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A Review of the Current Use of Gonadotropin-Releasing Hormone Vaccines for Reproductive Management of European and North American Zoo Animals
American Association of Zoo Veterinarians Conference 2019

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Abstract

The use of gonadotropin-releasing hormone (GnRH) vaccines in free-living wildlife is well documented. There is an increasing trend of their use in zoo animals given the relative ease of delivery of these products; however, there are few published reports of GnRH vaccine efficacy in zoo species and whether successes and failures are as a result of dosage, frequency of booster vaccination, or due to variation in species physiology. Reversibility of contraception and a return to full fertility after GnRH vaccination for individuals in captive breeding programs is crucial, but mostly unknown. Using the Association of Zoos and Aquariums (AZA) Reproductive Management Center (RMC) and European Association of Zoos and Aquaria (EAZA) Group on Zoo Animal Contraception (EGZAC) Contraception Database, we reviewed the use of GnRH vaccines (Improvac®/Improvest®, GnRH conjugate vaccine, Zoetis®, Parsippany, NJ, USA) in European and North American zoos over the last 10 years. In total, 686 bouts of vaccination were recorded in 148 (56:92) individuals, comprising 47 different species. Vaccines were principally used in ungulates (88% of records), but were also used in elephants (9%), pinnipeds (1.3%), rodents (0.6%), felids (0.3%), and macropods (0.2%). Vaccines were primarily used for contraception of male (121 records) and female (386 records) animals, but also for aggression management (82 records) and for the therapeutic treatment of reproductive tract disorders (97 records). Full contraceptive reversal was documented with live births in three out of nine animals that were allowed to breed; however, several more conceived due to contraception failure or incorrect product use. The review has helped identify successful contraception as well as causes of failure and our current understanding of how best to use GnRH vaccines in different zoo species.

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A Review of the Use of Selected Neuroleptic Drugs in the Management of Nondomestic Hoofstock
American Association of Zoo Veterinarians Conference 1991

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The ability to control or reduce the effects of the stresses frequently encountered by captive wild animals is of paramount importance to the field of zoological and wildlife medicine. Many of the procedures performed on both free-ranging and captive animals result in dramatic, traumatic, and stressful events.

Captured free-ranging animals often show pronounced excitability when confined, especially during initial periods of adaption to captivity. The stress resulting from confinement, human presence, disruption of social groups, etc., may result in overexertion and myopathy or injuries as a result of attempting to escape. In translocation procedures, the additional stress resulting from prolonged confinement during transport, unfamiliar surroundings and individuals at the release site, and qualitative changes in the environment may result in injuries from intraspecific combat or a generalized loss of condition.

Captive (zoo) animals similarly exhibit marked stress reactions when their conditions of captivity are altered. Whether as a result of prolonged hospitalization, changes to exhibit or holding facilities, or shipment between facilities, captive animals often suffer from severe injuries that could be eliminated if the effects of stress could be reduced.

Neuroleptic drugs have often been used to relieve anxiety, decrease motor activity, and moderate excitement. Because of higher incidences of capture-related stress and trauma in certain species, the use of neuroleptic drugs in wildlife medicine has been focused primarily on ungulates.

The use of these drugs in ungulates has been shown to[6]:

- Alter the mood or attitude of the animal
- Cause the animal to be indifferent to its surroundings
- Reduce the animal's fear of humans and tolerate them at close proximity
- Reduce belligerent, dominant, and aggressive behavior
- Reduce self-inflicted trauma

A range of products are available for use in the control or reduction of the effects of stress. Drugs of the phenothiazine, butyrophenone, and benzodiazepine families have all had widespread use in both domestic and wildlife species. The primary practical considerations differentiating pharmaceuticals from these families are time to effect, duration of effect, level of sedation produced, and incidence of deleterious side effects. The remainder of this paper will address several of the neuroleptic drugs in use with nondomestic ungulates.

Short-Acting Neuroleptics

Relatively short-acting neuroleptic drugs have been used successfully in the management of non-domestic hoofstock for many years. The value of these drugs is limited, however, because of the limited duration of their effects. Several of the more commonly used short-acting neuroleptics are described below.

Acepromazine Maleate

Acepromazine maleate, a phenothiazine derivative, is used extensively in veterinary medicine. Like other phenothiazines, acepromazine reduces motor activity and aggression, yet allows the animal to retain much of its alertness and coordination.[1,11] Acepromazine exerts its primary effect through a blockade of the neurotransmitter dopamine, has little or no analgesic activity, and is well known for disruptions of thermoregulatory control. Acepromazine is also well known for its rapid effect in the reduction of arterial blood pressure and has been shown to cause intermittent bradycardia and transitory sinoatrial cardiac arrest.[2]

Dosages for mild sedation range from 0.05–0.1 mg/kg across a wide range of species. However, even at the top of this dose range, acepromazine may fail to control hyperexcited animals. The duration of effect for acepromazine is relatively short; for continual effects, the dose should be repeated every six hours.[2]

Acepromazine has been used extensively as an adjunct to etorphine and carfentanil for immobilization of hoofstock; however, it has suffered some reduction in popularity due to its interruption of thermoregulatory control and the subsequent danger of hyperthermia, especially in hot climates.[11]

Azaperone

Azaperone is a member of the family of butyrophenone derivatives. These compounds have a number of related neuroleptic properties in animals; motor activity is reduced, mortality from stress or trauma is reduced, and cataleptic effects may be produced. These effects are the result of blockage of catecholamine transport, thereby reducing the activation of certain neuronal receptors. Azaperone is a relatively nontoxic, short-acting drug that is readily detoxified and eliminated. At normal dosages, azaperone is active for 2–3 hours and is nearly eliminated from the body in 16 hours.[2]

When used alone, azaperone has a wide dosage range (2–40 mg/kg in swine) and a corresponding, dose-dependent range of effects. Azaperone has been used in combination with various narcotics (fentanyl, etorphine, and carfentanil) for the immobilization of a wide variety of species, including buffalo, kudu, sable antelope, Burchell's zebra, and black rhinoceros, with very satisfactory results.[11] Typical doses for azaperone range from 0.5–2.5 mg/kg.[2,3,11] It should be noted that azaperone has been found to suppress the usual ejaculatory response to electrical stimulation, and as such, should be avoided in procedures where reproductive parameters are to be assessed.[15]

Mid-Duration Neuroleptics

Unlike the short-acting neuroleptics which have a duration of effect that is limited to several hours, mid-duration neuroleptics typically have pharmacological effects lasting 12–24 hours. They tend to be more specific in action, with less sedative effects and usually have an onset of action that is relatively rapid.

Haloperidol Lactate

Haloperidol lactated (Haldol) is a potent and specific neuroleptic drug that is a member of the butyrophenone group of compounds. It is an effective CNS dopamine blocking agent which has a high affinity for membranes surrounding the synaptic cleft of dopaminergic neurons in the midbrain. (This is in contrast to the relatively specific, peripheral effects seen with the low potency, "sedative" neuroleptics such as acepromazine.) Haloperidol is extensively used in human medicine as an antipsychotic agent and is the drug of choice in the emergency treatment of psychomotor agitation and aggression, regardless of its origin. Haloperidol is not an active hypotensive agent and has little effect on thermoregulatory mechanisms or cardiac rhythmicity.[12]

Over the past decade, haloperidol has gained widespread use as an adjunct to the capture and transport of a number of nondomestic species. In a study conducted by Hoffmeyer, adult springbok were successfully treated with haloperidol at a dosage rate of 0.25 mg/kg. Following treatment, the springbok were exceptionally calm and tractable and were not significantly alarmed by physical examination or venipuncture. Therapeutic effects were maintained for approximately 12 hours. Subsequent studies have shown that haloperidol at dosages ranging from 0.1–0.3 mg/kg IM is effective in reducing anxiety, aggression, and capture/transport-related stress in a wide range of species.

Although most studies of haloperidol in hoofstock have used parenteral administration, oral preparations are effective for use in nonruminants and may present a more economical (and convenient) approach for treating certain species due to the recent availability of generic haloperidol. It has also been suggested (Jensen, personal communication) that oral preparations of haloperidol may be effective in certain ruminant species when given at doses of 1.0 mg/kg.

Side effects of an extrapyramidal nature have been observed after treatment with haloperidol. Typically, these effects (opisthotonos, torticollis, hyperreflexia, chewing, dysphagia, and parkinsonism) are seen after administration of high dosages or after prolonged treatment with haloperidol and usually dissipate once treatment is discontinued. However, tardive dyskinesia, a potentially irreversible extrapyramidal syndrome, can occur subsequent to haloperidol administration.

Perphenazine Enanthate

Another mid-duration neuroleptic drug that has received substantial use in veterinary applications is perphenazine enanthate (Trilafon). When first introduced over 25 years ago as a human drug, perphenazine was evaluated for potential veterinary applications. This compound, which is a member of the phenothiazine group, was evaluated for clinical applications in domestic animals and was found to produce apparent indifference to unusual surroundings, reduction of psychomotor activity, apparent indifference to minor pain or irritation, and a decreased response to threatening situations, all without substantially sedating the animal. The effect of perphenazine appears to be the depletion of hypothalamic stores of catecholamines and decreased synthesis of prolactin-inhibiting factor. Perphenazine has also been shown to be capable of inhibiting the estrous cycle of certain laboratory species.[2]

Perphenazine has been used extensively to moderate the behavior of numerous domestic and nondomestic ungulate species, and its depot formulation (see below) has become part of the standard protocol for the translocation of several species (Kock M, Raath JP, personal communication). However, perphenazine is no longer available as a veterinary preparation in the United States due to its untoward side effects, such as extreme excitation and prolonged prolapse of the penis in certain individuals (Bigbee, personal communication). A human formulation is available in the United States. Dosages for parenteral use in hoofstock range from 0.1–0.5 mg/kg.[17] Neuroleptic effects typically begin within 15–30 minutes and last for 8–12 hours (Bigbee, personal communication).

Long-Acting Neuroleptics

In recent years several long-acting preparations of neuroleptic agents have received attention for use in nondomestic ungulates. These formulations generally are longer-acting versions of agents which have been developed with short- or mid-duration activities. Long-acting formulations of these drugs consist of fatty acid esters of the basic neuroleptic compounds which have been dissolved in a lipid vehicle such as sesame oil. The prolonged activity results from the slow release of the ester as it diffuses from the vehicle into the tissue fluid and is then absorbed and hydrolyzed into the active form of the neuroleptic drug.[6] As a result of this slow release of active drug, all long-acting neuroleptics currently available should be combined with a shorter-acting but more rapidly available neuroleptic drug. Such combinations of the two drugs will allow for a more continuous control of psychomotor activity, anxiety, and stress.

As with many of the other neuroleptic drugs, deleterious side effects of an extrapyramidal nature are of great concern with long-acting formulations. Unfortunately, if these effects do occur as a result of treatment with a long-acting formulation, treatment for these untoward effects will also be similarly prolonged. If extrapyramidal effects do occur, they may be controlled with biperiden, benztropine mesylate, or other antiparkinsonian drugs.

Perphenazine Enanthate (Long Acting)

As discussed above, perphenazine enanthate (Trilafon) is a member of the phenothiazine group of neuroleptic drugs. The effects of this formulation are generally not seen for 10–16 hours after (deep) intramuscular injection, and the peak effect is usually reached after approximately 72 hours. The duration of effect for this form of perphenazine is described as being up to 14 days; however, observations suggest that the duration of effect for nondomestic animals is about seven days.

Long-acting perphenazine enanthate is by far the most extensively used of all of the longacting neuroleptic drugs. It has produced favorable results when used in impala (*Epicures melampus*), hartebeest (*Alcelaphus* sp.), eland (*Taurotragus oryx*), greater kudu (*Tragelaphus strepsiceros*), blackbuck (*Antilope cervicapra*), sable antelope (*Hippotragus niger*), black rhinoceros (*Diceros bicornis*), and numerous other species.[3,10,14] Dosages for these species vary considerably but typically range from 0.5–2.0 mg/kg. (Note: There appears to be an inverse relationship between the dosage of L.A. perphenazine enanthate and the average size of the species, with larger species requiring lower doses per unit weight.) This depot formulation of perphenazine enanthate is not commercially available in the United States.

