



Antibiotic and Analgesic Use in Wild Animals

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Case: BIRD



A juvenile Blue Jay is brought to you by a family who saw their cat playing it. You examine the bird but do not find any significant findings.

What is important to consider? Are antibiotics necessary?

No lesion; No treatment?

- There is one rule to remember in cases of a wild animal exposed to a cat or dog : **ALWAYS TREAT WITH ANTIBIOTICS!**
- This rule applies especially to birds. The reason is because, their skin is so thin, and cat teeth are so fine, you can easily miss a small puncture wound.

20-80% of all cat bites will become infected compared with **3-18%** of dog bite wounds.

Act fast!

- The other thing to remember in bird cases is to act quickly. Their metabolism is higher than mammals and they tend to develop infections faster.
- This fact is also important to consider when deciding the dose and administration of a drug; you should not just extrapolate from mammal data.

Some facts about cat and dog bites

By doing bacteriological analysis of infected dog and cat bites in humans, Talan *et al.* (1999) collected the following results (only most common bacteria listed):

Bacteria	Dog bite (number of patient in %)	Cat bite (number of patient in %)
<i>Pasteurella</i>	50	75
<i>P. multocida</i> subs <i>multocida</i>	12	54
<i>P. multocida</i> subs <i>septica</i>	10	28
<i>P. canis</i>	26	2
<i>Streptococcus</i>	46	46
<i>Staphylococcus</i>	46	35
<i>S. aureus</i>	20	4
<i>Fusobacterium</i>	32	33
<i>Bacterioides</i>	30	28

Some facts about cat and dog bites

- A combination of aerobes and anaerobes were isolated from 56 % of the wounds.
- Also, many species isolated from infected bites, including staphylococci and most anaerobes, were β -lactamase producers.
- Considering all that, what would be the antibiotics to use?

Empirical therapy for dog bites and cat bites should be directed against *pasteurella*, *streptococci*, *staphylococci* and *anaerobes*, and should be β -lactamase resistant.

Antibiotics suggestions

Antibiotic combinations to use for dog or cat bites

β -lactam antibiotic and a β -lactamase inhibitor

Second-generation cephalosporin with anaerobic activity

Penicillin and a first-generation cephalosporin

Clindamycin and a fluoroquinolone

Empirical treatment with penicillin, ampicillin, a first-generation cephalosporin or a fluoroquinolone alone is not appropriate

IM or SC ?

- Some concerns have recently appeared in the literature regarding pain and muscle necrosis associated with IM administration of drugs.
- More studies are necessary to assess that fact. Until then, SC injections are recommended if possible.

More cases with BIRDS !

You receive a young bald eagle with a fracture of the tibiotarsus with some open skin lesions around the area of the fracture.



What would be your antibiotic of choice to prevent/treat any bacteria contamination of the fracture ?

What are the questions you should ask yourself ?

- First, **what bacteria** are more likely to be present in that lesion ?
 - **Gram + and anaerobic** bacteria are your major concern with a skin wound/open fracture.
- Second, **which antibiotics** have a **good distribution to bones** (since you absolutely want to prevent osteomyelitis)?

Answers !

- There are **2 classes** of antibiotics that can be used to address both questions :
 - Lincosamides (Clindamycin)
 - Gram + and anaerobe spectrum
 - Excellent distribution in bones and synovial fluids
 - Penicillins/Cephalosporins
 - Gram + and anaerobe spectrum
 - Good distribution in bones and synovial fluids
 - Clavamox is a good choice, especially if there is any *Staphylococcus* in the wound

Do you always treat blindly ?

NO !

- **Always try to do a culture** with orthopedic cases since there **might be resistance** to the antibiotics you are using.
 - For example, a strain of *Staph* could be resistant to the Clindamycin you are using.
 - Resistance means **treatment failure** if you are not able to identify it !

What about analgesia in both cases?

- Administration of analgesics is **necessary** in birds that have experienced a **fracture** or **soft tissue trauma**.
- However, some analgesic drugs will not have the same effect on a bird as on a mammal.

What you should know about opioids in birds...

