Montesinos, A., Encinas, T., Ardiaca, M., Gilabert, J. A., Bonvehí, C., & Orós, J. (2019). Pharmacokinetics of meloxicam during multiple oral or intramuscular dose administration to African grey parrots (Psittacus erithacus). *American journal of veterinary research*, *80*(2), 201-207.

**OBJECTIVE** To determine the pharmacokinetics of meloxicam in African grey parrots (*Psittacus erithacus*) during administration of multiple doses.

**PROCEDURES** Meloxicam was administered at each of 3 dosages (1 mg/kg, IM, q 24 h, for 7 days; 1 mg/kg, PO, q 24 h, for 12 days; and 1.6 mg/kg, PO, q 24 h, for 7 days) with an 8-week washout period between treatments (n=6 Af greys). Blood samples were collected 12 and 24 hours after each drug administration (times of presumptive peak and trough drug concentrations) for pharmacokinetic analysis. Birds were visually assessed during all experiments and monitored for changes in selected plasma and urine biochemical variables after administration of the drug at 1.6 mg/kg.

**RESULTS** Mean trough plasma concentrations at steady state were 10.7 and 9.16 μg/mL after meloxicam administration at 1 mg/kg, IM, and 1 mg/kg, PO, respectively. Plasma drug accumulation was evident (accumulation ratios of 2.04 ± 0.30 [IM treatment] and 2.45 ± 0.26 [PO treatment]). Plasma and urine *N*-acetyl-β-d-glucosaminidase activities were significantly increased at the end of meloxicam treatment at 1.6 mg/kg.

**CONCLUSIONS AND CLINICAL RELEVANCE** Plasma concentrations of meloxicam were maintained at values greater than effective analgesic concentrations described for other avian species. Although **administration of meloxicam at a dosage of 1 mg/kg IM and PO daily for 1 week and 12 days, respectively, was not associated with adverse clinical effects** in this population, further studies are needed to assess the efficacy and safety of the drug during prolonged treatment and the clinical relevance of its accumulation.

Question:

Which of the following is true regarding the pharmacokinetics and pharmacodynamics of meloxicam in birds?

1. Meloxicam was associated with increased prostaglandin levels in lipopolysaccharide-challenged cockatiels (*Nymphicus hollandicus*).
2. Oral administration to captive lesser flamingos (*Phoeniconaias minor*) resulted in a shorter half-life compared to intramuscular administration.
3. Repeated oral dosing in African grey parrots (*Psittacus erithacus*) was not associated with adverse clinical effects.
4. Sustained-release meloxicam extends the interval between treatments as compared to the regular formulation in American flamingos (*Phoenicopterus ruber*).
5. Evaluation of meloxicam residues in eggs following administration to domestic chickens (*Gallus gallus domesticus*), showed no withdrawal time is required.

Answer: C

Distractors from the following articles:

Gasthuys, E., Houben, R., Haesendonck, R., De Baere, S., Sys, S. U., Morrens, J., & Antonissen, G. (2019). Development of an in Vivo Lipopolysaccharide Inflammation Model to Study the Pharmacodynamics of COX-2 Inhibitors Celecoxib, Mavacoxib, and Meloxicam in Cockatiels (Nymphicus hollandicus). *Journal of avian medicine and surgery*, *33*(4), 349-360.

Sim, R. R., & Cox, S. K. (2018). Pharmacokinetics of a sustained-release formulation of meloxicam after subcutaneous administration to American flamingos (Phoenicopterus Ruber). *Journal of Zoo and Wildlife Medicine*, *49*(4), 839-843.

Zordan, M. A., Papich, M. G., Pich, A. A., Unger, K. M., & Sánchez, C. R. (2016). Population pharmacokinetics of a single dose of meloxicam after oral and intramuscular administration to captive lesser flamingos (Phoeniconaias minor). *American journal of veterinary research*, *77*(12), 1311-1317.

Souza, M. J., Bailey, J., White, M., Gordon, K., Gerhardt, L., & Cox, S. K. (2018). Pharmacokinetics and egg residues of meloxicam after multiple day oral dosing in domestic chickens. *Journal of avian medicine and surgery*, *32*(1), 8-12.

Summa, N. M., Guzman, D. S. M., Larrat, S., Troncy, E., Bird, D. M., Lair, S., & Fitzgerald, G. (2017). Evaluation of high dosages of oral meloxicam in American kestrels (Falco sparverius). *Journal of avian medicine and surgery*, *31*(2), 108-116.

**Abstract**: To evaluate the toxicity of short-term high doses of meloxicam in American kestrels (Falco sparverius), 32 male captive-born, 1- to 4-year-old American kestrels were randomly assigned to 4 groups: 3 groups treated with meloxicam (n = 9 per group) and a control group (n =5). Meloxicam was administered orally via feeding tube in the proventriculus at 2, 10, and 20 mg/ kg every 12 hours for 7 days for the treatment groups, while the control group received saline solution. The birds were evaluated for the presence of clinical signs, abnormalities in the complete blood cell count and in the plasma biochemical panel for the 20-mg/kg group, and gross and histopathologic lesions. **No clinical signs or mortality were observed in any group. No significant differences of clinical relevance were found in results of the packed cell volume, total solids, and biochemical panel, and no evidence of renal toxicity was found in the treatment or control groups. A significant correlation was found between hepatic lipidosis and meloxicam dose** (P =.02). **Two of 9 birds in the 20-mg/kg group developed gastric ulcers, although this result was not significant.** None of the birds in the 2- and 10-mg/kg groups had similar lesions. **Finally, meloxicam dosages up to 20 mg/kg did not result in nephrotoxicity in American kestrels.** Further toxicologic studies to evaluate hepatotoxicity and gastrotoxicity of meloxicam in avian species are needed.