Pipothiazine Palmitate

Pipothiazine palmitate (Piportil depot), an extremely long-acting neuroleptic formulation, is a member of the phenothiazine family. It is the second oldest depot neuroleptic and has been used in human medicine since 1969. It has the lowest incidence of extrapyramidal side effects of all depot neuroleptics.[4]

Pipothiazine palmitate has also been used on numerous species of nondomestic ungulates and has been found to have the longest duration of effect of all depot neuroleptics currently in use. The onset of pharmacological effects typically occurs 48–72 hours after intramuscular injection and has a duration of up to 30 days. Dosages for long-term control of maladaptive behavior in nondomestic ungulates range from 1.0–2.5 mg/kg.[6] Pipothiazine palmitate is not commercially available in the United States; however, it is readily available in Canada.

Other Depot Neuroleptics

Several additional compounds which are readily available in the United States may present options for the zoological or wildlife veterinarian who is either unable or unwilling to import the compounds mentioned above. Each of them has a long history of use in human medicine; however, they have been rarely used in the management of veterinary patients. Although the author has no personal experience with the use of the compounds and there are no readily available references as to their use in nondomestic hoofstock, information from the manufacturers suggests reasonable starting doses and expectations as to onset and duration of effect. Further study of the applicability of these compounds for use in zoological and wildlife species is needed.

- **Fluphenazine decanoate (Prolixin)**—available as a 25 mg/ml formulation. The onset of pharmacological effect is 24–72 hours with a duration of 21 days.
- **Haloperidol decanoate (Haldol)**—available as either a 50 mg/ml or a 100 mg/ml formulation in a sesame oil vehicle. The estimated dosage range is 1.0–4.5 mg/kg (10–15 times the dose used for haloperidol lactate). Onset of pharmacological effect is 24–48 hours, with a duration of approximately 30 days.

Future Developments in the Control of Anxiety, Aggression, and Maladaptive Behavior

In recent years psychopharmacologists have begun to find commonalities in a variety of psychological pathologies including anxiety and inappropriately aggressive behavior. Experience has shown that these groups of symptoms, seemingly so different from one another, can be treated with the same drugs. That such different groups of symptoms are controlled in nearly the same way is easily explained. Fear (anxiety) and fighting (aggression) are the most ancient responses of higher organisms when faced with danger or the unknown, and as demonstrated by the “fight-or-flight response,” fear may easily turn into fighting.[13] The common neurobiological substrate for these behaviors is thought to be serotonin, and modulation of serotonin transmission may result in control of both anxiety and aggression.[8] Several compounds have been developed recently which block or modulate serotonin transmission and thereby have the effect of controlling these behaviors.

R51163 (Tameridone)

R51163 is a newly synthesized compound that functions as a serotonin antagonist. It has been shown to be an effective aid in both the handling and adaption to captivity of caribou (*Rangifer tarandus*), eland (*Taurotragus oryx*), and impala (*Epicures melampus*).[14] Although the duration of this drug is only 6–7 hours, it has the effect of producing animals that are extremely calm, disinterested, and unresponsive to external stimuli and does not generally suppress appetite (Raath, personal communication). Unfortunately, the responses to treatment with R61163 vary widely among species. Cattle have been found to exhibit profound sedation,[5] and moose (*Alces alces*) show a marked decrease in food intake for up to one week following treatment with R51163. Other species have been shown to exhibit violent and unpredictable outbursts of excitatory behavior. Consequently, interest in the development of R51163 for use in nondomestic hoofstock has decreased considerably (Lance, personal communication).

Buspirone (Buspar)

Buspirone, a member of a novel class of compounds known as azapirones, is a partial serotonin agonist which works primarily at the 5HT-1a receptors. In humans and laboratory animals, it has been shown to have antianxiety, antiaggression, and anticonflict properties without marked sedation, muscle relaxation, incoordination, anorexia, or cardiovascular effects. Additionally, buspirone does not cause any of the extrapyramidal side effects frequently associated with typical neuroleptic drugs (Demestihas, personal communication).

As a partial agonist, buspirone binds to receptor sites and exerts an agonist-like effect, but it influences the activity of the target site less than a full agonist. The result is that the partial agonist (buspirone) competes for binding sites with the full agonist (serotonin), and displaces the more active full agonist from the binding sites while contributing less synaptic activation than the full agonist. Thus, the partial agonist functions (paradoxically) as an antagonist.[7]

In animal trials, low doses (40 mg/kg) of buspirone have been shown to reduce anxiety and aggression more effectively than diazepam without producing ataxia or hypoactivity. This effect typically lasts for 6–8 hours. Higher doses (80 mg/kg and 160 mg/kg) of buspirone appear to inhibit aggression and anxiety for more than 22 hours; however, mild hypoactivity is noted for the first 6–8 hours.[9,16] Clinical trials examining the efficacy of buspirone for controlling anxiety and aggression in nondomestic hoofstock will begin in late 1991.

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A Systematic Approach to Behavior Cases: The Key to the Right Diagnosis—Clinical Cases
2016 Joint AAZV, EAZWV, IZW Conference

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ABSTRACT

The so-called "behavior cases" are often challenging for zoo veterinarians. The inappropriate behaviors displayed by zoo animals, such as pacing, aggression, or compulsive disorders, should be interpreted as clinical signs. In order to treat patients with behavioral problems, it is important to first acquire an accurate diagnosis. A systematic approach can be used to build a thorough differential diagnosis list. The first step is to obtain detailed history on the animal, including behavioral development, medical history, feeding, grooming, exploratory and play behaviors, breeding history and sexual/maternal behavior, and then the relevant social and physical environments. The second point is to obtain a precise description of the problem behavior, including details about frequency, duration, and context of the behavior. Observation of the behavior by the veterinarian is of critical importance, directly or on a video format. Filming the animal over a 24-hour period has proven insightful in several cases. Behavioral analysis can be performed at that point, identifying the antecedents and the consequences of the problem behavior, as well as the general context. Then, a full physical examination of the animal should be performed. Depending on the case, diagnostics can include blood analyses, radiographs or more advanced imaging, gastroduodenal endoscopy with biopsies, and skin biopsies.[1,4,6] When all the information has been gathered and analyzed, a differential diagnosis list can be made. All potential medical or surgical causes should first be excluded and/or treated. Potential environmental causes should be addressed as much as possible. If the problem remains or if the improvement is incomplete, anxiety disorders or other behavioral diagnoses could be considered. Several clinical cases were successfully diagnosed and treated with this systematic approach.

An 8-year-old female Amur tiger (*Panthera tigris altaica*) presented for aggression towards keepers and unfamiliar people. Signs were first observed a few months before presentation, but increased over time. This female tiger was also aggressive towards her 2.5-year-old daughter with whom she was housed. Minor injuries between the two animals were reported. Physical examination of this adult tiger was unremarkable. Tiger cubs generally leave their mother at 2–3 years of age in the wild. Keeping the mother isolated from her daughter obviously resolved intraspecific aggressive behavior, but also resulted in a return to her usual nonaggressive behavior towards the keepers within only a few days.

An 18-month-old male Canadian lynx (*Lynx canadensis*) was presented for increased pacing over a few months since the departure of his family (mother and two sisters). Medical history revealed short bouts of dysorexia during the same period. Video analysis demonstrated that the pacing also occurred at night, and that the behavior was not stereotypic. Physical examination including gastroduodenoscopy and bronchoscopy revealed several medical conditions, such as *Helicobacter* gastritis, bacterial pneumonia and congenital cardiac malformations. Treatment with antibiotics and omeprazole resulted in a significant decrease of the pacing behavior. Environmental and social adjustments were also made in this case as part of the therapeutic plan.

A 24-year-old Asiatic black bear (*Ursus thibetanus*) was presented for stereotypic pacing behavior. Few changes had occurred in the bear's environment in the previous years. More efforts had already been placed to enrich the environment and stimulate natural behaviors, but were unsuccessful in decreasing the daily duration of the pacing. Physical examination and radiographs detected multiple dental root infections. Treatment was associated with a complete resolution of the pacing behavior. A few years later, the bear started pacing again. Another dental infection was rapidly diagnosed and treated, and the pacing behavior disappeared.

An 11-year-old female Amur leopard (*Panthera pardus orientalis*) was observed pacing in circles with her 6-week-old cub in her mouth. The behavior increased over time despite numerous environmental adjustments and alpha-casozepine therapy (Zylkene, Vetoquinol Canada, Saint-Hyacinthe QC, Canada). A visual examination revealed signs consistent with a localized mastitis. Pacing with the cub ceased 24 hours after initiation of the antibiotic therapy.

A 2-year-old male jaguar (*Panthera onca*) presented with self-inflicted tail wounds. This jaguar had been licking his tail since he was a cub. Behavioral observations showed that he spent 7% of his daytime hours licking his tail. Changes in the environment increased the behavior. Physical examination, including skin biopsies and gastroduodenoscopy, revealed a severe infection of the tip of the tail and possibly a mild eosinophilic gastritis. Radiographs were unremarkable. Local wound care and antibiotic therapy significantly decreased the licking behavior, but did not lead to a complete resolution. Successive treatments with omeprazole and gabapentin did not show any improvement. Though some medical causes could not be excluded at that time (food allergy, neuropathic pain), a compulsive disorder was suspected and treated with fluoxetine.[2,3,7] Further behavior analyses were conducted while the jaguar was treated with the SSRI and a new pattern was observed: the tail-licking/chewing behavior mainly occurred after meals or food enrichments. Therefore, treatment with omeprazole at a higher dose, based on the new feline literature recommendations was initiated and, in combination with the fluoxetine, led to almost complete resolution of the behavior.[5]

Many behavior cases can be managed and/or treated when a diagnosis is found, with the help of a systematic approach. When environmental adjustments have been made and medical conditions excluded, consulting with a board-certified behaviorist could be recommended to choose the most appropriate treatment for the animal and to monitor the recovery.

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Adverse Effects of Contraceptives in Carnivores, Primates, and Ungulates
American Association of Zoo Veterinarians Conference 1993
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Contraceptive use in zoos has evolved with the increasing commitment of zoological parks to conservation programs. The immediate need to prevent reproduction of surplus animals and to postpone pregnancy in some individuals, as part of single-species conservation plans, required using available contraceptives in species for whom these contraceptives had not been safety tested. Consequently, our understanding of the effects of these contraceptives on zoo species are only now gradually emerging from the large clinical trial we are conducting.

It should be remembered that no medical procedure or pharmaceutical is completely without risks. Our goal should be to use existing knowledge to choose contraceptives that have minimal detrimental effects on the health of the animals. This report summarizes currently available information on the adverse effects of contraceptives on zoo species. Adverse effects of contraceptives in free-ranging wildlife are included in the review by Kirkpatrick and Turner.[2]

Steroid Contraceptives

The most widely used contraceptives in all zoo species are the progestins, melengestrol acetate (MGA), megestrol acetate (MA), and medroxyprogesterone (MPA). Combined estrogen-progestin contraceptives (birth control pills) also have been used in primates. All steroid hormones exert their contraceptive effects by disrupting the normal cyclical hormonal levels of the hypothalamic-pituitary-gonadal axis. Tissue sensitivity to steroids depends on the presence of specific receptors, and receptor numbers, in turn, are modulated by exogenous and endogenous steroids. The response to receptor binding also depends on the species and tissue. All progestins are presumed to exert their action by binding to the progesterone receptors in tissues. Progesterone receptor numbers usually are up-regulated by estrogen and down-regulated by progesterone. For zoo species, the regulation of progesterone receptor numbers and responses to receptor binding are not known, but are assumed to be analogous to those of similar domestic and laboratory species.

The response of the endometrium and mammary gland to sex steroids varies among taxa and has only been studied in domestic and laboratory animals and women. For most species, estrogens promote hyperplasia and hypertrophy of the uterus, whereas progesterone antagonizes the estrogen effects, promotes secretory differentiation of the endometrium, and causes uterine atony. In canids and felids, however, progesterone also promotes endometrial proliferation. Mammary gland growth in all species requires estrogen, progesterone, and the pituitary hormones, prolactin and growth hormone.

