Antimicrobial Therapy for Birds

Lauren Powers, DVM, DABVP
Carolina Veterinary Specialists
Huntersville, NC

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Antimicrobial agents are commonly used in avian practice for the treatment of certain infectious diseases. Despite limited pharmacokinetic and safety data in birds, it is still the clinician's responsibility to administer, dispense, and prescribe the most effective and safe antimicrobial agent based on current evidence. Recent developments in avian antimicrobial therapy now offer minimally invasive or less invasive methods of treatment, including medicating of food and drinking water and slow-release formulations. Dosing strategies reported in this manuscript are greatly limited for the purposes of this discussion. Please refer to current drug formularies for a complete list of suggested dosages.

Selected antibiotic agents

- **Fluoroquinolones** – Bactericidal, concentration-dependent efficacy. Banned from use in food-producing animals such as poultry (eg. backyard chickens, Pekin ducks)
    - **Enrofloxacin** – Bactericidal against both Gram-positive and Gram-negative bacteria. Less activity against Gram-positive organisms. Poor efficacy against anaerobes. Occasionally used in the treatment of other avian bacterial diseases such chlamydiosis, mycoplasmosis, and mycobacteriosis. Pharmacokinetics have been evaluated in several avian species. No commercially available liquid formulation but the drug can be compounded. Stable for 56 days at room temperature in corn syrup and water, cherry syrup and water, or a commercially available compounding syrup. Can also be dosed in the drinking water (less effective).
    - **Others** – Few pharmacokinetic or safety studies have been done for other fluoroquinolones in avian species. Marbofloxacin has longer elimination half-life, greater bioavailability, and tissue penetrating ability than enrofloxacin but has not been extensively studied in birds. 2.0 to 2.5 mg/kg PO q24hr was considered effective for most Gram-negative bacterial infections in Muscovy ducks. Orbifloxacin has a similar antibiotic spectrum to enrofloxacin and marbofloxacin. It has excellent oral bioavailability and tissue penetration in Japanese quail. Ciprofloxacin is an active metabolite of enrofloxacin in some avian species and can be used, but studies have not been conducted in companion avian species.
- **Tetracyclines** – Bacteriostatic, time-dependent antimicrobial efficacy.
    - **Doxycyline** – Semi-synthetic tetracycline, highly lipid soluble. First line of choice for the treatment of avian chlamydiosis. Treatment duration for avian chlamydiosis is 30 days for budgerigars and 45 days for other psittacine species. Refer to the most recent edition of the "Compendium of Measures to Control *Chlamydophila psittaci* Infection among Humans (Psittacosis) and Pet Birds (Avian Chlamydiosis)" for more information on treatment options for avian chlamydiosis. 400 mg/L in the drinking water was effective for the treatment of oral spiral bacteria in cockatiels.
    - **Others** – Other tetracycline drugs are less commonly used in birds. Chlortetracycline-medicated feed historically has been used to treat avian chlamydiosis. Oxytetracycline is available in a long-acting injectable formulation (Liquamycin LA-200, Zoetis, Kalamazoo, MI, USA) but can cause injection site tissue necrosis.
- **Macrolides** – Bacteriostatic. Time-dependent antimicrobial efficacy. Most effective against Gram-positive and anaerobic bacteria.
    - **Azithromycin** – Broad spectrum against Gram-positive and Gram-negative bacteria. Also effective against spirochetes and some anaerobes. Effective against *Chlamydia psittaci* in cockatiels at 40 mg/kg PO q48hr x 21 days.
    - **Others** – Pharmacokinetic and safety information are lacking for other macrolides such as erythromycin and lincomycin, and so they are less frequently used and recommended in companion birds. Erythromycin is marketed for use in sick birds and was available over-the-counter (Ornacyn-Plus, Mardel Laboratories, Glendale Heights, IL, USA) but may no longer be available. Tylosin powder (Tylan, Elanco Animal Health, Indianapolis, IN, USA) is available over-the-counter for the treatment of respiratory illness in chickens.
- **Lincosamides** – Bacteriostatic. Most effective against Gram-positive and anaerobic bacteria.
    - **Clindamycin** – The most commonly used lincosamide in birds. Effective against Gram-positive cocci and obligate anaerobes. No studies have been done in psittacine species but the drug has been investigated in pigeons and a suggested dosage was 100 mg/kg PO q6hr in pigeons

