Analgesia and Anesthesia in Birds

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Objectives

• Latest literature review on pain management
• How to evaluate pain in birds
• Preemptive analgesia is more successful than pain management in response to pain
• Multimodal analgesia since one agent can’t do it all
• Common analgesics utilized in birds
• Use medications that can be reversed when possible
• Considerations to take prior to anesthesia
• Intubation or face mask induction, maintenance
• Monitoring of anesthesia
References:
What is pain?
• The old saying “It was fine before I went to sleep and was dead when I woke up” is true.
• This remphasizes the importance of preventive exotic animal medicine!
Balanced graced anesthesia

Preemptive analgesia
- Administer medication before, rather than after injury, whenever possible
- Prevents “pain windup” by preventing noxious stimuli from reaching the CNS

Multimodal analgesia
- Mechanisms of pain involve multiple pathways & a variety of neurotransmitters
- No one drug or class of drugs can be used to treat all pain
- Rely on drug combinations to provide greater pain relief
- By combining agents often uses lower doses, reduces the risk of undesirable side effects

I.e. Short-acting opioid like butorphanol, may act rapidly 10-15 m from injection with an NSAID which can be 1 h before significant analgesic effects
Causes of pain in birds

• Trauma including fractures, beak injuries
• Arthrititis (infection or gout)
• Pododermatitis (bumblefoot)
• Dystocia
• Visceral gout
• Inflammation associated with fungal infections, e.g. Aspergillosis air sacculitis
• I.E. “itis” means inflammatory
• Surgery
Signs of pain in birds:

- Stoic nature, behavioral signs may be subtle
- Will differ depending on location & type of pain
- May include withdrawal reaction when a localized injury is palpated, lameness, decreased weight-bearing, reluctance to move, impaired walking ability & guarding a painful area
- Vocalization may be increased or decreased
- +/- hyporexia, weight loss
- Lack of grooming, lethargy, lack of social interaction with other birds or owner & depression are common signs of general illness which can also indicate that a bird is in pain
- Feather picking & other compulsive behaviors
- Immobility can be a manifestation of extreme pain in birds
- Can be misinterpreted as evidence that birds do not experience pain
Management of pain in birds

- Reduce stress and apprehension
- Housed in a warm (unless head trauma) & quiet environment
- Provide easy access to food & water
- Low to no perches & areas to rest
3 types of nociceptors in the PNS: high-threshold mechanical, thermal & mechanothermal

Pigeons possess µ, δ & K receptors in the forebrain & midbrain, similar to mammals; however, there is a higher proportion of K & δ receptors compared with µ receptors, 76% K receptors

Chickens may not possess distinct µ & K receptors, or perhaps the receptors have similar functions
Pain Pathway

• Noxious stimulus at the periphery causes signal transduction at the nociceptor
• Signal is transmitted along peripheral sensory axons to the cell body in the dorsal root ganglion, which then relays the signal to the dorsal horn of the spinal cord for processing, modulation & projection to the brain along ascending spinal tracts
• When nociceptive signals reach the brain, they are modulated & processed for cognitive & emotional perception
Opioids: Butorphanol

- Mixed agonist/antagonist, low intrinsic activity at the µ receptor & strong agonist activity at the K receptor
- Historically analgesic of choice for acute & chronic pain
- Analgesic effects parrots using thermal & electrical noxious stimuli (Paul-Murphy 1999)
- Pain associated with arthritis & DJD was alleviated with butorphanol in green-cheeked conures, Hispaniolan parrots & turkeys (Buchwalder 2005, Paul-Murphy 2009)
- Isoflurane sparing effects of butorphanol 1mg/kg IM varied between 11 & 25% in cockatoos & African grey parrots, but no significant effect was found in blue-fronted Amazon parrots (Curro 1993 and 1994)
- Pre-operative 2mg/kg IM appears safe & did not cause significant changes in cardiopulmonary parameters in Hispaniolan parrots anesthetised with Sevo (Klaphake 2006)
Butorphanol

(Riggs 2008)
- PK properties in red-tailed hawks & great horned owls
- Rapidly absorbed and distributed after IV & IM administration
- Concentrations greater than 10 ng/ml were maintained for only 2-4 h after drug administration via any route
- Concluded that published dosing intervals of 4 - 24 h may be inadequate & should be dosed more frequently

