

Group Treatment Strategies for Animals in a Zoologic Setting



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KEYWORDS

- Group treatment • Zoo • Multispecies • Amphibian • Avian • Hoofstock
- Herd health • Aviary health

KEY POINTS

- Group treatments vary between taxa, but all have benefits and risks that should be considered before therapy administration.
- Treatments administered topically on or milled into food, solubilized in drinking water, and mixed into a bath are common routes of administration for groups of animals.
- Sick animals should be treated individually to ensure compliance, because group treatments are often only effective against highly susceptible pathogens.

INTRODUCTION

Providing care for groups of animals is a major part of practicing zoologic medicine. Herd health is key to the mindset of a zoo clinician no matter the species encountered, be it avian or artiodactylid. In addition to the classic examples of group treatment involving chemotherapeutics (discussed in detail later), zoo clinicians also practice herd health by preventing disease from entering the collection. Before traveling to a new institution, most animals undergo a preshipment examination, which serves as a screening tool for common infectious diseases specific to that taxa, and provides a snapshot of that individual's health. Diagnostics commonly included in a preshipment examination are a complete blood count, serum or plasma biochemistry, imaging, and fecal examination. On arrival to a new institution, most animals undergo a quarantine period, often 30 to 90 days, in addition to another thorough examination. All of these precautionary measures are vital to ensure that infectious disease does not enter an institution, and also provide the opportunity for targeted therapy if

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needed, before the animal is placed within its new social group. It is highly recommended that all animals that die within a zoologic setting receive a thorough gross necropsy with histopathology to try and determine the cause of death. Then, if an infectious cause is diagnosed, therapy for the remaining group of animals is based on the pathology findings.

Another way that zoo clinicians can try to limit the need for group treatment is to have a working knowledge of which taxa can be safely housed together. In addition to such factors as size and potential for trauma, knowledge of how certain infectious diseases interact with various species can prevent future outbreaks. For example, *Entamoeba invadens* is transmitted from clinically healthy herbivorous tortoises to snakes when they are housed together, causing the snakes to develop severe ulcerative colitis and hepatitis.¹ If a disease outbreak does occur, practicing vigilant biosecurity to try and limit transmission is key to decreasing the number of animals affected and needing treatment. Depending on the etiologic agent footbaths, isolation, and appropriate personal protective equipment may be used.²

When treatment is needed in a zoologic setting it presents unique challenges. One obstacle commonly encountered is that few pharmacokinetic studies have been performed in the species commonly found in zoos, so doses are often extrapolated from their closest domestic relative. Although extrapolation from domestics is done easily for some taxa, such as exotic canids, felids, or equids, there are species with no domestic counterpart, such as marsupials or invertebrates. Several different types of interspecies scaling have been described in the literature, with allometric scaling considered the most accurate.³ However, there are limiting factors to consider when using allometric scaling, such as the route of elimination and the extent of metabolism of the selected therapeutic agent.³ An additional challenge is that often accurate body weights cannot be obtained, so estimated weights are used, which can increase the risk of underdosing or overdosing an animal.⁴ Group treatment is not common for some taxa, such as large carnivores, and individual treatment is advised when possible. Once a dosage has been selected and a weight obtained or estimated, the next question is how to administer the drug to the animal. Treatment options are heavily dependent on the species, and are covered in detail in the following sections. Group treatment is not standard for all taxa, so only the most common species are discussed.

AMPHIBIANS

Terrestrial and aquatic amphibians may be housed in single-species or mixed species exhibits, and individually. Regardless of species, morbidity and mortality is best prevented with appropriate environments, husbandry, nutrition, and biosecurity.⁵⁻⁸ Separating ill or injured individuals from a group for individualized treatment is advised. Aquatic amphibians including premetamorphic larvae, neotenic salamanders, and aquatic newts and frogs inherently have a greater potential need for group treatments because of their aquatic existence; however, the potential exists for the need to treat a variety of amphibians as a group.