Adverse Effects of Progestin Contraceptives in Carnivores

Our ongoing reproductive pathology surveillance of MGA-contracepted zoo felids at the time of this writing includes 137 felids representing 22 species (MGA-contracepted=64; non-contracepted=73). Our data to date indicate that MGA is highly associated with more severe forms of endometrial hyperplasia and the development of endometrial hyperplasia at earlier ages than non-contracepted felids. All ten felids with uterine cancer from this survey had been contracepted with progestins, as had 22 of 25 felids with mammary gland cancer. Our data also suggest that more advanced endometrial hyperplasia and cancer are associated with lower doses of and prolonged exposure to MGA (5.5 or more years). These findings confirm the predicted pathologic effects of progestins on felid reproductive organs and indicate that progestins should not be used as permanent contraceptives for felids. Minimal endometrial lesions were noted in felids contracepted with MGA for less than 3 years, and these lesions most likely would resolve with withdrawal of MGA and resumption of estrous cycles. Thus MGA may cause acceptable levels of changes that pose a minimal health risk when used as a temporary contraceptive.

Diabetes mellitus also has been reported in MGA and MA contracepted felids, and has been presumed to be due to the potential of progestins to promote insulin resistance and aggravate latent diabetes. However, a case-control study has not been conducted to confirm this correlation.

Cystic endometrial hyperplasia, pyometra, and mammary cancer have been noted in progestin-contracepted canids and other carnivores (e.g., binturong, civet, and fox), but extensive epidemiologic studies have not been conducted to confirm the association of these lesions with progestin exposure. However, in canids particularly, progestins would be expected to be a major risk factor for these diseases. Delineation of the role of progestins in disease development in other carnivores awaits further studies.

Adverse Effects of Mibolerone in Canids and Felids

The androgenic steroid, mibolerone, has been used as an effective contraceptive in wolves, jaguars, leopards, and lions.[1] Anorexia, masculinization of lions, and increased aggression among wolves were notable side effects in this study.

Adverse Effects of Progestins in Ungulates

Insufficient information on the effects of contraceptive doses of MGA in zoo ungulates is available because use has been limited to a few zoos. In domestic cattle, prolonged exposure to progestins can result in the accumulation of endometrial secretions (mucometra or hydrometra) and secondary endometrial atrophy. Two cases of mucometra/hydrometra have, in fact, been reported in zoo ungulates ingesting MGA. This condition may be reversible if atony and atrophy are not prolonged and if secondary infection does not occur. Male barasingha ingesting MGA have been reported to have abnormal horn growth (B. Raphael, personal communication).

Adverse Effects of Progestins in Primates

Progestin-only contraceptives, such as levonorgestrel and medroxyprogesterone, have been extensively tested in laboratory primates and are currently approved for use in women. Adverse effects have been minor, such as amenorrhea and weight gain. However, some investigators are concerned that progestins may increase the risk of breast cancer when used in young women. The effects of long-term exposure of primates to MGA are not known, but would be predicted to be similar to other progestins.

Reproductive pathology surveillance of zoo primates on either progestin-only or combined progestin-estrogen contraceptives has only recently been initiated, so data is limited. Notable adverse effects of progestin-only contraceptives in lemurs have been weight gain and color changes (Porton, personal communication). MGA implant removal by primates (selfremoval or by cagemates) has been common and has resulted in superficial wounds. One case of retained placenta and endometritis was noted in an MGA-contracepted tamarin that was (or became) pregnant while exposed to MGA. The fate of the fetus was unknown. One orangutan with an MGA implant had profound endometrial atrophy and an intraluminal endometrial "cast," but had no clinical signs associated with these findings. These are presumed to be rare events, and progestin-only contraceptives are expected to be acceptable contraceptives for zoo primates.

Vas Deferens Plugs

Surgically-placed silicone vas deferens plugs have been tested extensively as reversible contraceptives in humans with no adverse reactions. Knowledge of pathologic effects in other species are very limited because clinical trials with formed-in-place soft silicone plugs have just been initiated at zoos. However, no serious adverse reactions are anticipated. In preliminary tests on impala and horses, small granulomas and mild inflammatory reactions were noted near the site of insertion and minimal tissue changes associated with healing were present. None of these lesions impinged on the lumen of the vas, nor were any pathologic changes within the vas containing the plugs. These preliminary findings suggest that this method will be safe for temporary or permanent contraception of males.

Surgical Contraception

The most prevalent methods of permanent contraception are surgical ovariohysterectomy or vasectomy. Male gonadectomy (castration) is usually not chosen because social

hierarchies can be disrupted and secondary sexual characteristics will be lost. Female gonadectomy without removal of the uterus also is not optimal for some species, because of the potential for developing infections in the post-pubertal, atonic uterus. The risks involved in any of these surgical procedures are minimal because current anesthetics are safe, and the procedures are relatively simple. The risks would be the same as for any minor surgical procedure.

Other Contraceptives

Clinical trials with the anti-spermatogenic contraceptive bisdiamine and immunocontraception with zona pellucida vaccines in zoo species are in the initial stages, and pathology surveillance for adverse effects has just been enacted. Therefore at the time of this writing, no information is available on their systemic or gonadal effects in zoo species. Because drug metabolism differs among species, extrapolation of bisdiamine safety data to zoo species may be inappropriate. The same is true for species variation in response to zona pellucida (ZP) vaccines. In laboratory dogs, mice, and primates, the ovarian effects of ZP immunization depended on the species, origin, and purity of the immunogen, dose, and type of adjuvant. In some cases, permanent destruction of the ovary occurred. The information gained from these studies should be used to choose the best system for temporary or permanent immunocontraception in zoo species. The variation in ovarian response noted in these laboratory animal studies also confirms the importance of conducting carefully controlled clinical trials that include histopathological analysis of gonads to determine the species-specific effects of ZP vaccines.

AAZPA Contraceptive Committee Adverse Reaction Reporting System

To address the critical need for more information on the safety of contraceptives in zoo species, the AAZPA Contraceptive Committee has established a system for reporting adverse reactions. Any reproductive problems or unexplained diseases in contracepted animals should be reported to this center by completing the enclosed form. Each contribution to this database increases our collective understanding of the risks of using certain contraceptive methods. Information from this databank will be reported annually at the AAZPA meeting.

REPORT OF ADVERSE REACTIONS IN CONTRACEPTED ANIMALS

REPORTING INSTITUTION: _____

REPORTING VETERINARIAN/CURATOR: _____

ANIMAL SPECIES: _____

ANIMAL ID: STUDBOOK # _____ ISIS # _____

Contraceptive type and dose	Animal weight	Inclusive dates of contraceptive use
_____	_____	_____
_____	_____	_____
_____	_____	_____

ADVERSE REACTIONS: (PLEASE INCLUDE MEDICAL RECORDS)

MAMMARY GLAND CANCER: _____

UTERINE CANCER: _____
UTERINE INFECTION: _____

ENDOMETRIAL HYPERPLASIA: _____

DIABETES MELLITUS: _____
SKIN DISEASE: _____
BEHAVIORAL CHANGES: _____

OTHER DISEASES: _____
_____
_____

PLEASE MAIL TO:

DR. LINDA MUNSON
DEPT. PATHOBIOLOGY
CVM/UNIVERSITY OF TENNESSEE
P.O. BOX 1071
KNOXVILLE, TN 37901
615-974-8235

Ongoing Safety Assessment Trials

The optimal method to assess the safety of contraceptive methods in new species is to conduct controlled prospective clinical trials, rather than retrospective epidemiological analyses. Toward this aim, we have proposed that safety trials be conducted for the following contraceptives:

1. Zona pellucida vaccines from native or recombinant proteins with various adjuvants
2. Vas deferens plugs
3. High dose melengestrol acetate in a 24-month trial

4. Bisdiamines and indenopyridine

5. Medroxyprogesterone in primates and seasonal carnivores

6. LHRH vaccines

These trials need surplus animal volunteers that are targeted for permanent contraception. If you are interested in contributing your animals to these trials, contact Dr. Cheri Asa, St. Louis Zoological Park, Forest Park, St. Louis, MO 63110 (314-781-0900 X 488) or Dr. Linda Munson, Department of Pathobiology, CVM, University of Tennessee, P.O. Box 1071, Knoxville, TN 37901 (615-974-8235).

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Animal Behavior Management is Not Just for Keepers: The Role of the Zoo Veterinarian in an Animal Behavior Management Program
American Association of Zoo Veterinarians Conference 2002
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Abstract

The role of training and enrichment in zoo animal husbandry is widely increasing in scope and magnitude. During the past several decades, the zoo industry has steadily improved the standards by which we care for captive animals. Gone are the days where animals reside in concrete and iron-barred exhibits, in favor of more naturalistic and interactive exhibits that allow animals to make choices about and within their environments. However, with the increase in behavioral opportunities comes a liability and challenge for the animal care staff. Visual and physical access to the animals can become limited in these new habitats, causing medical care to be more challenging. To combat this potential problem and ensure proper medical and psychologic care, zoos have turned to working hands-on with many species in animal training and enrichment programs.

The authors broached this subject at the American Association of Zoo Veterinarians conference in 1993 with a paper titled “Behavioral Training of Primates and Other Zoo Animals for Veterinary Procedures” highlighting the vast amount of medical and husbandry behaviors that could be trained in zoo animals.[4] In recent years, numerous papers have echoed the importance of training specific behaviors for medical care or improved animal husbandry, and the importance of behavioral enrichment. In fact, it seems as though animal training and enrichment are at the forefront of zoo animal husbandry. With this surge of animal behavior management, several zoos throughout the country are employing a more programmatic approach toward training and enrichment.[2,3,5] Furthermore, the American Zoo and Aquarium Association now includes enrichment as a requirement for accreditation.[1]

The development of an Animal Behavior Management Program requires the input and expertise of numerous zoo departments. The essence of this type of program is teamwork. It is crucial that each department recognizes its role in the program, as well as every other department’s role. From keepers, to curators, to maintenance and horticulture, to the veterinary staff, the behavioral health of the animals becomes a part of each area’s responsibilities. The keepers are the front line in this type of program: it is they who care for the animals daily and know the individual animals’ behaviors, the layout of the exhibit and holding areas, and the constraints on their time. The keepers are the trainers and the implementers of enrichment. However, without input and assistance from other departments, they can do only so much for the animals. This paper will examine the role of the veterinarian in an animal training and enrichment program, including interactions with and expectations of keepers, curators, and other zoo staff.

Program Framework

Consistency throughout all departments in the zoo is crucial to developing a quality animal training and enrichment program. Therefore, a program framework can help to lay out the expectations of the program in general. The basis of the framework should be the program vision or philosophy that will guide the staff to the final product—for example improved animal care and welfare through the implementation of training and enrichment. In addition to the vision, there are several key components to a successful program, including the following.

Program Coordinator

Although few zoos employ a single person to coordinate the training and enrichment programs, a central contact or point person is often essential. The coordinator can help to organize the program in terms of writing the vision, developing documentation, and writing procedures and protocols. The coordinator should also serve as a contact for all departments, and ensure that the other program elements are in place and consistent throughout the zoo. This person should be experienced in operant conditioning and familiar with the principles of enrichment and behavioral husbandry.

Goal Setting

Program Goals

Goal setting can take on many forms—from the programmatic approach to the individual behaviors targeted through training and enrichment. Setting overall goals for the program will set the standards for the program and establish a common ground for consistency and communication. For example, one goal might be to increase the occurrence of natural activity of resident animals.

Project Goals

Once the program vision and goals have been identified, individual behavioral goals can be determined. These may include enrichment priorities or behaviors for specific animals, management or medical behaviors to be trained, etc. A clear set of project goals with timelines helps to create a more cohesive team in which all are aware of future priorities, who will be responsible for each project, project timelines, involvement of other staff, etc. When setting project goals, it is important to include not only the keepers and curators, but veterinarians as well, as they can advise the staff on the specific behaviors to target for animal health and wellbeing. For example, behavioral goal setting at the Toledo Zoo includes desired medical behaviors from the veterinarians and input from the keepers, curators, and animal behavior manager regarding daily husbandry and animal management behaviors (i.e., shifting, behavioral problem solving, etc.).