(Sladky 2006)
- Liposome-encapsulated butorphanol 15mg/kg SC in Hispaniolan parrots provided analgesic effects for 3-5 d following a single dose
- Liposome-encapsulated butorphanol may provide long-term pain relief without subjecting birds to the stress of handling & multiple daily injections
Butorphanol

(Guzman 2014)

• PK and antinociceptive effects IM to American kestrels
• Did not cause thermal antinociception suggestive of analgesia
• Sex-dependent responses were identified
• Avian telencephalons revealed large variation receptor types in the forebrains
• Proper pain management may be species-specific
• Hypothesized that higher plasma concentrations, buprenorphine may "crossover" to act at different opioid receptors
• PK, BH American kestrels .6mg/kg IM/IV 9 h (Gustavsen 2014)
• Thermal antinociceptive effects BH, American kestrels 0.6 mg/kg IM/IV 6 h (Ceulemans 2014)
• SR-LAB 1.8 mg/kg administered IM/SC 12-72 h, mild sedation (Guzman 2017)
• Red-tailed hawks 0.3 mg/kg SC but no antinociptive studies done so far (Gleeson 2018)
(Guzman 2018)

- PK and thermal antinociceptive effects BH IM to cockatiels
- 9h, did not significantly change the thermal nociceptive threshold or cause sedative or agitative effects
Hydromorphone

- Antinociceptive, sedative effects and duration of action on hydromorphone IM American kestrels
- 0.6 mg/kg significantly increased the thermal foot withdrawal threshold by 3-6 h, mild sedation (Guzman 2013)
- PK hydromorphone after IV/IM American kestrels, very short half life (Guzman 2014)

- PK & thermal antinociceptive effects IM to cockatiels
- Did not increase the thermal withdrawal thresholds despite plasma drug concentrations considered therapeutic for other species (Houck 2018)
Tramadol

- Studies evaluated PK of tramadol and its metabolite in peafowl & bald eagles (Black 2009, Souza 2009)

- Bald eagles high oral bioavailability, authors concluded that a dose of 5mg/kg PO q12 provides adequate plasma levels (Souza 2009)

- Red-tailed hawks 15mg/kg PO q12 h (Souza 2010)

- Hispaniolan Amazon parrots oral bioavailability was found to be only 23.48%, compared to 97.94% in bald eagle

- 30 mg/kg produced plasma levels consistent with human analgesia for 6 hours, so q8 h! (Souza 2012)

- Plasma levels associated with analgesia is not known in avian patients and further studies are needed
Tramadol

- Kestrels 5, 15 and 30 mg/kg PO
- **Only the lowest dose** of 5 mg/kg was observed to significantly alter thermal foot withdrawal thresholds for 1.5 h
- Higher doses had decreased antinociceptive effects (Guzman 2014)

- Hispaniolan amazon parrots 10 & 20 mg/kg PO, no significant change in thermal foot withdrawal times were observed
- 30 mg/kg PO cause a **significant change in foot withdrawal times** for up to 6 h (Guzman 2012)

- 5mg/kg IV significant effects in thermal nociception 4h, #11 HAP (Geelen 2013)
Gabapentin

(Baine 2015)
- Hispaniolan Amazon parrots
- 30 mg/kg IV, 10 & 30 mg/kg PO; recommend q 8h
- Mild sedation only noted after IV admin.
- Good oral bioavailability and volume of distribution
- PO appropriate; liquid contains xylitol
- Effective plasma concentrations for anti-neuropathic pain properties of gabapentin have not been established in zoological species

(Yaw 2015)
- Great horned owls, 11 mg/kg PO q8 plasma concentrations at the human therapeutic threshold
NSAIDs history (Flunixin, carprofen, ketoprofen & meloxicam)

- Acute post-operative & traumatic pain
- GI & renal side effects, caution with renal, hepatic or perfusion problems
- Flunixin meglumine (high dose) 10mg/kg caused regurgitation & tenesmus in budgerigars and hematochezia in a crane (Bauk 1990, Clyde 1999)
- Renal changes such as glomerular congestion tubular dilation & tubular degeneration were seen in budgerigars given flunixin meglumine, ketoprofen & meloxicam after several days of treatment (Pereira 2007)
- Ketoprofen was associated with lethal renal damage in spectacle seiders (Mulcahy 2003)
- Histological evidence of renal damage was present in bobwhite quail given low doses of flunixin meglumine & the severity of the renal changes correlated to the dose (Klein 1994)
- Flunixin meglumine also caused muscle necrosis at the injection site in Mallard ducks (Machin 2001)
- Flunixin meglumine should be used only at low dosages & with caution
NSAIDs history