Question:

Which of the following is true regarding the administration of high dosages of oral meloxicam to American kestrels?

1. Mortality was observed following repeated dose administration.
2. Hepatic lipidosis was correlated with meloxicam dose.
3. All birds developed ventricular ulcers and nephrotoxicity.
4. Urine *N*-acetyl- β-d-glucosaminidase activities increased at high dosages.
5. Packed cell volume decreased significantly over time.

Answer: B

**Evaluation of the thermal antinociceptive effects and pharmacokinetics after intramuscular administration of buprenorphine hydrochloride to cockatiels (Nymphicus hollandicus).**

Guzman DS, Houck EL, Knych HK, Beaufrère H, Paul-Murphy JR.

American journal of veterinary research. 2018;79(12):1239-1245.

Buprenorphine 0.6 mg/kg IM had which effect in cockatiels (Nymphicus hollandicus)?

A. Increased thermal withdrawal at 9 hours

B. Increased agitation at 9 hours

C. Increased sedation at 9 hours

D. Maximum plasma concentration at 9 hours

E. Target plasma concentrations at 9 hours

Answer: E - > 1ng/ml is therapeutic in humans and American kestrels and was maintained in cockatiels up to 9 hours

A. no effect on thermal nociception was seen (so possibly this is not the therapeutic plasma concentration in cockatiels)

B, C. No agitation or sedation was seen.

D. Max plasma conc was achieved by 5 minutes.

**Pharmacokinetics of hydromorphone hydrochloride after intramuscular and intravenous administration of a single dose to orange-winged Amazon parrots (Amazona amazonica).**

Sanchez-Migallon Guzman, D., Knych, H., Douglas, J., & Paul-Murphy, J. R.

*American journal of veterinary research*, 2020;81(11):894-898.

In orange-winged Amazon parrots, which of the following is expected 3 hours after hydromorphone administration at 1 mg/kg IM.

A. Nausea-like behaviors, ataxia, pupillary constriction, and agitation

B. Non-therapeutic plasma concentrations due to low bioavailability

C. Non-therapeutic plasma concentrations due to slow time to Cmax

D. No change in thermal withdrawal latency due to low plasma concentrations

E. No change in thermal withdrawal latency due to rapid elimination

Answer: E

1 mg/kg IM reaches theoretical therapeutic plasma conc (> 1ng/ml) rapidly and maintains up to 6 hr

Increased thermal withdrawal latency was seen up to 3 hours at 1 mg/kg IM

High bioavailability, rapid time to Cmax, rapid elimination but maintains plasma conc up to 6 hr

Compare the use of buprenorphine for analgesia in cockatiels (*Nymphicus hollandicus)* and American kestrels (*Falco sparverius*).

* Cockatiel:
  + achieved therapeutic plasma concentrations for at least 9 hours after 0.6 mg/kg IM
  + no effect on withdrawal time with 0.6, 1.2, or 1.8 mg/kg IM
  + no sedation or agitation caused by above doses
* Kestrel:
  + 0.1, 0.3, and 0.6 mg/kg IM provided increased withdrawal latency for at least 6 hrs
  + 0.6mg/kg IM and IV exceeded therapeutic plasma concentrations for at least 9 hrs
  + 0.6mg/kg causes mild sedation
  + buprenorphine SR
    - 1.8mg/kg IM increased thermal thresholds at 6, 12, and 24 hours
    - resulted in mild sedation
    - slow onset of action - no effect at 1.5hr

A pharmacokinetic analysis of a single injection of fentanyl citrate in red-tailed hawks (Buteo jamaicensis) and Hispaniolan Amazon parrots (Amazona ventralis) showed what difference between species?

1. Elimination was much slower in hispaniolan amazon parrots
2. Fentanyl did not reach target concentrations in either species
3. Fentanyl does not appear to reduce mean alveolar concentration of isoflurane in birds
4. Anesthetic recovery was prolonged with the use of fentanyl
5. Fentanyl concentrations were significantly higher in red tailed hawks

Answer: E

After administration of lipopolysaccharides (LPS) in cockatiels (Nymphicus hollandicus), which of the following non-steroidal anti-inflammatory drugs (NSAIDs) most effectively inhibited prostaglandin E2 (PGE2)?

1. Meloxicam
2. Mavacoxib
3. Celecoxib
4. All were equally effective
5. None of these NSAIDs inhibited PGE2 concentrations

Answer: A

**Practice Question:**

Which of the following is targeted by grapiprant mechanism of action?

1. Cyclooxygenase (COX)‐1 inhibition
2. Cyclooxygenase (COX)‐2 inhibition
3. Arachidonic acid activation
4. Gamma aminobutyric acid (GABA)
5. Prostaglandin E2 receptors

Answer: E

*Which drug has been shown to have equivalent analgesic efficacy to meloxicam in Muscovy ducks with arthritis? Why might you pick it over meloxicam in a geriatric individual?*

Answer: Tramadol, kidney friendly