Planning and Implementation of Goals

The establishment of training and enrichment goals paves the way for the daily work to begin. Prioritizing goals and clarifying the roles of all involved are important during this step. Primary trainers can be identified and staff training implemented as necessary. During this stage of a training project, primary trainers are outlining training steps and determining the best methods for training. Veterinarians can provide valuable input at this point. For example, during training for an ultrasound exam, the veterinarians can offer advice in terms of where on the animal’s body to place the probe, where to position the machine, etc. When proposing new enrichment items, the veterinarians can be integral in assessing potential health risks. In such cases, many zoos have resorted to enrichment approval forms in which new items are described and submitted for approval by curators, veterinarians, and program coordinators.

Documentation

Throughout any behavior management project, documentation provides numerous benefits. Recording what enrichment items were offered, whether or not an item was used by a particular animal, or writing the results of a training session is key to a successful behavior program. Not only does this provide accountability and allow others on the behavioral team to monitor progress, it also allows staff to review the documents at a later date to look for behavioral patterns, correlations between different aspects of training (i.e., does the animal perform better for a specific reinforcer?), evaluate the use of enrichment, etc.

Evaluation and Readjustment

Evaluation can be a challenging aspect of a behavior management program. However, it is no less important than any other component of the framework. Both training and enrichment projects aim to target a specific response from the animals. By evaluating whether or not the appropriate response was achieved, the staff can adjust their methods to reach the desired behavior. Following a training project from start to finish, the veterinarian can review training records (documentation) to ensure that training is proceeding in a manner that will allow the final behavior to be achieved. In an enrichment program, we often place items in exhibits but fail to determine whether the animals react as intended. For example, enrichment to increase foraging behavior may be successful for one animal in an exhibit but may be ignored by others or become a catalyst for aggression between

cagemates. Evaluating the effectiveness of enrichment items can ensure that the animals' physical and psychologic needs are being met.

Role Clarification

With so many components of an animal behavior management program, it can become confusing trying to delineate the many responsibilities. Therefore, a document clarifying the roles of all involved in the program should be included in the basic framework of the program. The Toledo Zoo has developed "participant guidelines" for both training and enrichment that outline the responsibilities of all involved in both the training and enrichment aspects of the Animal Behavior Management Program. Included are the responsibilities of each of the following to each other:

- Animal behavior manager.
- Area keeper or primary trainer.
- Senior keeper.
- Area curator.
- Veterinarian/Animal health staff.

Protocols and procedures for training and enrichment are also outlined in various documents to ensure that expectations are communicated to each member of the behavior team and to again clarify the roles of all involved.

Role of the Veterinarian

The design of an animal behavior management program can take many forms depending on the needs and priorities of the institution. Thus, the role of the veterinarian can differ significantly among zoos. At the Toledo Zoo, the veterinary staff, including veterinary technicians, plays an integral role in the program for both training and enrichment and are seen as support for the keepers, the implementers of the program.

The primary role of the veterinarian in the Toledo Zoo's training projects is to provide guidance for the Animal Behavior Manager (ABM) and Primary Trainer (PT) in developing training projects. One or two members of the veterinary staff are assigned to serve as liaisons for each medical behavior being trained. Within this role are several responsibilities, including to:

1. Provide input during goal setting sessions regarding training priorities.

2. Work with PT, ABM, and area curator to develop guidelines for medical behavior training.

3. Consult on safety concerns (human and animal) and how to mitigate risks.

4. Review and provide input on training plans for medical behaviors to ensure that training steps are appropriate for the desired medical behavior/procedure.

5. Work with the PT on medical behavior training goals according to established training steps and participate in training sessions as necessary both to assist in the training, as well as to establish a positive relationship with the animals (vet staff are often written into training plans for invasive behaviors, such as blood collection, injections, or ultrasound).

6. Communicate with ABM regarding the progress of medical behaviors in training and veterinary needs as they apply to these behaviors.

7. Work with keepers to modify diets to accommodate reinforcers for training.

8. Participate in the design of restraint devices used during training sessions and procedures.

The veterinary input in the enrichment program is similar to that of the training program:

1. Provide input during goal setting sessions regarding enrichment that is targeted to alleviate medical problems or undesirable behaviors that adversely affect animal health (feather or fur plucking, aggression toward conspecifics, etc.).

2. Review and approve proposal forms for new enrichment items.

3. Work as part of a team with keepers, curators, and ABM to develop behavioral management plans for animals that exhibit behavioral abnormalities or undesirable behaviors, such as aggression toward conspecifics, stereotypic behaviors, or other behaviors that can adversely affect animal health or wellbeing.

4. Work as part of the above-mentioned team to develop isolation plans for animals that are removed from cagemates for a period of time, either for quarantine or behavioral reasons.

5. Work with keepers to modify animal diets as needed to accommodate novel enrichment.

6. Provide input regarding exhibit and holding area design for training and enrichment needs.

Cost:Benefit of an Animal Behavior Management Program

With an understanding of the importance of a zoo-wide training and enrichment program, it becomes obvious that while there are costs to this type of program (primarily staff time), they are far outweighed by the benefits. The ability to calmly separate animals for physical exams or procedures can reduce the need for immobilization drugs. Animals that choose to participate in such procedures tend to be calmer than when subject to physical or chemical restraint. In fact, many animals can be examined, treated, or diagnosed during regular training sessions, unaware that they are experiencing anything other than a routine part of their daily interaction with the staff. Such experiences can in fact be enriching for many animals, providing them with opportunities to make choices within a training session, and offering them activities that are mentally challenging or time consuming.

In addition to these obvious benefits to animal health, a training program can mean safer interactions for the animal care staff and enrichment can mean the difference between an animal exhibiting appropriate behavior and stereotypic behavior. Training and enrichment gives keepers additional contact with the animals, and therefore, allows for opportunities to observe the animals and detect potential medical problems. Through this program, animals will have increased trust in the veterinary staff, as they have been a positive aspect of the animals' lives.

Common Questions and Concerns of Both Veterinarians and Keepers

While this paper is intended to address the role of the veterinarian in an animal behavior management program, other concerns will likely arise that affect staff members, and ultimately animal wellbeing. Additional challenges with this type of program include:

1. How to gain support of upper management for the animal behavior management program.

2. How to address staff and animal safety when embarking on a more hands-on approach to animal care.

3. How to address keeper territoriality issues.

4. How to get all area keepers on the same page in terms of support of the program and policies.

A programmatic approach to training and enrichment can help answer these and other concerns.

Conclusion

The nature of the animal behavior management program requires a team effort from all staff. Therefore, not only is the clarification of roles crucial; support of each other is just as important. As primary caregivers, both veterinarians and zoo keepers can become inundated with daily tasks and the increased responsibility that accompanies the improvement in zoo animal husbandry, medical care, conservation, and public education. Common concerns for veterinarians and keepers is how to make time for training and enrichment, and how to work together and gain each other's support for this type of program. Because each comes from different perspectives of animal care, but have the same goal in mind, clear and honest communication is imperative. Realizing that animal wellbeing is the responsibility of all staff, veterinarians, keepers, and curators must work together to reach this and other common goals. Doing so can only benefit the animals.

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Animal Training Techniques at the Toledo Zoo in Different Species to Aid in Introductions, Movement, and for Behavioral Enrichment
American Association of Zoo Veterinarians Conference 1990
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Following successful training and subsequent introduction of a somewhat hyperactive 13-year-old adult breeding male lowland gorilla to his family (2 adult females, 18 and 20 years, and 3 juveniles ranging from 5 months to 2 years) in March 1989, the Toledo Zoo began exploring a more active, open animal training policy, not only for the great apes, but for several different animal species. Using basic universally accepted training techniques in conjunction with recommendations and techniques emphasized by behavioral consultant Tim Desmond[a] (consulted in February 1989 for the gorilla introductions), management and keepers have begun to outline and work on goals for behavior modification of various species of animals in our collection.

The Toledo Zoo has had a history of experience (although somewhat limited) with animal training which served to lay the groundwork for the work being done now. Former zoo veterinarian Dr. Charles Hardin,[b] Glenous Favata,[c] and others worked in the early 70s (1971–1973) on artificial insemination of chimpanzees using the group of 1.3 chimps housed at the zoo. The male, “Coco,” was successfully trained to masturbate on command into an artificial vagina for semen collection. The females were taught with varied success to hang upside down and present their perianal regions for inspection, injection and/or insemination. The primary positive reinforcement was attention and keeper interaction. This work was later abandoned, but the 3 females still housed at the Toledo Zoo still present their perianal regions on command, and “Ellie” stands for injections.

The Toledo Zoo also instituted an elephant training program in 1982, still active today, with the arrival of 0.2 African elephant females (current ages average 11 years). Initial training and guidance were given by professional elephant trainer Richard “Army” McGuire[d] and has been carried on by senior elephant keeper Don RedFox[e] and others. The program was instituted initially for safety reasons as well as for management/husbandry considerations and continues to be a dynamic program, changing and growing to suit the zoo’s needs, the age of the animals, and the experience of the keepers in the program. At present it is a 2-keeper system, and training consists of a series of “tricks” or behaviors the elephants can perform which are categorized into graduated levels of difficulty. Some of these behaviors include opening the mouth (to check teeth), lifting a specified foot for trimming and inspection, lying down for injections, drawing blood, etc. The keeper being trained to direct the elephant through these behaviors must exhibit complete control of the animal at one level before proceeding to the next.

By using this structured, yet flexible, approach for other species of animals, the keepers at Toledo Zoo have used animal training to achieve a number of successes:

1. Introduction of an adult male gorilla to his family (as previously mentioned). The male has a history of hyperactive juvenile behavior and killed one infant he was exposed to in the past. Using target training, keeper interaction, and environmental enrichment techniques, keepers were able to reduce stress and promote better cooperation from the group, averting major conflicts. This successful introduction allowed more natural relationships to occur between the animals—similar to those in the wild, and created an excellent group for exhibit.

2. Training of 0.3 adult female gorillas to present their perianal regions for labial inspection and to urinate in specific off-exhibit holding areas on a daily basis so urines can be collected and analyzed for estrus detection.

3. Crate-training of 1.1 geriatric American river otters (ages estimated at 20 years) for the purpose of shipping, avoiding immobilization and its inherent risks.

4. Reintroduction of an infant Bornean orangutan being hand-raised to its mother at 3 months of age.

The, 36-year-old, multiparous female, “Maggie,” was attentive and had been worked with before with other babies, but had difficulty positioning her infants for nursing because both breasts were so pendulous. By working closely and intensely with Maggie while hand-raising the baby, the keepers were able to manipulate her breasts and manually express milk and even place the nipple or a bottle of formula into the infant’s mouth once he was reintroduced. In this instance, not only food treats, but keeper interaction and contact with the infant were used as the positive reinforcement.

5. Training of 1.1 reticulated giraffes (2.5- and 1.5-year-old) to move easily down a lengthy (approximately 375 ft) outdoor fenced path with a series of mechanical gates to get to a large natural outdoor mixed exhibit area, and then to move back off exhibit to the indoor holding area at night. A cowbell is used as the audible signal, and a gray bucket is used as the target containing treats.

6. Conditioning of above 1.0 giraffe to allow examination of incisor teeth without sedation/immobilization.

7. Moving, manipulating, performing minor veterinary procedures on 0.3 African elephants using vocal commands only as primary means of control.

8. Teaching an adult male white rhinoceros to move and back up on vocal command and to knock over a set of bowling pins on cue as a promotional demo for the conservation fund-raising project, “Bowling for Rhinos.” Female urine and feces were used initially to reinforce the behavior.

9. Training of 1.1 ostriches, 1.2 zebras, and 1.2 kudus to move to indoor holding facilities from a large outdoor mixed exhibit in the evenings, an audible bell is used as a signal for some of these animals. 1.1 hippos and 1.2 lions have been trained to move inside their respective areas using similar methods.

Training projects currently in progress or being planned include:

1. Target training and training “games” with 1.1 and 2.4 lowland gorilla groups for behavioral enrichment, better cooperation and gating, and future veterinary procedures and introductions.