• Carprofen 1mg/kg SC substantially improved the walking ability of lame broiler chickens (McGeown 1999)

• In contrast, carprofen 3mg/kg IM did not significantly reduce the weight-bearing load in HAP with experimentally induced arthritis, but was superior to butorphanol for reducing feather picking on the arthritic limb (Paul-Murphy 2009)

• Domestic fowl minimum effective dose for carprofen was 30mg/kg in, but the death of at least one bird was observed during the experiment

• Extreme caution should be exercised when such high doses are used in a clinical setting (Hocking 2005)

• Ketoprofen 5mg/kg IM, had analgesic effects in Mallard ducks anesthetized with Iso when a noxious stimulus was applied, but lower doses of ketoprofen 0.5-2mg/kg IM did not provide any detectable analgesia (Machin 1998 & 2002)

• Domestic fowl the minimum effective dose of ketoprofen was 12 mg/kg, but such high doses can result in death (Hocking 2005)
Meloxicam

- PK ring-necked parakeets, (chickens, ostriches, ducks, turkeys & pigeons) showed considerable variation among different species
- Half-life in ring-necked parakeets was of longer duration than in any of nonpsittacine species for both PO & IV routes
- Chickens & pigeons had a longer half-life than ostriches
- IV bioavailability was 100% & was also high for PO in ring-necked parakeets (Baert 2003, Wilson 2005)
- 0.5mg/kg PO q12 or IV q4 recommended in psittacine birds (Wilson 2005)
- 1 mg/kg IM/PO q24 pscittacines, AGP (Montesinos 2017)
Meloxicam

(Summa 2017)

- Toxicity of short-term high doses in American kestrels
- PO 2, 10, and 20 mg/kg q12 h x 7 d
- 20mg/kg significant correlation with hepatic lipidosis
- 2/9 developed gastric ulcers, although this result was not significant
- No nephrotoxicity

- Celecoxib, suggested dosage for PDD 10 to 20 mg/kg PO q24 h x 6-12 w

- NSAIDs, monitor for melena, FOB
Corticosteroids

- Such as bethamethasone, have anti-inflammatory effects and can reduce pain associated with DJD (Duncan 1991)
- Adverse effects may occur after a single treatment with corticosteroids and include severe immunosuppression, adrenal insufficiency and delayed wound healing (Dorrestein 2009)
- Panalog (Triamcinolone) very potent, may lead to immunosuppression, hepatopathy & secondary fungal infections
- Use NSAIDs over corticosteroids!!!
Lidocaine considerations, cat study

- A previous study showed topical 2% as effective as 10% to facilitate intubation.
- 2% lidocaine lower maximum plasma concentrations; is recommended.
- Topical alone or in combination with intratesticular results in dose-dependent increases in maximal plasma concentrations.
- Recommended doses of 2% are 0.1 mL ($\approx 0.6$ mg/kg) administered topically on the larynx and 0.1 mL/kg administered intratesticularly, adjust for smaller patients.
- Although time to reach peak plasma concentrations does not significantly differ between topical application alone or in combination with intratesticular.
- Plasma concentrations may be affected by other patient factors & should be considered on an individual patient basis.
- Must know max dose recommended!

Plasma concentrations of lidocaine following laryngeal administration or laryngeal and intratesticular administration in cats. (Soltaninejad 2018)
Local anesthesia

- Lidocaine 2-3mg/kg, bupivacaine 1-2mg/kg & benzocaine
- May be more sensitive to toxic side effects than mammals
- Lidocaine can be used safely below 4mg/kg IM/SC (Paul-Murphy 2001)
- Overdosing reported to cause seizures & cardiac arrest
- Intraarticular bupivacaine 2mg/kg provided analgesia in 
  chickens with MS pain (Hocking 1997)
- Ducks bupivacaine 2 mg/kg SC suggested that analgesic 
  effects might be shorter acting than in mammals
- The length of action of local anaesthetics is unknown in 
  birds
Local anesthesia

- EMLA cream (lidocaine/prilocaine) for venipuncture/IVC, wait > 5 m (Imani 2013)
- Evaluate total toxic dose of lidocaine and serum lidocaine concentrations resulting in clinical signs of toxicity in chickens
- Systemic toxicity ~30 mg/kg and corresponding serum lidocaine concentration were ~38 µg/mL
- Greater doses of lidocaine are needed to produce toxic manifestations in chickens as compared with mammals
Alfaxalone