- Studies in pigeons have demonstrated that birds have **more *kappa* opioid receptors** than *mu* opioid receptors.
- What does that imply?
 - Birds **do not respond** to *mu* agonists (morphine, buprenorphine or fentanyl) in the same manner as mammals.
 - **Butorphanol** has been shown to be a **useful analgesic** in birds since it is a *kappa* agonist.

Liposome-encapsulated butorphanol for long lasting effects in birds

- Sladky et al. (2006) studied the effects of regular butorphanol tartrate compared with **liposome-encapsulated butorphanol (LEBT)**.
- In their study, SC administration of LEBT provided **analgesia** and **detectable serum concentrations** in parrots for up to 5 days.
 - This finding is of great interest with birds, especially wildlife, since they are **highly stressed** with handling.
 - Use of LEBT (if available) means **long term pain management** with much **less manipulation** required.

NSAIDS

- **NSAIDS alone** are indicated for the relief of **mild to moderate pain**.
- Owing to a ceiling effect, NSAIDS should **never be used alone after major surgery**; they should be **combined with opioid analgesics**.
- Most commonly used NSAIDS in birds:
 - Meloxicam (Metacam)
 - Carprofen (Rimadyl)

Case: RABBIT



One week later, the same cat comes home with a baby rabbit. It seems depressed.

You see a skin wound between his shoulder blades and on the left leg, but no fracture is found. You also feel some abdominal distension.

What is important to consider? Which antibiotic and analgesic treatment would be appropriate?

Rabbit Gastroenterology

- The caecum and colon have well-established **strict anaerobes** and some **facultative anaerobes**.
- An important factor in the bacterial pathogenesis of rabbit diarrhea is the **establishment of an infective dose of intestinal pathogens** (dysbiosis)
 - Most likely *E. coli* or *C. spiroforme*
- The **use of therapeutic antibiotics**, especially gram-positive and anaerobic spectrum drugs, **may produce a dysbiosis**.

Antibiotic associated Dysbiosis

- Mechanisms for antibiotic-associated enteritis include (some study results) :
 - Alteration in intestinal mobility and enterocyte ion transport with lincomycin, clindamycin, erythromycin and gentamicin.
 - Altered microbial flora and overgrowth of *C. difficile* following oral ampicillin.
 - Altered microbial flora and overgrowth of *C. sporogenes* following intravenous cephalosporins.

Antibiotic associated Dysbiosis (con't)

- These findings suggest that many antibiotics should be **avoided** in rabbits for systemic uses:
 - Ampicillin, Amoxicillin, many Penicillins
 - Clindamycin, Erythromycin, Fipronil and Lincomycin
 - Gentamicin
 - Cephalosporins

What else can we use then ?

- General antibiotic therapy
 - **TMS**
(may cause tissue necrosis if SC)
 - **Enrofloxacin**
(may cause arthropathies in young, SC and IM can cause muscle necrosis or sterile abscesses)
- Treatment for anaerobic infections
 - **Metronidazole** (can be combined with azithromycin)
- General antibiotic therapy (to be used with caution)
 - Penicillin G (parenteral use only) once a week
 - Cephalexin (parenteral use only)

Is that cat bite painful ?

- **Pain recognition** in small mammals, such as rabbits and rodents, **can be challenging** because many small mammals are prey species and they have evolved to **hide signs of illness and pain**.
- **Bruxism** (teeth grinding) is a sign of severe pain in rabbits, often gastrointestinal in origin.

The « pain management » Dilemma

- **Opioids** working on *Mu* and *Delta* receptors have the potential to cause **ileus in rabbits**.
- However, **pain management** is particularly **important** in rabbits because when in pain :
 - They often develop anorexia and ileus.
 - They are more prone to stress-induced clostridium overgrowth in the bowel, which can lead to toxemia, diarrhea and potentially death.

Then, what should I do ?

- One should not be afraid to treat pain in rabbits.
- Pain should be addressed with a **combination of NSAIDS and Opioids.**
- **Food intake and hydration status** should always be closely monitored.