Terrestrial and aquatic amphibians living in a group may be separated for individualized treatments and this is generally well-tolerated. Individual animals may be temporarily moved out from the group enclosure to a separate enclosure for treatments and may remain separated for the duration of the treatment or be moved for short periods of time on a routine basis (Fig. 1). Individualized housing for medical care may be simplistic, but is acceptable as long as husbandry needs are adequately met.⁵ Benefits of individualized treatments are assurance of medication compliance, ability to closely monitor clinical condition, reduced risk of infectious disease spread,



Fig. 1. A Panamanian golden frog (*Atelopus zeteki*) is moved into a plastic covered container for daily medicated bath treatments. After treatments, the animal is moved back into a more elaborate enclosure.

and elimination of extraneous treatments for healthy animals or nontarget species as compared with group treatments. Risks of individualized treatments include potential social and behavioral stress, and epithelial trauma from handling.⁹

Skin of amphibians is vascular and highly permeable, allowing for gas, water, and electrolyte exchange, and should absorb medications effectively transcutaneously.^{10,11} In terrestrial and semiaquatic systems, topical medications may be administered to individuals living within the group as spot-on treatments without handling and may be a useful strategy when handling or removal from the group is not desired. Alternatively, animals may be restrained on a routine basis for medicating and be replaced back into the group. If spot-on topical medications are desired for aquatic animals, some duration of dry docking out of water is needed for the drug to absorb before being returned to water. This should not be done if the animal is unable to tolerate a period out of water because of lack of respiration or dehydration. Topical medications are particularly useful for very small animals.¹² Care should be taken to accurately calculate the intended dose. Dilute compounded drug formulations and calibrated micropipettes for delivery help facilitate small animal treatments and prevent overdosing.¹³ Evidence for spot-on topical treatments in amphibians is primarily anecdotal, but common in practice and suggested dosages are available.¹⁴

Bath treatments are a common therapeutic modality for amphibians, terrestrial and aquatic. For terrestrial species, bath treatments are achieved by placing the individual to be treated in a container, such as a vented plastic carrier, filled with the solution just to the point where it covers the ventral drink patch to allow for adequate absorption (Fig. 2). Multiple animals may be treated in the same bath simultaneously, as space and temperament allows (Figs. 3 and 4). For aquatic species, the medicated bath should ideally be separate from the animal's home enclosure to prevent treatment of nontarget species, adverse effects on the biofilter, or damage to living plants. Additionally, using an animal's home enclosure water may be necessary for aquatic species to prevent sudden changes in water quality leading to electrolyte imbalance and stress. An air stone to provide oxygenation may be considered for lengthy treatments. However, if treatment in the primary enclosure's water system is desired, medications may be added directly into the water system. After the desired length of treatment, the medicated water should be cleared by a water change or high flow rate filtration to prevent an unnecessarily long exposure.¹⁵ Typical bath treatments include electrolyte, antibiotic, and



Fig. 2. A single Houston toad (*Anaxyrus houstonensis*) soaks in an electrolyte solution with the ventral drink patch completely submerged. Ideally, the container should have a cover to prevent the animal from exiting the space and to ensure adequate contact or compliance throughout the entire treatment period.

antifungal solutions that are calculated to be a certain dosage per volume of water over a specified period of time at set intervals. For example, chytrid fungus (*Batrachochytrium dendrobatidis*) treatment may include a bath of 0.01% itraconazole (100 ppm or 1 mg/L) in an electrolyte solution for 5 minutes daily for up to 14 days.¹⁶ The total volume to be administered depends on the size container for medication and the size of animal, so that the drink patch is covered. The benefits of group bath treatments are that it is time and resource efficient and reduces handling. For topical spot-on and bath treatments, the pH of the desired medication should be checked and ensured to be neutral. This may be done with in-house pH strips to prevent caustic dermal from either acidic or alkaline products.

Injectable medications may also be administered with intramuscular or intralymphatic injections being common.¹² These routes of administration are more invasive and require additional handling compared with topical treatments, thus making these



Fig. 3. Two axolotls (*Ambystoma mexicanum*) are treated with a medicated electrolyte solution bath in tandem. These animals were moved from their primary enclosure into a clean plastic container containing the medicated solution. A 60-mL syringe is being used to apply the solution topically to the dorsum because these animals are not completely submerged for the duration of treatment.