- **Potentiated sulfa drugs** – The combination is probably bacteriostatic at dosages used in birds but can be bactericidal at higher dosages. Time-dependent efficacy. Broad spectrum of activity, effective against Gram-positive and Gram-negative bacteria and some anaerobes and parasites.
    - **Trimethoprim-sulfamethoxazole** – Popular for use in companion birds, particularly pediatric patients. Available in a liquid form but high volumes often required. Pharmacokinetic studies have not been done in psittacine birds.
- **Penicillins** – Bactericidal. Time-dependent antimicrobials. Effective against many Gram-positive bacteria but Gram-negative resistance is common. Extended-spectrum and combination drugs often used in avian medicine to enhance Gram-negative spectrum. Major disadvantages are cost and frequency of administration, as the elimination half-life is usually very short.
    - **Amoxicillin-clavulanic acid** – Achieved therapeutic plasma concentrations in Amazon parrots when dosed at 125 mg/kg PO q8hr
    - **Piperacillin** – Demonstrates excellent activity against some Gram-negative bacteria. Often combined with tazobactam (eg. ZOSYN, Pfizer, Philadelphia, PA, USA).
- **Cephalosporins** – Bactericidal, time-dependent efficacy. First-generation drugs have good Gram-positive spectrum, third-generation drugs have excellent Gram-negative spectrum. Like the penicillins, most cephalosporins are rapidly eliminated, requiring frequent dosing of at least three times daily. Extra-label use banned in major food-producing animals including chickens and turkeys as of 2012.
    - **Cephalexin** – First generation cephalosporin. Good Gram-positive spectrum, useful for treating infections with sensitive strains of *Staphylococcus aureus*.
    - **Cefovecin sodium (eg. Convenia, Zoetis, Kalamazoo, MI, USA)** – Third generation cephalosporin. Highly protein bound in dogs and cats, which results in long elimination half-life. Elimination half-life in chickens was very short (0.9 hours vs. 5.5 days in dogs). Similar findings in African grey parrots and red kites. Half-life in greys at 20 mg/kg IM was 64 minutes. Cannot be recommended in birds at this time.
    - **Ceftiofur crystalline-free acid (eg. Excede, Zoetis, Kalamazoo, MI, USA)** – Third generation cephalosporin. Bactericidal. Broad-spectrum. Oil base allows extended release. In helmeted guineafowl, plasma concentrations remained above MIC for many bacterial pathogens for at least 56 hours in all birds, and a dosage of 10 mg/kg IM q72 hours was suggested for this species. In red-tailed hawks, plasma concentrations were maintained above targeted ranges for 36 to 45 hours at 10 mg/kg IM and for 96 to 120 hours at 20 mg/kg IM. In black ducks, plasma concentrations were maintained above target for 73.3 hours at 10 mg/kg IM.
- **Aminoglycosides** – Bactericidal, concentration-dependent efficacy. Generally have excellent Gram-negative efficacy, not effective against anaerobes. Not absorbed from the GI tract and must be injected. Disadvantages include increased risk of toxicity such as nephrotoxicity. Gentamicin and amikacin are the most commonly used aminoglycosides in companion birds.

Selected antifungal agents

- **Azoles –** Inhibit synthesis of ergosterol in fungal cell membranes by inhibiting fungal cytochrome P450 isoenzyme.
    - **Itraconazole** – Probably the most commonly used antifungal in companion birds, particularly for the treatment of aspergillosis. Hepatic conversion into a number of active metabolites. Pharmacokinetics have been done in different avian species, species-specific variability evident. Use only the commercially available liquid or capsules, extemporaneous compounding not advised.
    - **Fluconazole** – Has very good activity against *Candida* spp., *Cryptococcus* spp., *Blastomyces* spp. Poor *in vitro* activity against most filamentous fungi. Well absorbed from the GI tract. Very water soluble. Minimally metabolized, excreted unchanged by the kidneys.
    - **Voriconazole** – Newer generation antifungal agent. Good *in vitro* and *in vivo* activities against yeast and filamentous and dimorphic fungi including *Candida* spp., *Cryptococcus neoformans*, and *Aspergillus* spp. Little to no efficacy against zygomycetes. Nonlinear pharmacokinetics with saturable hepatic metabolism, indicating that species-specific studies are needed.
    - **Others** – Use of ketoconazole and enilconazole is occasionally reported in the literature in companion avian species and raptors, but pharmacokinetic and safety data are lacking.
- **Terbinafine** – Blocks ergosterol sysnthesis by interfering with squalene monooxygenase and is believed to be fungicidal. Not mediated through cytochrome P450. *In vitro* activity against *Microsporum* spp., *Trichophyton* spp.,

Candida spp., *Aspergillus* app., *Blastomyces* spp., and *Histoplasma* spp. Used primarily for dermatophytosis in veterinary medicine, but is also used in the treatment of aspergillosis. Can be administered orally or nebulized.

- **Amphotericin B** – Polyene macrolide antifungal agent, most often used for the treatment of disseminated aspergillosis and candidiasis. Currently the only fungicidal drug used in veterinary medicine effective against systemic infections. Poor GI absorption. The major risk is the potential for nephrotoxicity. Most frequently used as an injectable systemic treatment for aspergillosis in companion birds. Also administered orally for the treatment of macrorhabdosis (infection with the proventricular ascomycetous yeast *Macrorhabdus ornithogaster*).
- **Nystatin** – Polyene antifungal agent. Popular treatment for gastrointestinal yeast infections in birds, particularly in pediatric patients. Minimally absorbed from the GI tract.