Pain management

- Opioids -

- Opioids used with rabbits include :
 - **Butorphanol**
 - Since it is a *Mu* antagonist, it **should not cause ileus** in rabbits, however it's analgesics properties are questioned
 - **Repeated doses** are required since it's duration is about 2 to 4 hours

Pain management

Opioids (con't)

– Buprenorphine

- Mixed agonist-antagonist

– Hydromorphone

- Excellent analgesic
- Can be reversed using naloxone or partially reversed using butorphanol

Pain management

- Tramadol -

- There are almost no studies done on the use of this drug in small mammals or birds.
- Doses have been **extrapolated** from humans (10mg/kg). However, a dose of 11 mg/kg PO **did not result** in plasma concentration high enough to provide sufficient analgesia for a clinically acceptable period.
- Studies in raptors are currently being conducted.

Pain management - NSAIDS -

- NSAIDS used with rabbits include :
 - **Carprofen**
 - **Meloxicam** (most commonly used in small mammals)
 - Both products have PO and injectable formulations
- Advantages include :
 - Not a controlled drug and **long duration** of action
- Disadvantages include :
 - Should not be used if hypovolemia, bleeding disorders, renal disease or if severe surgical hemorrhage is anticipated.

Case: REPTILE



A box turtle is brought to you with a shell fracture. She has been hit by a car. There is no opening of the abdominal cavity and you try your best to stabilize the fracture lines by gluing metal stabilizing bars on the shell.

What is important to consider? Which antibiotic and analgesic treatment would be appropriate?



First, how to deal with the *Salmonella* issue ?

Remember *Salmonella spp.* is a zoonotic agent.

ALWAYS REMEMBER :

When manipulating any kind of reptile, take appropriate disinfection and hygiene measures.

Do we treat *Salmonella*?

- Another important fact is that *Salmonella spp.* is a component of the **indigenous microflora** of reptiles and it rarely causes clinical signs in reptiles.
- It is not recommended to treat Salmonellosis because of the risk of creating antibiotics resistance in indigenous flora, including *Salmonella*.

General Considerations

- Bacteria commonly associated with infections in turtles are often **Gram-negative** opportunists of the Enterobacteriaceae family, therefore your choice of antibiotics should include those effective against these specific bacteria.
 - The **cutaneous microflora** of chelonian include : *Pseudomonas*, *Proteus*, *Aeromonas* (especially in aquatic chelonians), *Providencia*, *Morganella*, *Salmonella* and *Klebsiella*.
- These bacteria are sensitive to aminoglycosides, piperacillin, third and fourth generation cephalosporins, quinolones, trimethoprim and chloramphenicol.

General Considerations (con't)

- Anaerobes are increasingly recognized as important reptile pathogens.
 - **Metronidazole, chloramphenicol** and many **β -lactams** antibiotics are potentially effective in treating such infections.

General Considerations (con't)

- In general, Ceftazidime (a third generation cephalosporine) and Enrofloxacin (a quinolone) are probably the best choices.
 - They are relatively **safe**,
 - Bacteria more frequently present **are susceptible** to these antibiotics,
 - Can be used in a **multitude of clinical presentations**
 - Wounds (skin/shell), stomatitis, respiratory tract infections, osteomyelitis/septic arthritis, otitis media and septicemia .

Antibiotic of choice

- Ceftazidime -

- Excellent against respiratory infection with *Staphylococci* and *Streptococci*.
- Enhanced activity against **Gram-negative bacteria**.
 - Effective against *Pseudomonas* and *Pasteurella*.
- **Widely distributed** in the body (bone, bile, skin and kidney).
- Can be used IM every 72 hours (20 mg/kg).

Antibiotic of choice

- Enrofloxacin -

- Wide spectrum against **Gram-negative** and **Gram-positive** bacteria.
- Indications: *Pasteurella spp.*, *Pseudomonas spp.*, *Mycoplasma spp.* and *Chlamydia spp.*
- **Widely distributed** within the body, including the eye and central nervous system.

Antibiotic of choice

- Enrofloxacin -

- **Keep in mind :**
 - Poor activity against *Enterococcus spp.*
 - Poor activity against anaerobic bacteria.
 - **Contraindicated** at high doses in **growing animals** as they may cause cartilage abnormalities.