Fig. 4. Four Houston toadlets (*Anaxyrus houstonensis*) share a medicated bath solution that is deep enough to cover the ventral drink patch within a vented plastic carrier.

less common for group treatments. Long-acting medications in depo-formulations, such as ceftiofur crystalline-free acid antibiotics, may allow for less frequent handling and minimize disruption to the amphibian group, but have not been well-studied in amphibians, so any potential use should be done with caution.

Oral medications may be given to terrestrial and aquatic individuals into the oral cavity with a syringe or pipette or gavaged deeper into the esophagus or stomach with a metal ball-tipped feeding tube, a pliable red-rubber catheter, or similar device. Individuals require handling for this route of administration, which may prove challenging in vigorous aquatic species. Handling trauma, regurgitation with aspiration into the glottis or contamination of the gills, are risks. In debilitated animals, oral medications may be given with nutritional support.

Oral group treatments may be administered prophylactically, such as part of a preventative medicine program, or may be in response to disease. These treatments are generally administered as topical applications onto insects or fed to insects before feeding out to amphibians. This method allows for a completely hands-off approach to treatment and is rapid for large groups. However, the method is also problematic because the medication may easily dissolve or dislodge off the insect and relies on all amphibians consuming medicated prey items immediately and equally, so dosage received by an individual may be over or under the target. Animals that consume more than the anticipated number of medicated insects should be monitored for adverse reactions or toxicities.¹⁷ For example, a study in Houston toads (*Anaxyrus houstonensis*) demonstrated that fenbendazole reduced the number of nematode eggs, larvae, and adults observed on fecal examination. This was achieved by dusting crickets with finely ground fenbendazole granules and feeding them once daily for 3 consecutive days. The dosage for this treatment was higher than most other published doses and was estimated based on how much fenbendazole dust adhered to the cricket.¹⁸ Considerations should also be made for the welfare of insects being treated before being fed out to prevent undue distress.

Environmental changes, such as temperature adjustments, are reported as effective therapies and may be applied readily to groups of terrestrial and aquatic amphibians.^{19,20} For example, caecilians (*Typhlonectes natans*) with subclinical chytridiomycosis have been successfully treated by gradually elevating their tank water temperature by 2°C to 3°C per day until a temperature of to 32.2°C (90°F) was reached and this was sustained for 72 hours. After treatment, the tank water was gradually

returned to normal over 3 to 4 days.¹⁹ Not all species tolerate therapeutic temperature changes and it may be most useful in combination with other therapies.⁸

Preventative medicine in terrestrial amphibians varies by species and institution, but may include routine deworming. Groups of amphibians may be treated topically with anthelmintics, by injections, oral medications either directly gavaged to the animal or on prey items, or via bath solution. Fecal parasite screenings are recommended to determine which treatments to administer and efficacy of medications.

When treating larval amphibians, dosages may be lower than that used for adults and are likely species specific. Therefore, caution and conservative dosing may be prudent when treating groups of larval amphibians. For example, midwife toad (*Alytes muletensis*) tadpoles cleared *B dendrobatidis* infections at less concentrated intracranial bath solutions than adults, but developed epidermal depigmentation, thought to be caused by hepatotoxicity.²¹

BIRDS

Aviary populations are highly variable and may consist of single or multiple species. Avian group medicine focuses on prevention of and rapid response to disease in flocks of birds.²² Birds housed in groups may have drugs administered individually via injectable, topical, oral, or inhalational routes or as group treatments via oral routes in water or food based on several factors, including, but not limited to clinical condition, population of birds within the group, drug availability, frequency of administration, and risks of treatment.²³