Selected antiparasitic agents

- **Avermectins** – Macrocyclic lactone derivatives with potent anthelmintic activity. Few pharmacokinetic and safety studies have been conducted in companion avian species. Ivermectin is popular for the treatment of air sac mites in finches and canaries and for the treatment of *Knemidocoptes* (scaly face, scaly leg) mite infestations. It is generally dosed orally. Spot-on application to the featherless tract over the jugular vein is popular but carries a significant risk of inaccurate and excessive dosing. The topical avermectin selamectin has reportedly been used for the treatment of knemidocoptic infections in budgerigars and for the treatment of air sac mites in zebra finches. Moxidectin (SCATT, Vetafarm, Wagga Wagga, NSW, Australia) is not currently available as a FDA-approved drug in the United States but is popular for use as a topical treatment for mite infestations. Pharmacokinetics of topical selamectin have been investigated in helmeted guineafowl and the drug appeared to maintain effective plasma concentrations for 19 days and no adverse effects were seen.
- **Benzimidazoles** – Broad class of highly effective anthelmintics and widely popular in avian medicine for the treatment of enteric parasitic infections such as infections with ascarids and *Capillaria* spp. The most popular benzimidazole agents used in companion avian medicine are fenbendazole and albendazole. Fenbendazole is also conveniently available in commercially available liquid formulations. Radiomimetic dosage-dependent bone marrow suppression has been reported with the use of benzimidazoles in avian species including pigeons, doves, and cockatiels.
- **Nitroimidazoles** – This class of drugs demonstrates both antiprotozoal and antibacterial activity. Metronidazole is frequently used for the treatment of anaerobic infections in companion birds. Carnidazole and ronidazole are not available as FDA-approved drugs in the United States, but carnidazole is widely used internationally for the treatment of trichomoniasis in racing and show pigeons. The use of nitroimidazole drugs such as metronidazole is prohibited in food-producing animals including poultry such as backyard chickens.

Suggested reading

Flammer K. Antibiotic drug selection in companion birds. J Exot Pet Med 2006;15(3):166–176.

Hahn A, D'Agostino J, Cole G, et al. Pharmacokinetics of selamectin in helmeted guineafowl (*Numida meleagris*) after topical administration. J Zoo Wildl Med 2014;45(1):176–178.

Hawkins MG, Barron HW, Speer BL, et al. Birds. In: Carpenter JW (ed). Exotic Animal Formulary, 4th ed. Elsevier, Maryland Heights, MO, 2012.

Hope KL, Tell LA, Byrne BA, et al. Pharmacokinetics of a single intramuscular injection of ceftiofur crystalline-free acid in American black ducks (*Anas rubripes*). Amer J Vet Res 2012;73(5):620–627.

Keller KA. Therapeutic review: Terbinafine. J Exot Pet Med 2012;21(2):181–185.

Keller KA. Therapeutic review: Itraconazole. J Exot Pet Med 2011;20(2):156–160.

Kirchgessner M. Therapeutic review: Amphotericin B. J Exot Pet Med 2008;17(1):54–56.

Lenarduzzi T, Langston C, Ross MK. Pharmacokinetics of clindamycin administered orally to pigeons. J Avian Med Surg 2011;25(4):259–265.

Mitchell MA. Therapeutic review: Enrofloxacin. J Exot Pet Med 2006;15(1):66–69

Mitchell MA. Therapeutic review: Azithromycin. Sem Avian Exot Pet Med 2005;14(3):212–214.

Petritz OA, Sanchez-Migallon Guzman D, WiebeVJ, et al. Stability of three commonly compounded extemporaneous enrofloxacin suspensions for oral administration to exotic animals. J Am Vet Med Assoc 2013;243(1):85–90.

Rinaldi ML. Therapeutic review: Doxycycline. J Exot Pet Med 2014;23(1):107–112.

Sadar MJ, Hawkins MG, Drazenovich T, et al. Pharmacokinetic-pharmacodynamic integration of an extended-release ceftiofur formulation administered to red-tailed hawks (*Buteo jamaicensis*). Proc Assoc Avian Vet 2014:11.

Sanchez-Migallon Guzman, D. Advances in Avian Clinical Therapeutics. J Exot Pet Med 2014;23(1):6–20.

Thuesen LR, Bertelsen MF, Brimer L, et al. (2009). Selected pharmacokinetic parameters for Cefovecin in hens and green iguanas. J Vet Pharm Therap 2009;32(6):613–617.

Watson M. Therapeutic review: Praziquantel. J Exot Pet Med 2009;18(3):229–231.