ANAESTHESIA AND ANALGESIA CHALLENGES FOR EARLY NEUTERING PROGRAMS

Sheilah Robertson, BVMS (Hons), PhD, DECVAA, DACVA, MRCVS

TALKING POINTS
- What is “early-age” spay/neuter?
- Unique neonatal physiology
- Pain in neonates
- Drug pharmacokinetics and metabolism
- Practical protocols

PAEDIATRIC SPAY AND NEUTER CONCERNS
- Developmental concerns
- Few detailed studies on anaesthesia
- Pain in neonates
  - Assessment
  - Needs
  - Drugs
**CONCERNS**
- Obesity
- Stunted growth
- Musculoskeletal disorders
- Delayed closure of growth plates
- Lower urinary tract disease
  - Penile urethral diameter
- Perivulvar dermatitis

**BENEFITS**
- Population control
- Mammary neoplasia
- Behaviour

**ANAESTHETIC CONCERNS**
- Survey of New York veterinarians
  - > 90% agreed there were benefits to early neutering
  - ~ 60% believed this would carry an increased anaesthetic risks

Spain et al 2002; JAAHA; 38: 482-488
Cats under <2 kg have a higher risk of death.

Time of death — first 3 hours after surgery

SURGERY AND ANAESTHETIC COMPLICATIONS

775 cats - Complications based on age

- < 12 weeks – shortest anaesthesia time and few complications
- 13-24 weeks – very few problems
- > 24 weeks – highest complication rate, longest surgery times

Howe 1997; JAVMA 211; 57-62

Early Spay and Neuter Position Statements

“The AVMA supports the concept of early (8 to 16 weeks of age) spay/neuter in dogs and cats in an effort to reduce the number of unwanted animals of these species.”

“The AAFP supports neutering early in life (6-14 weeks of age) as a safe and effective method of decreasing cat overpopulation, and one that confers long-term medical and behavioural benefits to the individual cat.”

Also endorsed by BSAVA, AAHA and CVMA
ASSOCIATION OF SHELTER VETERINARIANS

- Animals adopted into homes should be spayed or neutered
- Voucher or pre-paid programs have a compliance rate of < 40%

NEUTERING PROCEDURES

- Ovariectomy or ovariectomy
- Castration

THE IDEAL ANAESTHETIC

- Safe
- Simple
- Effective for males and females
- Efficient
  - Large numbers of animals
- Cost-effective
  - Drugs and equipment
- Rapid recovery
- Analgesia
PRE-REQUISITES FOR SUFFERING

<table>
<thead>
<tr>
<th>Sentience</th>
<th>Consciousness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phylogenetic status</td>
<td>Awake</td>
</tr>
<tr>
<td>Functional nervous system</td>
<td>Asleep</td>
</tr>
<tr>
<td>Stage of development</td>
<td>Anaesthesia</td>
</tr>
</tbody>
</table>

ONTOGENY OF NOCICEPTION AND PAIN PERCEPTION

- Varies between species
  - Degree of maturity at birth
- Varies within a species
  - Gestational age
NEUROLOGICAL MATURITY AND ONSET OF CONSCIOUSNESS DETERMINE WHEN MAMMALIAN YOUNG CAN SUFFER AFTER BIRTH

<table>
<thead>
<tr>
<th>EEG Features</th>
<th>Species</th>
<th>Exceptionally immature</th>
<th>Immature</th>
<th>Mature</th>
</tr>
</thead>
<tbody>
<tr>
<td>electrical silence</td>
<td>marsupial</td>
<td>kitten</td>
<td>puppy</td>
<td>mouse pup</td>
</tr>
<tr>
<td>spikes</td>
<td>calf</td>
<td>fawn</td>
<td>foal</td>
<td>lamb</td>
</tr>
<tr>
<td>continuous REM/nonREM sleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>short epochs</td>
<td></td>
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</tbody>
</table>

Adapted from Mellor, Patterson-Kane and Stafford: The Sciences of Animal Welfare

WHAT DOES THIS MEAN FOR KITTENS?

- Conscious wakefulness not present at birth
- Kitten welfare is likely protected until 7 days of age

WHAT DOES THIS MEAN FOR KITTENS?