For birds requiring medical treatments, separating the individual from the group is advantageous to ensure compliance and provide close monitoring, but may also come with social and behavioral stress, along with risks of repeated manual restraint. In ill birds, if compliance cannot be achieved by a particular route of administration, an alternative route, hospitalization, or isolation from the group may be needed.²⁴ Intramuscular and subcutaneous injections ensure compliance, but are invasive and may traumatize or irritate tissues. Long-acting depo-formulations of drugs are available, such as ceftiofur crystalline-free acid, which may be given less frequently than other antibiotics and may reduce handling for a bird still living within a group.^{25–27} Intravenous and intraosseous injections have similar risks and benefits as other injections, but these are most commonly performed in sedated or critically ill patients.²³ Nebulization, intratracheal, and topical routes of administration are also possible for individuals.²³ Oral medications may be administered to the individual directly in the oral cavity or via gavage tube passed into the crop or esophagus. Advantages include ensured accurate compliance and an opportunity to provide nutritional supplementation for sick individuals. Disadvantages include frequent restraint, stress, aspiration, or regurgitation.²³

Oral medications may also be provided topically on food items, to individually or group housed bird (Fig. 5). Powders, crushed tablets, and oral suspensions may be added to favored or high value food items. This administration strategy is simple; depends on the bird self-medicating through food consumption; and does not require handling, which may be a significant advantage in large, potentially challenging flocks, such as with ratites.²⁸ Chicks may be medicated via the parents by adding medications to the adult diet. Disadvantages include that food items may reduce drug absorption, sick birds in most need of medication may consume less food, and food may be unpalatable or refused or conversely overconsumed resulting in toxicoses.^{23,29,30} In general, it is difficult to achieve therapeutic concentrations of drugs with this strategy and only very susceptible pathogens are likely treated.²³ However,



Fig. 5. A group of Attwater's prairie chicken chicks (*Tympa-nuchus cupido attwateri*) may be treated as a group topically on pelleted food to avoid catching individuals housed in large communal enclosures.

there are some situations where this strategy may be useful, such as when treating flocks of cockatiels (*Nymphicus hollandicus*) for *Chlamydia psittaci* with doxycycline-medicated pelleted diets.³⁰ Dosing is often based on the mass of food to be treated or on the average body weight of birds in the flock multiplied by population size. Specific references are available.³¹

Formulated diets that contain medications milled directly into the food item are also commercially available.²³ Compliance with this type of food item may be increased by gradually introducing the medicated food in replacement of or in addition to the regular diet.³²

Oral medications may be provided in water-sources and are most successful in treating mild infections where local effect in the gastrointestinal tract is desirable or when widespread zoonoses treatment is imperative, such as adding antifungals or doxycycline to drinking water for pigeons with candidiasis or chlamydiosis, respectively.^{33,34} Like medications applied on food; administering medications in water is simple; depends on the bird self-medicating through drinking, and does not require handling. Medicated water may decrease disease transmission via medicated drinking water.²³ Disadvantages include that water consumption is more erratic than food consumption for birds in general and may not be appropriate for every species. For example, frugivorous birds stay hydrated through fruit consumption and raptors do not consistently drink water.^{32,35} Environmental temperatures may affect water consumption, whereas in hot weather, birds may consume large volumes of medicated water resulting in toxicoses.³⁶ Moreover, medicated water may be unpalatable and reduced water consumption may decrease the achieved drug concentration and may result in dehydration. Furthermore, not all drugs are stable or soluble in water, so drug choice may be limited and potency may degrade over time.³² In most cases, medicated water does not reach therapeutic concentrations in the animal to adequately treat most diseases, because birds usually fail to drink enough, especially if ill. If water is consumed, low drug concentrations are sustained, which will likely be effective only to a highly susceptible pathogen. Remaining pathogens could develop resistance and become established within a flock, which would be detrimental to flock health if treated nonspecifically or at subtherapeutic levels.²³ Because of these factors, water-based treatments are not appropriate for sick birds alone, but may be used as an ancillary treatment to direct drug administration or in situations where individual treatment is impossible. For example, in Attwater's prairie chickens (*Tympa-nuchus cupido attwateri*) with *Clostridium coli* infections, tylosin powder was provided in the only source of drinking water in addition to the birds receiving parenteral

antibiotics. Dosing is often based on the volume of water to be treated and references are available.³¹

In mixed-species aviaries, birds occupying the same ecologic niche may compete for space, food, water, and other resources resulting in antagonism.² Birds occupying different niches may allow for the targeted species to be adequately medicated, they would not contact the same feeders or occupy the same space³⁷; however, this does not prevent nontarget species from accessing medicated food items. For example, in a mixed species exhibit, arboreal birds may be medicated on food in elevated feeders, but if food is spilled from the feeder, terrestrial species may have access to this and consume it.