2. Similar target training and games for behavioral enrichment of an older male mandrill (20 years) who recently lost his long-term cagemate.

3. Target training and eventual movement on command of 1.1 adult sea lions and 2.0 subadult sea lions for transfer to a new exhibit. They will be taught to move onto and off a stock trailer to be transferred. Eventually a squeeze cage will be available, and their behavior will be modified to move through this for veterinary procedures and exams.

4. Work on flight training of an adult female kestrel and later other raptors for flight demos used in the zoo’s education program.

5. Movement and gating of an adult male nyala who has become too aggressive to handle via direct contact.

In all the above situations, food and/or treats and keeper interaction are used as the primary forms of positive reinforcement. In most instances natural behaviors are reinforced. The training sessions also serve as an excellent form of environmental and behavioral enrichment.

To summarize, the Toledo Zoo has begun to outline objectives and goals desired for different animals in the collection (individuals and groups of animals). Each case is then evaluated individually, considering the personalities and limitations of each species and also their exhibit or enclosure design. Basic animal training techniques are then systematically applied by experienced keepers when possible to achieve the goal desired. We have found that animal training can be a viable, positive and often successful alternative to noxious stimuli or immobilizations for movement, introductions, and conditioning of animals to new situations. It has the potential for reducing stress and creating a strong trainer-animal bond while making procedures much safer for all involved. It also serves as an excellent means of behavioral and environmental enrichment and can be very rewarding for both animal and keeper.

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e. RedFox D. Toledo Zoo

Animal Training, an Overlooked Science: Bringing Training Out of the Closet
American Association of Zoo Veterinarians Conference 2002
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Abstract

When most people think of animal training, it either conjures up images of performing animals in the circus or a pet dog rolling over on cue. While those images certainly reflect one small component of training it hardly represents the complete picture; no more than describing a doctor's job as "prescribing a few pills" accurately reflects a physician's duties or the extent of his or her knowledge. Modern trainers in a zoologic setting should be skilled professionals with a background in both animal care and animal behavior. Trainers must know the science behind training and understand the practical applications with a variety of species. Training is one of the cornerstones to a good animal care program; just as one would never put together an animal care program without proper veterinary care, good nutrition, and the proper environment, a behavior management component is just as essential. Today, thanks to modern training, many diverse and seemingly amazing feats have been accomplished: nurse sharks swimming into a stretcher for weights, a baboon presenting its arm for insulin injections, a killer whale allowing its tooth to be drilled, a tiger submitting to ultra sound exams, and an endangered black rhino allowing blood to be drawn from its ear. These are just a few examples of the possibilities. However, for more programs to realize this type of success, all animal care personnel must recognize the importance of training and recognize the skills needed to implement a good behavioral management program. Additionally, the barriers that tend to get in the way of good communication must be avoided—trainers, keepers, veterinarians, curators, and managers can all contribute to the roadblocks to good communication. Finally, everyone involved in an animal care program should be aware of the most common pitfalls that can cause a good training program to fail.

Training is a Science

Training is a technology based on proven scientific principles.[3] The serious trainer must understand both operant and classic conditioning; these two very different concepts explain why animals behave the way they do and govern how an animal will learn within a training program. Classic conditioning was first defined by Pavlov and describes the automatic or involuntary response that animals have to certain stimuli.[1] An understanding of these principles will help a trainer better understand an animal's instinctive responses to certain situations or reactions to certain behaviors, such as aggression. Operant conditioning was first defined by Skinner and it describes the learning that occurs when an animal's behavior is modified by the consequences that follow it.[4] As an example, assume that a dog pokes his nose into a fountain and is sprayed with water. If he likes the sensation, he is likely to repeat the behavior—because the behavior was reinforced. On the other hand, if the dog pokes his nose into the fountain and it frightens him, he is less likely to repeat the behavior—because the behavior was punished. Understanding these principles and the things that affect, motivate, and modify behavior are a key to training animals.

Basic Training

Most training programs revolve around the application of operant conditioning principles. At first glance, the concepts seem simple and straightforward, which is precisely what causes some people to delve into training without being fully prepared for the problems and pitfalls. Although basic training concepts are simple, the proper application of those principles, under less than perfect circumstances, requires a great deal of expertise. One of the clearest introductions to operant conditioning for the beginner, is Karen Pryor's book *Don't Shoot the Dog*. She developed a list that she refers to as the "10 laws of shaping."[2] These laws provide a good introduction to basic training principles without getting too bogged down with operant jargon. Here is Pryor's list with my own explanation of each law's meaning.

1. **Raise criteria in small increments**. By using very small steps (successive approximations) you will set your animal up to succeed.

2. **Train one criterion at a time**. This will keep your goals clear and not confuse your animal. Most behaviors have multiple criteria, but you should focus on only one aspect of the behavior at a time. If you are asking an animal to position its hindquarters against one part of its enclosure so that you may give an injection, the position, the length of time in that position, touching the animal, the use of a syringe, and the use of an assistant are five separate criteria.

3. **Vary reinforcement before moving to the next approximation**. One way to maintain a strong response in an animal is to assure that reinforcement is varied. There are many ways of providing variety including varying the magnitude of reinforcement, type of reinforcers, or requiring varied duration or repetition of the behavior being trained.

4. **Relax old criteria when introducing new criteria**. When an animal is being introduced to something new, it is not unusual for an animal to fail to meet all previously learned criteria. This is acceptable at first and will minimize frustration in your animal.

5. **Plan ahead**. Have a training plan in mind and know the short-term and long-term goals.

6. **Don't change trainers in mid-stream**. In order to maintain consistency with the animal it is not wise to have different individuals training the same behavior.

7. **If a plan doesn't work change the plan**. Training is a dynamic process, so don't be afraid to change the plan.

8. **Don't stop a session gratuitously**. It is important to stay focused and not get distracted, don't end a session abruptly or the animal may get confused or frustrated.

9. **Regress when behavior deteriorates**. It is normal for animals to forget or get confused. Taking a few steps back can refresh their memory and get them back on the right track.

10. **End on a positive note**. Training should always be fun. Avoid ending a session when an animal is frustrated; try to end with success.

The Veterinarian's Role

It is typically not the role of the veterinarian to build the type of relationship with an animal necessary for successful training. However, veterinarians can have a tremendous impact on the ability of trainers to train their animals successfully. There are several programs that demonstrate a very good relationship between the veterinary staff and the animal care staff. Those programs seem to have the "cure" for building veterinarian/trainer relationships: communication, understanding, respect, and evaluation.

Communicate

It is critical that veterinarians communicate their plans, needs, and expectations to the animal care staff far in advance of a visit or exam. Likewise, the trainers must communicate their plans needs and expectations to the veterinary staff.

Understand

All staff should understand the role and responsibility of each person involved in making animal care decisions.

Respect

Each staff member has special skills and talents that they bring to the job; it is important to respect those skills and talents.

Evaluate

After each procedure it is important to evaluate what worked and what did not so that future procedures can be made more efficient and successful—which leads back to the top of

the list with communication.

Most Common Mistakes

Finally, there are many pressures and decisions that are made that can cause animal behavior to deteriorate. Some of these pressures are from eager inexperienced trainers who expect too much too fast, sometimes the pressure comes from managers who demand unrealistic results, and sometimes the pressure is from the veterinarian who is pushing urgently for assistance in a medical treatment. Whatever the reason, it is usually when dealing with problem behavior or medical issues that the biggest mistakes in training are made. Here is a list of some of the most common pitfalls that cause medical behaviors to deteriorate. They are in no particular order.

Looking for the Quick Fix

We all want behavioral problems solved quickly, but the reality is that it takes time to solve them. Searching for a quick fix often leads to the use of punishment or aversive stimuli, which can ultimately cause bigger problems.

Forgetting That Learning Is Always Taking Place

Animal care staff will often forget that an animal is learning all the time, not just when a training session is taking place. When trainers or veterinarians forget this fact, they often inadvertently shape undesirable behavior. Activities and interactions that take place with or near the animals can affect an animal's behavior in either a productive or destructive manner—the only way to make sure that learning is productive is to be conscious of each and every interaction.

Using Voluntary Medical Behaviors Before They Are Completely Trained

This is one of the most common mistakes made when training voluntary medical behaviors. Although it is more typical with beginners, even experienced trainers can fall into this trap. A behavior may be progressing very well, when suddenly there is a medical need that would benefit from the use of this "behavior in training." At the time, the temptation to use the behavior "even though it is not quite ready," is very strong—it seems easy, what can it hurt? Most of the time it fails to get the desired result and even when it does work, it often breaks down the trust and can turn the behavior into a frightening experience. If a medical behavior (taking blood, kennel or crate training, giving an injection, etc.) is planned for regular or frequent use, it is important not to use the behavior for actual sampling until all steps are completed and the animal has been desensitized to all stimuli.

Not Using a Conditioned Reinforcer (A Bridging Stimulus or an Event Marker)

Whether a trainer uses a whistle, a clicker, or simply says the word "good" the use of this signal is instrumental in shaping behavior. Sometimes trainers will feel that once a behavior is trained that a whistle is no longer needed. However, it is important to remember that medical behaviors are never truly complete; there are always new stimuli to desensitize or longer durations to approximate. The conditioned reinforcer becomes invaluable in providing the animal with information about what aspect of the behavior is being reinforced.

Using Too Many Trainers to Train One Task

This is a common mistake when working on medical behaviors. The urgency or desire to get the behavior completed sometimes necessitates multiple trainers. However, if you must use more than one trainer it is still wise to use as few as possible and to make sure that those who are involved communicate constantly and in a consistent manner.

Making Assumptions About What an Animal Likes

It is easy for trainers to fall victim to the concept of assuming they know what an animal finds reinforcing. But husbandry behaviors frequently involve novel or frightening equipment, some discomfort, or awkward positioning. For this to be worthwhile to the animal it requires that the reinforcement offered be high. Most experienced trainers know how to gauge this, but it is truly a difficult thing to define and a mistake made often by young trainers.

Taking Approximations That Are Too Large

It is not unusual for a skilled trainer or a sharp animal to move quickly through certain training steps. Often this encourages the trainer to make larger and larger approximations. However, these approximations are the foundation of a strong medical behavior, skipping steps or taking large approximations can weaken the foundation that these behaviors are built upon.

Forgetting the Importance of a Calm Response

One of the keys to successful medical training is a calm response by the animal. However, if a sample is successfully taken, trainers will often get so excited that they bridge and reinforce the behavior even if the animal is tense, nervous, or moving too much. This inevitably teaches the animal that this type of movement is acceptable.

Desensitization Is an Ongoing Process

The effort to desensitize animals to new stimuli and new situations is a continuous process that never ends. When trainers assume that a medical behavior is complete and everything has been desensitized, they are likely to be disappointed very quickly.

Trying Just One More Time or Pushing for a Few Extra Seconds

When a trained behavior fails to get the desired result or pushing for a few extra seconds seems like it will allow the veterinarian to get the sample he or she wants, trainers are often tempted to push the limit. However, one of the best ways to ensure long-term success is to reinforce a behavior well if the animal did its part correctly and not ask for the behavior again too soon. If a needle was inserted or the animal remained calm, but you did not get the sample you were looking for—it was not the fault of the animal. The animal should be reinforced well. Asking again can sometimes cause the behavior to deteriorate, unless the repetition or the extra time was already a part of the training.

Lack of Communication

As discussed in a previous section, communication is a key to successful interactions between trainers and veterinarians and a well-communicated plan can set the animal and the staff up for success.

Assuming That Training Can Be Done by Anyone

On the outside, training can seem so simple that the training of complex medical behaviors or the resolution of behavioral problems are often assigned to individuals with little or no training experience. While it is certainly wise for all animal care staff to understand the basics and importance of operant conditioning, there is no substitute for the knowledge and skill of an experienced professional trainer.