(Escalante 2018)
- Alfaxalone 15mg/kg vs. Butorphanol 2.5 + Midazolam 1.25mg/kg IM
  Budgerigars
- 3/10 birds butorphanol-midazolam recumbent by 5 m
- 10/10 birds alfaxalone
- Alfax more consistent, shorter duration 28 m vs. 72 m

(Villaverde-Morcillo 2014)
- 2 mg/kg IV with iso, HR & RR remained more stable than with iso alone
- Breath-holding was reduced, facilitating more rapid induction
- Lower flow rate of iso, overall fewer intraop & postop side effects were observed in the avian patients
Midazolam

- IM, IN, .5 - 6mg/kg (passerines), 2-3 most
- Minimal cardiorespiratory side effects
- Can combine with opioid to provide additional analgesia
- Flumazenil reversal IM, IN

(Grayson 2018)

- IN midazolam 3mg/kg & midazolam-butorphanol 3mg/kg each in cockatiels
- ~ 90 sec to sedated, combo slightly better
- Not as a sole agents may cause excitement (Santangelo 2009)
- Common buzzard 25 ug/kg & common kestrel 75 ug/kg with atropine as premed
- Sedation, adequate muscle relaxation
- Able to be handled without reacting
- NO arrhythmias
- Reliable reversal with atipamezole

α2-adrernergic agonists
Dexmedetomidine
α2-adrenergic agonists
Dexmedetomidine

(Hornack 2015)

• **Pigeons** IN 80ug/kg & midazolam 5mg/kg
• Significant reductions HR, RR, Temp
• Dorsal recumbency max level at 20-30 m
• IN atipemazole
• Butorphanol CRI in ducks, no isoflurane MAC sparing effect seen
  (Litchenberger 2008)

• Butorphanol CRI in cockatoos significantly lower MAC
  (Lichtenberger 2009)

• Propofol CRI 0.85 mg/kg/min produced stable anaesthesia suitable for painless clinical procedures

• In contrast, bolus administration was unsatisfactory
  (Muller 2011)
What analgesics do we recommend in birds

- Seems to be species dependent
- Butorphanol IM, q3-4h, acute, periop
- Buprenorphine AKs IM/IV q9h, other carnivores?
- Bup-SR, AKs, SC q72, other carnivores?
- Tramadol BAEA 5 mg/kg q12, RTHA 15mg/kg q12, HPA 30mg/kg q8
- Meloxicam .5-2mg/kg q12-24
- Gabapentin HPA 30mg/kg q8, no PD
- Lidocaine 1-2 mg/kg, higher in chickens?
- Bupivicaine 1-2mg/kg ?
- Methadone, stay tuned
- Others…
Avian Anesthesia

- Highly efficient respiratory system allows for rapid induction & recovery from inhalants
- Inhalants are the mainstay
- Inhalants considered direct CV depressants & cause hypotension d/t dose-dependent decreases in myocardial contractility, stroke volume & systemic vascular resistance
- Mean ± SD isoflurane MAC in pigeons is 1.8%, whereas in thick-billed parrots it is reportedly much lower at 1.07%
- Chickens, methadone 6 mg/kg IM reduce the mean MAC of Iso by 30%
- Iso been associated with 2nd & 3rd degree AV block in pigeons & BAEA

Finch SPH
Intubation

- Complete tracheal rings so ideally use non-cuffed endotracheal tubes
- Trachea tapers in diameter
- Inflated cuff can result in mucosal damage & potential tracheal stenosis
- Several reported cases of stenosis, treated with tracheal resection & anastomosis
Air Sac Cannula

- Used to ventilate birds by a route other than ET intubation
- For oxygenation & anesthesia, especially during surgery of the head or trachea where tracheal intubation would be cumbersome
- Means to medicate air sacs directly
- Aid dyspneic birds with tracheosyringeal obstruction from FB, granulomas or tumors
- NOT if lung disease
- May be left in place for 7 d, ideally 4 d d/t increased risk of bacterial or fungal infection
• Complications severe air sac damage, occlusion of the cannula with exudate or fluid, and abdominal organ damage
• Insert into the cdTAS or abAS
Air sac cannula step by step