Preventative medicine for the flock typically consists of, but is not limited to, anthelmintic treatments. Fecal parasite screenings are recommended to determine which treatments to administer and efficacy of medications. Preventative treatments may also include probiotics. Probiotics may improve gastrointestinal microbiota and health by providing balance and inhibiting pathogenic bacteria. This type of medication may be added prophylactically or responsively to food or water sources for flocks (Fig. 6).³⁸

MAMMALS

Group treatment of mammals is challenging and not practiced as widely as group treatment of other taxa. Most mammals are treated individually, or are not housed in cohorts as large as those commonly found in other species. However, exotic hoofstock are commonly housed in large herds, and therefore are the focus of this section. Two of the most common reasons for mass treatment of hoofstock are contraception and gastrointestinal parasites. Contraception can be administered to a group of animals by milling a chemotherapeutic agent into the feed, such as melengestrol acetate,



Fig. 6. Attwater's prairie chicken chicks (*Tympanuchus cupido attwateri*) may be treated as a group by adding medication, such as probiotics into the water source within the enclosure. When chicks are less than 2 weeks old, glass marbles are added to shallow plastic dishes to prevent chicks from turning over the dish or from soaking feathers.

which is a synthetic progestin.³⁹ This method has been used to reduce fertility in herds of barasingha (*Cervus duvauceli*), axis (*Cervus axis*), sambar (*Cervus unicolor*), and sika (*Cervus nippon taiwanus*) deer, and blackbuck antelope (*Antilopa cervicapra*) under human care.⁴⁰ These species were fed melengestrol acetate at a concentration of 0.000154% in pelleted feed, which significantly decreased birth rates. However, post-treatment reproductive rates were lower than pretreatment rates, an effect that has also been seen in cattle.⁴¹ A clinician should be aware of the potential risks of lowered fertility in a herd before mass treatment, and may elect for individual treatment instead.

Gastrointestinal parasitism is the most common reason for mass therapy for exotic hoofstock, and there are two main strategies. The first strategy is administering a large amount of medication to a group of mammals, for an average dose, and hoping that each animal consumes the correct amount. For example, this is done with deworming agents mixed into pelleted feeds.⁴² Risks include overdosing and underdosing animals, which in addition to having potential toxic effects, can select for anthelmintic resistance in the parasites.^{42,43} Social dynamics can have an impact on this medication strategy, because often the low-ranking individuals are denied access to the feeding stations, but they are usually the animals with the heaviest parasite burden.⁴² Dose range via group feeding can only be roughly estimated, and the drug used should have a wide margin of safety, so that if animals do not eat the same amount every day, they are to be sufficiently treated after a period of time. If the group is treated, then often group fecals are to be used to track anthelmintic efficacy. Group sampling involves taking several samples from the herd and recording the median and range number of parasites observed, or pooling samples from many different fecal piles and mixing the sample before examination.⁴² Although this route may be easier for the practitioner, it does not provide the most accurate representation of the effectiveness of the chosen drug therapy. Certain classes of animals tend to carry the highest parasite load (eg, calves), and if group samples are examined then the parasite load per animal is diluted and therefore not accurately represented.^{42,44}

The second strategy for administering deworming agents to a large herd of hoofstock is targeted therapy. Administration may be done via physical restraint if a facility has the proper equipment, such as drop chutes or hydraulic squeeze chutes. If physical restraint is not possible because of either facilities limitations or the animal's size or temperament, then chemical immobilization must be used. The risks and benefits of chemical immobilization of an individual animal must be weighed against the benefit of the deworming procedure. If the animal is heavily parasitized, then a thorough physical examination with ancillary testing, such as a complete blood count, serum biochemistry analysis, and mineral panel, may help elucidate the underlying reason an animal has a high parasite load. While the animal is anesthetized a fecal sample can be collected from the rectum for individual sample analysis.