Conclusion

Training offers an incredible tool to help us manage the animals in our care more responsibly. A behavioral management program that is overseen by an experienced trainer will assure that training needs are not placed on the backburner, but given the importance they deserve. As more facilities recognize the significance of training and approach it as a science and as one of the cornerstones to good animal care, there is no question that the animals will benefit. The veterinarian plays a key role in influencing animal care decisions, and he or she is in a position to help bring training out of the closet and to the forefront in animal care management and decision-making. The points described above are hardly a substitute for a good training manual or extensive training experience; but hopefully they serve as a starting point for thinking about how to integrate training into a strong animal care program.

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Search Result #8: **Applied Behavioral Analysis: The Science Behind All That Training**

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Applied Behavioral Analysis: The Science Behind All That Training
American Association of Zoo Veterinarians Conference 2010
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ABSTRACT

"Training" is now mainstream in many zoos and aquariums. Specifically, positive reinforcement training is being utilized to achieve a wide range of medical, husbandry, and public presentation behaviors in a multitude of zoological species.

Positive reinforcement training fits within a larger field of behavioral analysis and the techniques are applicable within and outside of the zoological field.[3,6,9,10,15] Behavioral analysis is the study of behavior change; how individuals learn behavior (i.e., operant behavior or conditioning).[2,5] Applied behavioral analysis is the utilization of this science "in the real world." The laws and rules that govern learning in individuals provide a robust method for examining behavior, productively evaluating and reducing problem behavior, and teaching (training) specific behavior.[2,6,9,15] They are conserved across species and thus applicable to all animals.

Behavior and why behavior develops or changes can be examined through a variety of sciences (e.g., neuroendocrine, genetic, physiology, etc.). As veterinarians, we are trained to consider medical causes for behavior or behavior change. For example, increased aggression (e.g., biting when touched) may be due to pain or a brain tumor. In the zoological field, we often consider natural history or evolutionary causes for behavior or behavior change. For example, biting may be from territorial defense during breeding season. In addition to these more familiar methods of behavior evaluation, behavioral analysis is critical for understanding how behavior develops, and is maintained in an individual animal.[5] For example, biting developed because it was reinforced in the past; the animal has learned to do the behavior. These approaches are not mutually exclusive and integration is often integral to successful training and problem behavior intervention.

An excellent review of applied behavioral analysis for veterinarians exists.[5] The review examples are from parrots, but as noted above the principles are conserved across species. Certain highlights are presented below.

Behavior is a function of its consequence (The Law of Effect). A consequence is a stimulus, event, or condition that influences the strength of future behavior.[5] Reinforcers are consequences that maintain or increase a behavior; punishers are those that decrease behavior. The consequence is defined by what it does to behavior, not what it is.[5] Consequences can also be categorized based on input; positive if added to the environment and negative if removed/escaped/avoided. Positive and negative are mathematic concepts; there is no connotation of "good/bad." Thus, there are four consequence options (also called quadrants); positive reinforcement ("reward"), negative reinforcement ("escape"), positive punishment ("discipline/correction"), and negative punishment ("penalty/fine") as displayed in Table 1. It is the learner who determines if something is reinforcement or punishment.[5] If you yell "stop it" when your dog barks and barking increases in frequency, intensity, duration, etc. then yelling is reinforcement to the dog, no matter what you want it to be!

Table 1. Summary of the four consequence options[a]

	Reinforcement (increase behavior)	Punishment (decrease behavior)
Positive (add)	Positive Reinforcement (R+) Addition is desired Commonly called: Reward	Positive Punishment (P+) Addition is aversive Commonly called: Discipline/correction
Negative (remove)	Negative Reinforcement (R-) Aversive is in antecedent Commonly called: Escape	Negative Punishment (P-) Removal is aversive Commonly called: Fine/penalty

[a]Modified from: Freidman SG, Edling TM, Cheney CD. Concepts in behavior: Section I. In: Harrison GJ, Lightfoot TL, eds. *Clinical Avian Medicine Volume I*. Palm Beach, FL: Spix Publishing Inc.; 2006:46–59.

Whether a consequence is reinforcement or punishment can only be fully evaluated by observing what actually happens to behavior in the future. Based on understanding an individual animal or species in general, it is possible to predict the likely impact of consequences on behavior. This predication is part of the basis for implementing purposeful training programs and developing problem behavior interventions. However, the actual impact on behavior must be evaluated to test if the prediction is correct.[5]

Behavior is never evaluated alone but is always considered within the context of the environment immediately surrounding the behavior and functionally related to it. Thus, the smallest unit to evaluate behavior is the behavior (B) with the environmental brackets of the antecedent immediately before the behavior (A) and the consequence (C) immediately after the behavior (A-B-C).[5] The observable behavior of interest is defined first, using clear, concise language to describe the relevant behavior. Then the consequence and antecedent are identified and described. The ability to list and understand the functional relationship between a behavior and the environment around it is extremely important when trying to reduce problem behavior.[5] The functional analysis (A-B-C) becomes, in effect, a hypothesis to identify what, exactly, the problem behavior is and what consequences may be maintaining that behavior as well as the environmental cues that elicit the behavior. This functional relationship between A-B-C is also the fundamental relationship that is developed when specific behaviors are purposefully trained.

This process of receiving feedback from the environment and feedback modifying future behavior (i.e., learning) is completely natural and happens constantly "in the wild" as well as "in captivity."[2] While we may use it to purposefully train behavior, it is functioning at all times and not just in training sessions. Every interaction humans have with the animals in their care creates a "learning" opportunity. In addition, the animal's interactions with other animals and the overall environment will also be providing constant feedback as to the effectiveness of behavior.

There are predictable negative side effects to living in environments that provide higher amounts of negative reinforcement, positive punishment, and/or negative punishment than positive reinforcement.[5] These include apathy/reduced activity, aggression, escape/avoidance, and over-generalized aversion to environment.[2,5] There is increasing focus in all areas of captive animal management on purposeful training using positive reinforcement and also establishing environments that are filled with opportunities for animals to "naturally" obtain positive reinforcement (i.e., enrichment). Enriched environments that provide opportunities for choice, control, and positive reinforcement have been linked to improved behavioral and physical health in a variety of studies.[1,4,7,8,11-14,16]

Increased understanding of the scientific principles that underline how individuals learn behavior can allow veterinarians to more productively help prevent or manage behavior problems in captive animals and assist husbandry staff in training desired medical behaviors.

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Azaperone for Standing Sedation in Asian Elephants (*Elephas maximus*)
American Association of Zoo Veterinarians Conference 1996
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Abstract

Azaperone was used for standing sedation of four Asian elephants (*Elephas maximus*) in 93 trials at Dickerson Park Zoo (DPZ). Procedures including surgical artificial insemination, semen collection, and routine foot trimming were completed while utilizing azaperone as a sedative. All procedures were performed within an elephant restraint device. Azaperone has proven to be a safe and reliable drug for facilitation of routine health and reproductive-related procedures in captive Asian elephants when administered at 0.30 mg/kg. The procurement of azaperone in the United States has been difficult due to changing manufacturing and distribution procedures. The utilization of an Investigational New Animal Drug permit from the Food and Drug Administration is described, to facilitate procurement of azaperone from Canada for use in the United States.

Resumen

La azaperona fue utilizada para lograr sedación sin recumbencia en 4 elefantes asiáticos en 93 pruebas en el Parque Zoológico Dickerson. Los procedimientos que se realizaron mientras los animales estaban sedados con azaperona incluyeron inseminación artificial quirúrgica, recolección de semen, y recorte rutinario de las uñas. Todas las actividades se realizaron dentro del sistema de contención de elefantes. La azaperona administrada a una dosis de 0.30 mg/kg ha demostrado ser una droga segura y confiable que facilita el manejo de elefantes asiáticos para exámenes de rutina y procedimientos reproductivos. La obtención de la azaperona en los Estados Unidos ha sido difícil debido a cambios en los procedimientos en su fabricación y distribución. Se describe la utilización de un permiso para la Investigación de Nuevas Drogas en Animales, dependiente de la Oficina de Administración de Drogas y Alimentos (FDA), que facilita la importación de azaperona de Canadá para su uso en Estados Unidos.

Introduction

Elephant handlers have traditionally applied the so called “free-contact” method of elephant control for providing care to captive elephants. The inherent dangers of this free-contact method with some individuals in the elephant population are reflected in the numbers of elephant related injuries and occasional deaths of handlers. These dangers, along with the controversy concerning discipline of dominance controlled elephants, have encouraged adoption of “restricted contact” for some individual elephants and programs of captive elephant management. In 1988 DPZ began a program of restricted contact with mature bulls and selected individual cows, with the installation of a moving wall elephant restraint. This conventional restraint provided twice daily confinement for basic care of Onyx, the zoo’s intractable bull Asian elephant. This care included periodic administration of xylazine for standing sedation during trimming of problem toenails. Xylazine was the drug used in each of the eight foot trimming sessions. However, xylazine proved ineffective during these sessions due to the bull’s frequent arousals when stimulated by activities related to routine foot care.

Xylazine was not considered for use in the zoo’s elephant artificial insemination (AI) project. Persistent urine dribbling under the influence of xylazine precluded its use for semen collection. Xylazine’s attributed inhibition of reproductive hormone secretion in females of other species and its profound changes in uterine motility made its application questionable. An additional problem was the prolonged drowsiness (up to 48 hours) following xylazine administration and yohimbine reversal. The negative aspects of xylazine necessitated finding an alternate method for sedating elephants.

In May 1992 completion of the zoo’s latest elephant restraint device ushered in a new era of captive elephant management at DPZ. The prototype restraint was designed and built for manipulation of elephants in standing and lateral recumbency. The effectiveness of the elephant restraint has been greatly enhanced by the situational use of the sedative tranquilizer azaperone in intractable individuals. Azaperone is classified as a neuroleptic tranquilizer of the butyrophenone series of tranquilizers. The proprietary product Stresnil contains 40 mg/ml of azaperone. Azaperone has been reported by Kock[2] to produce good sedation in various age groups in doses ranging from 30 mg for babies, 120 mg for juveniles, to 760 mg for adult elephants. Azaperone has been used in African elephants as reported in MedARKS records submitted and summarized by Page.[3] In the seven elephants of known weights the mean dosage was 0.10 mg/kg (range 0.06 to 0.15 mg/kg). A calming effect is produced through central nervous system depression. In swine a wide dosage range may be used (2–40 mg/kg). Azaperone is a relatively nontoxic, short-acting drug that is active for 2–3 hours and nearly eliminated in 16 hours.[1] It is approved and has been marketed in the United States for use in pigs to relieve stress and minimize introductory aggression by Pittman-Moore Company. Recently they have suspended producing and marketing Stresnil in the United States. However, Janssen Pharmaceutica of Mississauga, Ontario, Canada has gained the manufacturing rights and Stresnil is being distributed by the Upjohn Company (Animal Health Division, Orangeville, Ontario, Canada L9W 3T3; (519) 941-1030, FAX (519) 941-1074). To be able to import azaperone a **Notification of Intent to import a new animal drug(s) or an investigational new animal drug substance** (INAD) must be obtained from the Food and Drug Administration’s Center for Veterinary Medicine. Once the application is returned and approved by the Center for Veterinary Medicine, notification of an INAD# is received and the drug can be ordered. The INAD application can be requested by contacting:
Dr. Marcia Larkins, HFV112 Center for Veterinary Medicine Food and Drug Administration, 7500 Standish Place, Room 319, Rockville, MD 20855; (301) 594-1612 or 0614.

Methods

The use of azaperone as an elephant sedative was evaluated in 93 trials in a group of four sexually mature Asian elephants. The study animals included two bulls (ages 32 and 17 years), and two cows (ages 32 and 21 years). All the animals were housed at DPZ during the study period.

Occasions to use the drug included foot trimming and semen collection of bulls and surgical AI with subsequent follow-up care of cows. Semen collections were performed using electroejaculation or manual stimulation techniques. The rotational capabilities of the restraint positioned the bulls into left lateral recumbency for the foot trimming sessions.