- They are sentient and conscious when early neutering is performed
- The neonatal nervous system may be vulnerable to damage
  - Plasticity
MANAGING PAIN IN HUMAN NEONATES

- 1985 – Jeffrey Lawson, 1.9 kg neonate
- Surgery for PDA correction
- Sole “anaesthetic” agent was pancuronium
- Reasons
  - “Jeffrey was too sick to tolerate powerful anaesthetics”
  - “It has not been demonstrated that babies feel pain”

BARRIERS TO PREVENTING AND TREATING PAIN IN HUMAN NEONATES

- Pain assessment in non-verbal humans
- Fear of adverse side-effects from drugs
- Belief that neonates are not sufficiently developed to experience pain
  - “they will not remember it”
NEONATAL INJURY

Rat pup model
- Injury in one tissue alters sensory processing throughout the body
- Injury early in life alters sensory processing throughout life

IMPACT OF EARLY PAIN EXPERIENCES

- Three groups (87 infants)
  - Uncircumcised boys
  - Circumcision with local anaesthesia
  - Circumcision with no analgesia
- Studied response to vaccination pain at 4-6 month (videotapes)
  - Cry duration
  - Facial action
  - VAS

Effect of neonatal circumcision on pain response during subsequent routine vaccination

Joulaa T, Todd J, Lamarche C, Green N.
Pain scores
- Uncircumcised < local anaesthesia < no anaesthesia

Conclusion
- Infants retain a memory of previous painful events
- Response to subsequent painful stimuli are altered

Altered pain sensation
- Anticipation of pain, threat cues
- Stress disorders
- Attention deficit disorders
- Self destructive behaviours

Why this matters
What we do here has impacts later in life
PAIN ALSO CAUSES PHYSIOLOGIC CHANGES

- Metabolic and hormonal stress response
  - Catabolism and weight loss
- Increased catecholamines
  - Hypertension, tachycardia, arrhythmias
- Altered respiratory function
- Ileus
- Immunosuppression

ANALGESIC STRATEGIES

<table>
<thead>
<tr>
<th>Drugs</th>
</tr>
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<tbody>
<tr>
<td>Non-drug therapies</td>
</tr>
<tr>
<td>Swaddling</td>
</tr>
<tr>
<td>Suckling</td>
</tr>
<tr>
<td>Sucrose</td>
</tr>
<tr>
<td>Skin-to-skin contact</td>
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</tbody>
</table>

BMC Pediatrics

Research article
Kangaroo mother care diminishes pain from heel lance in very preterm neonates: A crossover trial
Celeste Johnson1, Fransine Filion1, Martha Campbell-Yvon1, Cathleen Coates2, Kathleen McNaughton1, Jasmine Byron1, Marilyn Atla2, G. Allen Finlay3 and Clare-Dominique Walker4
Compared warmth, sucrose and a pacifier for vaccination
- Warmth decreased crying and grimacing
- Heart rate reflected analgesia

**Other Considerations**

Isolation (psychological stressor) resulted in hyperalgesia

**Surgical Trauma**

- Pain is driven by inflammation
- The greater the trauma the greater the inflammation
- SMALL INCISIONS
THE IDEAL ANAESTHETIC
- Safe
- Simple
- Effective for males and females
- Efficient
  - Large numbers of animals
- Cost-effective
  - Drugs and equipment
- Rapid recovery
- Analgesia

PAEDIATRIC PATIENTS - CONCERNS
- Unique physiology
- Hypothermia
- Hypoglycaemia
- Immature metabolism
- Monitoring

NEONATAL PHYSIOLOGY
CARDIOVASCULAR
- Sympathetic innervation to the heart is incomplete at birth
- Parasympathetic innervation is anatomically mature
- Cardiac output is heart rate dependent

HYPOTHERMIA CAUSES BRADYCARDIA
Neonatal Physiology
- High oxygen requirements
- Increased risk for hypoxaemia

Shivering increases oxygen demand

Neonatal Physiology Metabolism
- P450 enzyme activity is low at birth
- Takes several months to reach adult function

Fasting and Feeding
- Fasting
  - Low glycogen stores
  - No, or minimal fasting
  - Do not remove kittens from Queen
- Feed as soon as possible after surgery
**PRE-OPERATIVE ASSESSMENT**
- Accurate weight

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**ANAESTHETIC PROTOCOLS**

**INJECTABLE**

**INHALANT**

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**ANAESTHETIC CHOICES**

**INHALANT AGENTS**
- Large "dose" when used alone
- Cardio-respiratory depression
- Stressful induction
- Equipment needs and expense
  - Usually not a suitable option for high volume clinics
**ANAESTHETIC CHOICES INJECTABLE DRUGS**

<table>
<thead>
<tr>
<th>PROPERTIES</th>
<th>ROUTE OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short acting</td>
<td>Subcutaneous</td>
</tr>
<tr>
<td>Reversible</td>
<td>Intramuscular</td>
</tr>
<tr>
<td></td>
<td>Intravenous</td>
</tr>
</tbody>
</table>

**PROPERTIES**
- Short acting
- Reversible

**ROUTE OF ADMINISTRATION**
- Subcutaneous
- Intramuscular
- Intravenous

**ANAALGESICS**

- Opioids
  - Buprenorphine
  - Pethidine
  - Morphine
  - Methadone
  - Butorphanol

**INDUCTION**

- Ketamine
  - IM
  - Analgesic properties
  - Wide safety margin
PREMEDICATION
- Anticholinergic drugs
  - Atropine, glycopyrrolate
- Cardiac output = HR x SV
- May not be needed if using ketamine