**Head**

**Tail**
Temperature

- Monitoring is very important!
- If low temp, double check probe placement
- Rapid heat loss first 10 min, vasodilation, increases conduction heat loss & reduced muscle activity, which decreases heat production
- Minimizing anesthesia time
- Providing supplemental heat (water blankets or forced-air warming blanket)
- Warm IV fluids
- LRS or 0.9% NaCl at 20 mL/kg/h via IOC during isoflurane anesthesia in pigeons, no significant differences were found in electrolyte or acid base balance (Carregaro 2015)
- Plastic sticky drapes
- Minimizing the amount of feathers pluck, rinse with warm prep solutions & surgical flush instead of alcohol
Monitoring: Temperature

- Warming starts at time of premedication
- Lasting until the patient has fully recovered & normothermic
- Prolonged recoveries can be associated with low body temp., reduces metabolism of anesthetic drugs
- Skin burns from electric heat blankets or heated fluid bags if used in direct contact with the skin
- Heat lamps should remain at least 1 m from the patient to prevent burning
- Cloacal or esophageal probe, 40°C (104°F) to 43°C (109.4°F), being routinely higher in smaller birds
Monitoring: Blood pressure

• Have relatively large hearts and thick vessels
• Reduced elasticity of the arterial walls, SAP higher than in mammals
• BP range 90-180 mm Hg in conscious psittacine birds
• Normal SAP for psittacine birds under Iso or Sevo 90-150 mm Hg
• Systolic BP ≤ 90 or ≥ 145 mm Hg should be evaluated for causes of possible hypotension & hypertension respectively in psittacines
• Unfortunately, indirect readings in birds <2 kg do not correlate to direct measurements
• Indirect good for trends
Monitoring: Blood pressure

- Learning curve
- A finger is better than using nothing!
- Place finger or Doppler probe on Superficial ulnar or Deep radial a.
- Water birds or long-legged birds, Cranial tibial or Dorsal metatarsal a.
- Isoflurane-associated hypotension > dopamine or dobutamine CRI
- HAP, CRI of dobutamine at 5, 10 & 15 µg/kg/min and dopamine at 5, 7, and 10 µg/kg/min increased systemic blood pressures to normotensive levels (Schnellbacher 2012)
Monitoring: Pulse oximetry

- Not validated in birds
- Absorption characteristics of oxygenated and deoxygenated avian and human Hb differ leading to an underestimation of Hb saturation in avian patients
- Good for trends
Monitoring: Capnography

“Rate & depth of respiration are the best indicators of anesthetic depth, so nothing like a good technician”

- 30-45 mm Hg
- Birds hypoventilate under anesthesia
- Negative physiologic effects develop much more rapidly in anesthetized birds than in mammals
- Assisted ventilation, immediately after induction is strongly recommended to prevent hypercapnia & hypoxemia
- As in mammals, strong correlation between ETCO2 & PaCO2 in birds
- Side-stream capnography provides a good estimate of PaCO2
Monitoring: EKG

- Speed of $\geq 100$ mm/s (may need 200 mm/s very small patients)
- Slower speeds wave forms too close together to interpret but the tracing may be useful for monitoring anesthesia & to detect arrhythmias
- ECG tracing can have the appearance of ventricular tachycardia, primarily because of the large negative S wave
- This QRS morphology caused by the high density of sympathetic & parasympathetic nerve fibers in the avian ventricles & atria when compared to mammals
Monitoring: Doppler

- Every patient should at least have a doppler probe attached
- Much more sensitive than a stethoscope or finger “pulse”
- Same sites as for BP monitoring
• High % of anesthetics deaths occur during recovery
• Start turning down anesthesia gradually towards the end & monitor ventilation very closely
• It takes 2 breaths cycles to clear air sacs/lungs
• Mucous plugs are common so if in doubt reintubate
• Have a warm towel handy to prevent aggressive wing flapping
• Have warm incubator ready, it should have been warmed during premed administration
• Repeat opioids shortly after recovery
EVERYTHING must be ready prior anesthesia
ASA score your patient, premeds, Iso/Sevo
Keep warm pre/during/post anesthesia
Use reversible medications when possible
Have colloids/fluids pre drawn warm & handy
Have ER drugs pre drawn
Monitoring (Breath/ETCO2, Doppler/BP)
Give reversals ASAP
Conclusion:

- Thy shall not practice avian medicine w/o midazolam!
- Very limited PK & PD studies, but a good base
- Studies in “similar species” can give us guidelines to doses & anesthetic plans
- These studies should be used with care but not avoided
- Experience & future research with continue to advance the care of birds
- Attend CE wet labs to enhance skills
- Thank the internet for some great images
- Publish what you see, it is easier than you think