Weights of the animals were determined using a scale built into the restraint, allowing accurate dosing. Intramuscular injection of azaperone was administered via hand syringe in the triceps muscle using a 2-inch catheter needle. The bulls were injected while confined in the restraint. The cows were normally injected in a stall adjoining the restraint and permitted to enter on their own during the latter stages of induction. Intravenous injections of azaperone were avoided due to transitory excitement tendencies reported when this class of drug is administered in this manner. Following azaperone injection, each elephant was closely monitored to determine the time of initial effect, time of maximum effect, and total duration of effect. The initial effect was recorded at the time of first perceived change of the elephant’s normal behavior or posture. Maximum effect was recorded at the time frame of least response to external stimuli. The duration of effect was defined as the point in time when the drug’s effects were no longer detected.

The degrees of sedation were rated as good, fair, or poor. They were determined by the ability to begin and complete a particular procedure in relation to amount of interference from the elephant involved. A rating of good was given when the elephant demonstrated no or minimal response from the procedure’s stimuli. A fair rating was given if the response was noteworthy but did not hinder the procedure. A poor rating resulted if the elephant’s response resulted in an aborted or abbreviated procedure.

Results and Discussion

The dose range of azaperone utilized in this study was 0.017–0.046 mg/kg. The lower dose or half-dose was given due to a temporary shortage of azaperone. The half-dose provided adequate depth of sedation, but effects were short-term. The higher range was given to attain profound sedation required for electroejaculation of a bull Asian elephant. A normal dose range from our experience has been determined to be between 0.024 and 0.038 mg/kg for use in minor surgical procedures. Azaperone dosages within this range have provided a safe and reliable standing sedation for restraint of confined Asian elephants.

The sedative effects of azaperone on elephants in 93 trials were rated as good in 81 trials, fair in 12 trials, and poor in none. The calming initial effects of azaperone on the elephant could be seen in 10 to 15 minutes following injection. In most cases, appetite seemed to increase during this time. Maximum effect was attained in 15 to 25 minutes. Maximum effects were characterized by a stuporous or somnolent mental state often accompanied by snoring, an unwillingness to move or respond to stimuli, diminished bowel movement,

distended or relaxed penis or clitoris. No tendencies or desires to lie down have been noted. Maximum effects rapidly diminished after approximately two hours. Total duration of effects was approximately three hours. Repeated daily administration of azaperone during two to six day periods demonstrated no residual effects.

During the induction phase azaperone appears to have sensitizing effects on the elephants' response to stimuli, particularly noise. Any stimulation or activity tends to prolong induction time particularly with an intractable or nervous elephant. Consequently, it is important to have a quiet environment during induction until maximum effect is achieved.

Azaperone appears to diminish aggressive behavior in bull Asian elephants. A highly aggressive bull in musth becomes very placid, and tolerant of stimulation once maximum effects of azaperone have been reached. Azaperone and the restraint system combined, provides the capability to perform a wide variety of procedures regardless of the animal's normal intractable nature. Some of the potential uses for azaperone would include tusk trimming, minor surgery, and other routine treatments.

Two abnormal responses were shown from the same cow during azaperone induction. The episodes of confused or hallucinatory behavior were responses to mild stimuli. Although these experiences were isolated, for safety considerations the drug is administered only under controlled circumstances whereby direct keeper/elephant contact is not required. The reasons for these episodes have not been determined and call for further investigation. Once maximum effect has been attained, no behavioral problems have been noted.

Conclusions

Azaperone at a dose of 0.030 mg/kg (range 0.017–0.046 mg/kg) has proven to be safe and reliable in providing standing sedation for both male and female Asian elephants within a restricted contact protocol. Azaperone has shown no residual effects. Recovery is smooth and rapid. Azaperone provides effective sedation in a small dose (120–160 mg or 3–4 ml). The maximum effect is long enough for most procedures to be completed and no inclination for recumbency has been noted. Elephants under the influence of azaperone should be managed only in a restricted contact situation. Sedated animals show diminished aggression, even males in heavy musth. Azaperone has proven its value for routine utilization for intractable elephants within these guidelines.

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Search Result #10: **Behavioral and Medical Therapy for Self-Mutilation and Generalized Anxiety in a Bonobo (*Pan paniscus*)** Click to go to the TOP

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Behavioral and Medical Therapy for Self-Mutilation and Generalized Anxiety in a Bonobo (*Pan paniscus*)
American Association of Zoo Veterinarians Conference 1998

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Case Report

Treatment of abnormal or undesirable behaviors with behavior modification and medical therapy is relatively new to the field of veterinary medicine. Few published reports on the use of antidepressants and antipsychotic drugs in exotic animals exist.[2] This report describes the successful treatment of a nonhuman primate with a combination of behavior and medical therapy based on extrapolation of similar treatments used in human psychiatric medicine.

On July 8, 1997, the Milwaukee County Zoo (MCZ) received “Brian,” an 8.5-year-old, 35-kg male bonobo (*Pan paniscus*) from another institution. The animal was born at that institution and had been housed with its father and other troop members until 7.5 years of age. Reports from the staff indicated that the bonobo was regularly severely intimidated by its father. During this time, the bonobo developed the persistent self-mutilating behavior of inserting its fingers and/or entire hand into its rectum (termed “fisting”).

Believing that this behavior may have been caused by chronic stress and mental trauma, the animal was removed from the group in October 1996, and housed in isolation for 8 months prior to its arrival at the MCZ. The “fisting” behavior continued while in isolation, occasionally with enough intensity to cause rectal bleeding. Treatment with acepromazine 12.5 mg orally every 8 hours was begun in November 1996. Effects were minimal and treatment was discontinued shortly thereafter. Magnetic resonance imaging was performed in December 1996 to determine if an underlying physical problem was causing the behavior. The rectum and lower colon were palpably thickened, which was attributed to chronic trauma; however, no other abnormalities were noted. Treatment with fluoxetine (Prozac, Eli Lilly & Co., Indianapolis, IN, USA) 16 mg orally once a day was initiated in December 1996, and 14 days later it was noted that there was improvement in both the severity and frequency of the “fisting” behavior. Therapy was continued until just prior to shipment to the MCZ. To try to provide the animal with a better social environment, it was sent to the MCZ for integration into a large group of bonobos. The bonobo troop consisted of one juvenile and four adult females, and two juvenile and two adult males. In addition, the MCZ has an active operant conditioning and medical behavioral training program, and it was hoped that behavioral therapy would reduce the self-mutilation behavior.

When the bonobo arrived at the MCZ, it seemed both angry and frightened. The keeper staff noted several behavioral abnormalities which included: inserting its fist into its rectum, inducing vomition, pacing, constant hand clapping, rubbing genitalia on sharp objects, self-mutilation by ripping at fingernails and toenails, inability to sleep or rest during the day, spitting and generalized aggression toward the keepers. Volunteer observers were recruited to monitor the type and frequency of these behaviors.

Behavior modification was used in an attempt to alleviate the problems; medical therapy was not immediately instituted. While isolated during the quarantine period, short training sessions praising desired behaviors, and ignoring undesirable behaviors were begun. Frequent small feedings were offered to keep the animal active and occupied. It was observed that induced vomition increased after fruit was eaten; therefore, fruit was removed from the diet, and the frequency of vomition decreased. Training and enrichment were difficult because the animal was extremely fearful of all new objects, including toys and food items used for behavioral enrichment. Nonetheless, some improvements in behavior were obtained, but after several weeks, improvement reached a plateau.

One and one-half months after arrival, the animal was cleared from quarantine and introduced to the other troop members. The animal was fearful of adult male bonobos, it had problems eating in a group, and it had poor play and reconciliation behaviors. Solutions to help the animal adapt included placing it in small social groupings with calm, gentle animals and keeping life routine and predictable. This strategy appeared to work for a couple months, when improvement stopped and behavior regressed.

A decision was made to seek consultation with a psychiatrist. The consultation included a “case conference” with zoo staff where the psychiatrist reviewed the animal’s developmental history and the dynamics of its seeming self-mutilating and obsessional “fisting.” There was agreement that the behavior increased when the bonobo was anxious or under stress and seemed to have both regressive and auto-erotic components to it. A plan was devised to use medications to deal with the obsessional anxiety, and behavioral efforts to introduce the animal to females and the usual matriarchal society of bonobos with the goal of promoting a more normal mature sexual outlet. The behavioral changes were staged to occur as the bonobo bonded with its keeper, allowed itself to be pampered by two female (older) companions and gradually resocialized with other bonobos. The process was accompanied by regular discussions with the consultant and modifications in the staging of socializing events according to the animal’s progress and improvement. All keeper-animal interactions were kept calm and positive. Many (≥5/day) short, positive training sessions were performed to integrate the animal into the medical behavior training program, and to keep it occupied in an attempt to decrease the undesirable behaviors.

Paroxetine (Paxil, SmithKline Beecham Pharmaceuticals, Philadelphia, PA) 10 mg was administered orally once a day initially, but after five days administration increased to twice a day. Within 1 week, the animal appeared calmer. Induced vomiting stopped after 2 weeks. Changes noted by the observers included slower eating habits, ability to rest/sleep during the day, cessation of pacing, decreased aggression toward the keepers, and an increased attention span during training sessions, with the ability to focus on tasks and learn new behaviors. The “fisting” behavior was reduced, but still occurred at perceived high anxiety times, such as immediately before meals. Diazepam 2.5 mg once daily in the morning was initiated to curb anxiety levels, with moderate success. Paroxetine is an antidepressant which acts as a potent and highly selective inhibitor of neuronal serotonin reuptake. In addition to its antidepressive effects, it is also highly effective in treating obsessive-compulsive disorders and panic disorders. Reported side effects in humans include nausea, somnolence, insomnia, dizziness, asthenia and ejaculatory disorders. Its use is contraindicated in patients taking monoamine oxidase inhibitors.[1] Paroxetine was chosen over other selective serotonin reuptake inhibitors (SSRIs) because of its anti-obsessional effects, and because of its more immediate onset and the hope for quick reduction of anxiety.

The bonobo has now been introduced into the large bonobo group and is learning the social skills necessary to interact successfully with peers. The animal is successfully participating in the MCZ medical behavior training program. Although self-mutilation behaviors still occur occasionally, the animal continues to improve and adapt. Routine treatment with diazepam has been discontinued because of poor acceptance, without ill effects. It is hoped that with continued therapy, with adjustments as necessary, quality of life will remain high throughout the animal’s life span.

This case illustrates that behavioral and medical therapy, carefully chosen and implemented, can work effectively to treat undesirable and self-destructive traits exhibited by animals.

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 # Changes in Plasma Testosterone and Aggressive Behavior in Male Green Iguanas (*Iguana iguana*) Following Orchidectomy

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Changes in Plasma Testosterone and Aggressive Behavior in Male Green Iguanas (*Iguana iguana*) Following Orchidectomy
American Association of Zoo Veterinarians Conference 2000

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Abstract

Many male green iguanas (*Iguana iguana*) demonstrate aggressive behavior towards their owners and conspecifics following the onset of sexual maturity. The aggression is particularly severe during the natural breeding season (late November–February) in northern Florida. This aggressive behavior often involves vicious attacks with biting and tail whipping. Veterinarians have attempted to mediate this aggressive behavior with castration.

A 10-month study was conducted in order to investigate whether castration reduces aggressive behavior and the mean circulating plasma testosterone concentration as well as to determine if there is a temporal relationship between castration and breeding season in the amelioration of aggression. Sixteen clinically normal green iguanas, (based on physical examination, complete blood count and plasma biochemistry analysis) ranging in weight from 0.660–3.62 kg (mean=1.6 kg) and snout to vent length from 26.0–44.5 cm (mean=32.3 cm), were obtained from various sources. The iguanas were separated into three size classes: Small (<1 kg), medium (1–2 kg) and large (>2 kg). Animals from each size class were randomly placed into one of three groups. Group 1 (five animals) were castrated in September, 6 weeks prior to the onset of the natural breeding season. Group 2 (five animals) were castrated in December, during the breeding season, after the onset of aggressive behavior. Group 3 (six animals) served as the control group which had anesthesia induced and maintained, and had a sham operation performed (three animals prior to breeding season and three animals during breeding season) consisting of creating an abdominal incision closed in a manner similar to that of the castration groups.