Indiscriminant Use of Antibiotics

Antibiotics in reptiles should **ALWAYS** be used with many precautions since there is a **larger risk of antibiotics resistance** of the indigenous flora, more **specifically *Salmonella***.

Impact of reptilian metabolism on drug dosage

- The metabolic rate of reptiles is **significantly lower** than in endothermic vertebrates.
- Snakes maintained at 37°C have a metabolic rate **nearly 80% lower** than mammals of the same size.
- A mammalian dose may last **up to 10 times longer** in a reptile because of the slower metabolism.
- Body temperature can also **affect the half-life** of a drug, with the half-life increasing with decreasing body temperature.
 - At a higher body temperature, an antibiotic will reach its MIC faster but will also need to be administered more often, the reverse being also true...

Impact of reptilian metabolism on drug dosage (con't)

- This implies that drug dosage should not be extrapolated from mammalian formularies since it may lead to overdosage.
- When treating reptilians, it is strongly advised to refer to exotic's formularies for the dose and the interval that should be used .for a specific drug .

The Renal Portal System

- It is a component of the venous system of reptiles that can affect the drug **plasma concentration** and the distribution to the kidneys.
- The blood from the caudal regions of the body can **shunt** directly into the kidneys by the renal portal vein or bypass the kidneys and enter the liver and central venous system.

The Renal Portal System (con't)

- In reptiles, the tubular cells are perfused by the renal portal veins and also by afferent arterioles leaving the glomeruli.
- In times of water conservation, arginine vasotocin decreases glomerular filtration and increases tubular water resorption. Since reptiles do not have a Loop of Henley, they are not able to concentrate urine. As a result, the renal portal veins are essential to prevent tubular ischemic necrosis.

The impact of the Renal Portal System

- When administering a drug to a patient in the **hind legs**, the drug can **bypass** the liver and central venous system and go directly to the kidneys with a higher concentration - most likely during water conservation. Consider this with dehydrated turtles.
- The belief is that, as a result, some drugs can lead to a **nephrotoxicity** and others can be eliminated **more rapidly**, leading to **subtherapeutic drug levels**.

What to do?

- More data needs to be collected to fully understand the impact of the renal portal system on nephrotoxicity and pharmacokinetics in reptiles.
- To be safe, cranial sites should be used instead of the hind limbs or tail.

Are all reptiles the same ?

- The **reptilian class** is composed of 4 orders
 - Chelonians (turtle) – **about 300 species**
 - Squamates (lizards and snakes) – **about 7900 species**
 - Crocodilia - **23 species**
 - Sphenodontia – **2 species**
- With such a large class, we can assume that there would be **differences** between orders and species concerning drug metabolism.
 - Would you give the same dosage to a dog and a horse?
- Try to use a dosage that applies to a specific order or, even better, a specific species.

Reptile Pain Management

- Pain control in reptile can be especially **challenging**
 - Evaluation of pain in reptile is difficult because we have not identified typical pain behavior patterns in the reptile patient.
 - Information concerning pain control in reptile is scarce.
- **However, this should not prevent you from using pain control drugs on your reptile patient.**
- General rule of thumb: « *If it would hurt you, chances are good that it will also hurt the animal.* »

Reptile Pain Management - Turtle -

- Drugs mostly commonly used:
 - Buprenorphine
 - Reference books usually indicate to use 0.02 mg/kg, however a recent study indicate that 0.075 to 0.1 mg/kg SC should be used for analgesia q24hrs
 - Morphine
 - Carprofen
 - Meloxicam
- And what about Butorphanol?
 - NOT EFFECTIVE

Reptile Pain Management

- Snake -

- Drugs most commonly used:
 - Buprenorphine
 - Butorphanol
 - 5 mg/kg IM has not shown any effect
 - 20 mg/kg IM seems effective, however, this is a high dose and caution must be taken when used on a patient
 - Carprofen
- **And what about :**
 - Morphine?
 - **NOT EFFECTIVE**
 - Meloxicam?
 - **0.3 mg/kg IM has not shown any effect on snakes**

Conclusion

- We hope that this introduction to wildlife analgesics and antibiotics will help you to get started.
- For more information, we encourage you to consult our reference list (certainly not exhaustive.)



GOOD LUCK !!!

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