TOTAL INJECTABLE PROTOCOLS
- Balanced anaesthesia
- Can include an analgesic
- Can do more animals at one time
- May be partly reversible
  - Rapid recovery

DRUG DOSING - ACCURACY
- Dilute drugs
- Use insulin syringes
**MONITORING**

- Non-invasive
  - Auscultation
  - Observation
  - Pulse oximetry
  - Indirect blood pressure
  - Temperature
- Neonatal kittens
  - HR is 200 beats/minute

**KITTEN STUDY – UNIVERSITY OF FLORIDA**

32 kittens
- 7-12 weeks old
- 17 females
- 15 males

Body weight
- Mean ± SD: 906 ± 155g
- Range: 636-1205g

**ANAESTHETIC PROTOCOL - 1**

- Induction with isoflurane by mask
- Butorphanol 0.4 mg/kg IM
- Maintained on isoflurane / O₂
ANAESTHETIC PROTOCOL-2
- Medetomidine 40 µg/kg
- Ketamine 20 mg/kg
- Buprenorphine 20 µg/kg
- Mixed together
  - Subcutaneous injection
- Atipamezole after surgery

DURATION OF SURGERY
- Ovariohysterectomy
  - 6.8 ± 1.5 minutes
- Castration
  - 48 ± 23 seconds

RESULTS

<table>
<thead>
<tr>
<th>Group</th>
<th>Time to loss of toe pinch*</th>
<th>Time to sternal recumbency**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iso But</td>
<td>3.9 ± 1.1 min</td>
<td>3.9 ± 1.7 min</td>
</tr>
<tr>
<td>MKB</td>
<td>3.9 ± 1.0 min</td>
<td>8.8 ± 2.2 min</td>
</tr>
</tbody>
</table>

* NS
**P < 0.05
RECOVERY

ISOFLURANE / Butorphanol MKB

RECOVERY – 1 HOUR

RESULTS

<table>
<thead>
<tr>
<th>Group</th>
<th>T°C</th>
<th>HR</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>37.7</td>
<td>184</td>
<td>32</td>
</tr>
<tr>
<td>Butorphanol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MKB</td>
<td>38.2</td>
<td>175</td>
<td>39</td>
</tr>
</tbody>
</table>
CONCLUSION
- Both techniques were acceptable
- MKB may be more suited to a shelter environment where multiple kittens are handled at one time and inhalant anaesthetic equipment is unavailable or limited

ENDOTRACHEAL INTUBATION
- Increased odds (x3) for short procedures
  - < 30 minutes
- Respiratory obstruction as a cause of death more common in cats
- Have intubation supplies ready
- ± Oxygen by mask

OTHER ANALGESICS – LOCAL ANAESTHETICS
- "splash" blocks
- Intra-testicular blocks
Lack of information on NSAID use in neonates
Potential benefits and risks but few conclusive facts

COX-1 and COX-2 expression change during fetal development and after birth
Prostaglandins are important for normal CNS, renal and cardiovascular development
COX-2 is involved in organ development

Prostaglandins are involved in
- Sleep regulation
- Pain
- Cerebral blood flow
- Neuroprotection
- Thermoregulation
- Renal function
- Gastrointestinal function
- Osteogenesis
**NSAIDs in Young Cats**

Not as a “First Line” Analgesics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Age Limit</th>
<th>Weight Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carprofen</td>
<td>20 weeks</td>
<td>None</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>6 weeks</td>
<td>2 kg</td>
</tr>
<tr>
<td>Robenacoxib</td>
<td>16 weeks</td>
<td>2.5 kg</td>
</tr>
</tbody>
</table>

Labels state: “Do not use in…” or “Safety has not been established in…”

**Top 10 List for Anaesthesia Problems…….**

**Hypothermia**
Papers

Retrospective study of the prevalence of postanaesthetic hypothermia in cats

J. I. Bednarska, P. Szczech, J. Gil, S. Saló, J. Serra, E. Saló

Time to extubation (mins) | # of cats | Deaths | Mortality index %
--- | --- | --- | ---
Normothermia | 13 ± 11 | 5 | 0 | 0
Slight hypothermia | 12 ± 7 | 73 | 2 | 2.73
Moderate hypothermia | 13 ± 10 | 166 | 2 | 1.20
Severe hypothermia | 26 ± 25 | 29 | 2 | 6.89

ADVERSE EFFECTS OF HYPOTHERMIA

- Delayed recovery
- Post-operative shivering and increased oxygen demands
- Pain
- Bleeding
- Blood viscosity
- Wound infection
- Cardiac complications
  - Bradycardia, arrhythmias
**SIMPLE AND CHEAP!**

**BUBBLE PACKING**

**FORCED WARM AIR**
PRE-WARMING

SUMMARY

- Neonatal anaesthesia and surgery can be successful
- Analgesia is essential
- Injectable protocols are ideal in shelter environments
- Intubation is not required
- Keep them warm