If neither medicated feed nor chemical and physical restraint are possible, then anthelmintics may be darted to individual animals. The benefit of this technique is targeted therapy and limited stress to the animal. However, most injectable anthelmintics are not labeled to be administered intramuscularly, but subcutaneously, so the efficacy may be reduced. Additionally, darting an animal carries inherent risk of trauma if there is poor dart placement, and if follow-up treatment is needed, or multiple animals in a herd need to be darted, the subsequent darting attempts may be difficult because of the suspicious nature of the animals.

Because of the many difficulties of administering anthelmintics to large groups of hoofstock, nonchemotherapeutic methods should be judiciously used. For example, pasture management is a key strategy, because increased stocking density of animals on a habitat leads to increased fecal contamination and infective larval load.^{2,4,42,45,46} Pasture rotation and combining animals of different taxa, such as bovids and equids,

are highly effective strategies to reduce the fecal load in a habitat. Mixing browsing and grazing species can reduce grass length, which reduces worm burden on the pasture, and also increases refugia.^{43,47} Refugia are species that are not clinically susceptible to the parasites of interest, and therefore dilute the resistant alleles of the parasites.⁴³ There are tools, such as paddock vacuum cleaners, that can facilitate fecal pick up in large habitats; however, such equipment is expensive, and the benefit may be offset by the stress imposed on the animals living in that habitat.⁴²

Other nonchemotherapeutic options for managing gastrointestinal parasites in hoofstock include copper oxide wire pellets, condensed tannins, and nematophagous fungus. Copper wire oxide pellets are administered orally, most often in gelatin capsules, and when dissolved in the forestomachs, interact with parasites to cause expulsion or parasite death.⁴⁸ Copper oxide wire particles have been demonstrated to reduce trichostrongyle fecal egg count in several exotic hoofstock species including schmitzer horned oryx (*Oryx dammah*), blackbuck (*Antilopa cervicapra*), roan antelope (*Hippotragus equinus*), and blesbok (*Damaliscus pygargus*).⁴⁹ Condensed tannins, such as *Sericea lespedeza*, can be fed to hoofstock either as hay or in pelleted form.^{50,51} Once ingested, the tannins bind and disrupt the cuticle of the parasite causing reduced worm burden and reduced fecal egg count.⁴⁸ One last nonchemotherapeutic option for parasite control is nematophagous fungus. This fungus is ingested by the target animal, but actually does not work inside the animal that has consumed it. Instead, the fungal spores are passed in the animal's feces, where they germinate and then trap the developing nematode within the feces. Thus, because of the different mechanism of action of this agent, it does not impact the fecal load of the animal, and instead reduces the possibility of reinfection.⁴ One nematophagous fungus, *Arthrobotrys flagrans*, has been used to lengthen the time until egg reappearance in a herd of equids within a zoo. When a mixed herd of plains zebra (*Equus quagga*), Falabella miniature horse (*Equus caballus*), European donkey (*Equus asinus*), and African wild ass (*Equus africanus asinus*) were treated with antiparasitic agents combined with the fungus, the egg reappearance was delayed by several months, compared with just deworming agents alone.⁵² This and other studies have shown that combining chemotherapeutic and nontraditional deworming agents provides the zoo clinician with a variety of tools to try and facilitate group treatment of mammals.^{42,45,46,49,52}

SUMMARY

Group treatments are most common in amphibian, avian, and certain mammalian species that may live in a zoologic setting. All taxa have various group treatment strategies that exist with advantages and limitations that should be considered before therapy administration. Preventative measures, such as infectious agent screening and biosecurity, are advantageous to reduce the need for group treatments in response to disease. Medications administered topically on or milled into food, solubilized in drinking water, and mixed into a bath are common routes of administration for groups of animals. Sick or debilitated animals should be treated individually, because group treatments are often only effective against highly susceptible pathogens. Group therapies may be a beneficial strategy when treating animals in a zoologic setting and may be used, provided the risks and benefits are considered, in a variety of species.

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