases.

• Ferrets: (Eschar, 2010)
  – Epidural used successfully to treat clinical post-operative pain.
Wound Soaker Catheters

(Adelson, 2009; Carney, 2009)
Regional Analgesia *Recommendations*

- Efficacy and benefit demonstrated for multiple species.
- Commercially available and can make own – perform equally well.
- Low infusion speeds with CRI can create uneven distribution of local anesthetic, resulting in inconsistent pain relief.
- Intermittent boluses of local anesthetics may be more effective than CRI. (Hansen, 2013)
Hot Topics in Analgesia

- Pain Assessment
- Non-pharmacologic Analgesia
- Oral Dosing of Analgesia
- Sustained Release Analgesia
- Tramadol
- Multimodal Analgesia
- Transdermal Analgesia
- Regional Analgesia
Thank you!