Data collection consisted of aggression scores, plasma testosterone concentration and femoral pore diameter measurement. Aggression scores were obtained 2–3 times/week for the duration of the study. Aggression scores were determined by placing a large (66 cm×33 cm) mirror in each iguana's cage and counting the number of open mouth contacts to the mirror in a 5-min period. Baseline aggression scores were obtained for 3 weeks prior to any surgical manipulation. Blood was collected from the ventral coccygeal vein, on days that were not aggression score days, every 2 weeks for determination of plasma testosterone levels using a radioimmunoassay validated for iguana plasma. Two baseline blood samples were collected prior to any surgical intervention.

The resulting data were analyzed with a repeated measures analysis of variance (ANOVA) using SAS General Modeling Procedure. A borderline statistically significant difference in aggression was seen among groups indicating that a difference among groups occurred over time and this difference was seen during the breeding season. Comparison of group 1 and its own control group during the breeding season (December–January) detected a statistically significant difference in aggression, while comparison between group 2 and its control group was not significantly different. However, there was a trend towards reduction in aggressive behavior between the groups.

Plasma testosterone concentration from group 1 showed no statistically significant change over time while group 2 showed a significant decline over the course of the study. No significant difference in plasma testosterone concentration was detected between group 1, group 2 and their respective controls during the breeding season.

The data support that castration before the breeding season reduces aggression in male green iguanas and that the testosterone concentration remains low in castrated iguanas even during the breeding season.

 Chemical Castration and Aggression Control in Impala *(Aepyceros melampus*) Using Zeuterin™

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Chemical Castration and Aggression Control in Impala *(Aepyceros melampus*) Using Zeuterin™
2016 Joint AAZV, EAZWV, IZW Conference

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ABSTRACT

Breeding groups of antelope under managed care are usually comprised of one breeding male and multiple females. However, surplus males are often managed as bachelor groups, which can be problematic due to intra/interspecific aggression. Options for contraception and aggression control in male hoofstock species are limited. GnRH does not down regulate LH/testosterone; while progestin has variable effects on aggression control with questionable down-regulation of semen production for contraception. Castration and vasectomy require surgery which can prove difficult for larger herds. In contrast, Zeuterin™ (zinc gluconate neutralized by arginine, Irvington, NY, 10533 USA), an intra-testicular injectate, causes irreversible fibrosis, disrupting spermatogenesis without completely eliminating testosterone, thus preserving some secondary sexual characteristics. This study investigated impala (*Aepyceros melampus*) at 6–8 months of age following intra-testicular injection of 0.15±0.1 ml/cm^3 testicular volume Zeuterin™ (Group 1, n=3) using canid dosing and 0.31±0.24 ml/cm^3 testicular volume (Group 2, n=3) using twice the canid dosing. Body weight, testicular measurements and semen and sperm assessments, and horn and neck morphometrics were collected pre-treatment and 6 months post-treatment. Body weights increased in all individuals. Testicular measurements changed in both groups from small evenly-sized to larger asymmetric testes in 2/3 males in both groups. Mean testicular volume increased from 11.3±1.6 cm^3 to 26.3±4.8 cm^3. No spermic ejaculates were obtained for any of the prepubertal males. Six months later, low numbers of morphologically abnormal spermatozoa (3 and 4x10^6 sperm/ml, 49% and 16% abnormal morphology) were detected in 2/3 males in Group 1, but azoospermic ejaculates were obtained in group 2. Behavioral observations noted reduced aggression and mounting behavior in both groups and reduced inter-species aggression in the mixed exhibits. Results demonstrate a useful non-surgical tool to contracept and reduce aggression in impala males and may be appropriate for other antelope species.

Chronic Feather Picking: A Different Approach to Treatment
American Association of Zoo Veterinarians Conference 1987
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The chronic, “psychological” feather-picking psittacine presents a frustrating dilemma for the pet owner and the veterinarian. This paper is an attempt to show that the psychological disturbances which manifest as picking and self-mutilation may, in fact, be only symptoms of a brain and neuronal chemical imbalance, primarily involving the neurotransmitters norepinephrine (NE) and serotonin (5-HT), as a result of chronic stress. Treatment of these neurotransmitters’ imbalances and deficiencies with currently available psychotropic drugs may be of benefit in psittacines.

The psychological feather-picker definition that is widely accepted is a kind of catch-all for etiologies emotionally or behaviorally based in the absence of systemic organic disease. Although recognizable, organic disease problems may have been implicated as a factor in the initiation of the feather-picking behavior. Commonly listed as psychological causes for feather picking include habit; boredom; lack of routine; attention-getting vice; fear; nervousness; jealousy; frustrations involving a new bird, owner, toys, other pets; other environmental changes; diet; husbandry; unresolved and reproductive-based frustrations, including exaggerated preening/courtship, inappropriate pair bonding, lack of mate, temporary/permanent loss of mate, chronic egg laying; social isolation; inability to cope with caging, climate, captivity; defense of territory; and displaced aggressions. Self-mutilation may occur with the more intense pickers. Psychologic pickers may show intermittent response to isolation, uses of collars, tranquilizers, hormonal therapies, and availability of mating opportunities with their own species. Generally, treatments aimed at minimizing these contributing factors are temporary and largely unsuccessful in preventing recurrence.[5,7,8,12,19,20]

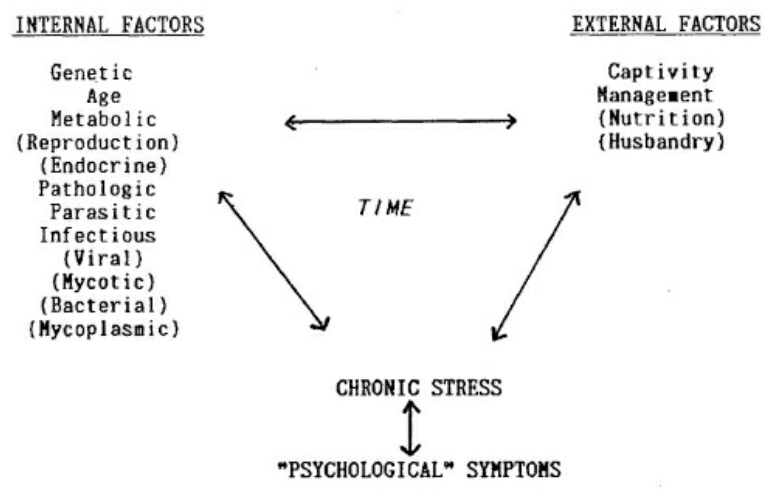
Without anthropomorphizing the emotional state of these birds, they do exhibit signs of frustration, fear, inability to cope with captivity, changes, social pressures, inappropriate and displaced aggressions, and other behavior patterns different from their non-feather-picking counterparts. In humans, these same described emotional disturbances are characteristic of anxiety and are frequently associated with clinical depression and, in some cases, manic depressive mood alterations.

It is now widely recognized that emotional disturbances such as those above may be symptoms of neurotransmitter deficiencies in the brain.[3,6,23]

It is possible that birds previously categorized as psychological pickers, in fact, are exhibiting symptoms of a physiologic process.

Chronic stress has long been associated with many physiologic changes in animals and has been particularly implicated in many avian disease processes, including feather picking (Illustration 1).

Illustration 1. Accepted etiology of psychological feather pickers



Behavior and emotional disturbances have been demonstrated with increased serum levels of corticosteroids.[4,11] Brain neurotransmitter (NE and 5 HT) depletion has been linked with chronic stress both clinically and experimentally.[6,22,23,27]

A review of neuroanatomy and physiology reveals that in birds and mammals, the limbic system and hypothalamus are directly involved with emotions, reproduction and sexual behaviors, rage, fear, aggression, defensive reactions, biological rhythms, and autonomic function modulation.[6,15] Norepinephrine and serotonin are major neurotransmitters in this region.

Although the avian brain differs in morphologic proportions and configuration when compared to the mammalian brain, the structures and functions have been shown to be similar.[15] Chronic stimuli (stress) requiring sympathetic (noradrenergic) “fight/flight” responses cause an increase in firing of these neurons in the limbic and hypothalamic areas and an increase in NE turnover, which may lead to a decrease in available NE. Chronic stress also increases the firing rate and alters 5-HT turnover in neurons, which has been found to lead to increased levels of 5-HT in some regions (hypothalamus) and decreased levels in other parts of the limbic system. Brain monoamines, in turn, play a functional role in modulating corticosterone response to stress. Chronic stress then puts a demand on the neurologic system as well as the commonly examined endocrine system, and the systems are interrelated in determining an animal’s reaction to stimuli.[22,27]

The most well-known endocrine modulator for the treatment of behavior disorders used in veterinary medicine deserves mention to relate its efficacy with neuroanatomy. Progesterone compounds often are used to control psychodermatosis, feather picking, aggression, and other behaviors, which are manifestations arising/moderated in the limbic system and hypothalamus. These compounds have been shown to exert a temporary effect in the brain by acting as “neuro” hormones and altering firing rates. These generally lose effect with time and are rarely recommended for continuous or prolonged use due to side effects.[6,14,16,25]

Documented symptoms of NE depletion in mammals following chronic stress include behavioral depression, decreased ability to adapt to new situations, frantic activity when first confined, followed by a decreased motor activity, changes in grooming, sleeping, eating, and sexual behaviors.[27]

In a study involving pigeons, deficiencies of NE in diffuse areas of the limbic system were manifested differently and by varying degrees in the individual birds. Behaviors noted included restlessness (which in some developed into escape responses), defensive and aggressive actions, increased preening and displacement preening, and inappropriate

courtship behavior ranging from ineffectual to frantic or even aggressive. Alterations in appetite, sleep patterns, and reactions to human presence in the form of nervousness, shaking, and vocalizing were also observed in some individuals. These symptoms of emotional and behavioral disturbances seen in other birds and mammals, along with human data correlates, seem to be quite similar to those seen in the chronic “psychologic” feather-picking psittacine.[15]

Testing for actual levels of neurotransmitters is impractical at this time. Postmortem brain catecholamine assays have been used in experimental animals. A by-product of NE catabolism (normetanephrine) and one of 5-HT catabolism (5-hydroxyindoleacetic acid) can be found in human urine. However, these by-products may result from other tissues catabolizing the same compounds, so the urinary level is not an accurate reflection of brain/neuronal concentrations.[3]

Response to medical therapy is probably the most accurate way of monitoring the neurotransmitter function and level.[17,23]

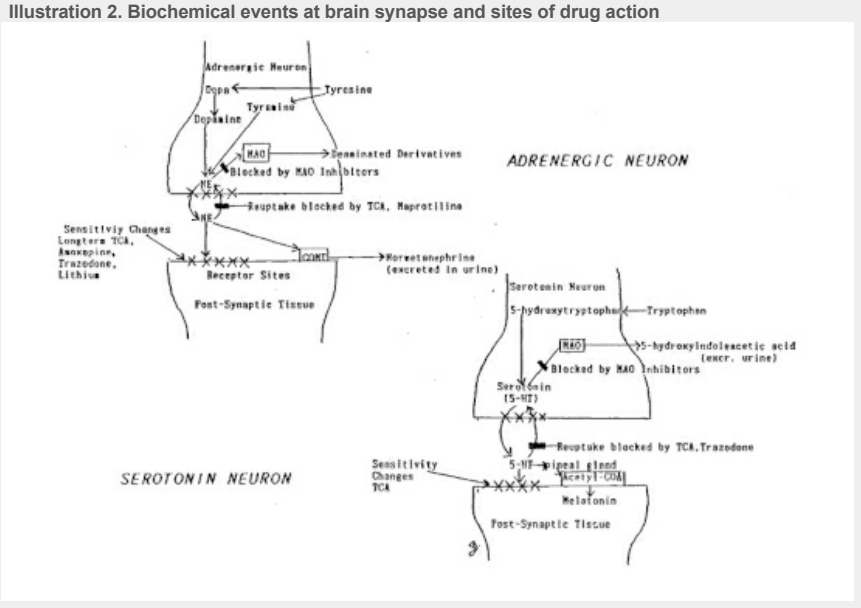
With the evidence presented, it seems possible that neurotransmitter deficiencies may contribute to many behavior problems encountered with psittacines, including feather-picking and self-mutilation. Therapy, then, should be aimed at increasing the levels of NE and/or 5-HT available to the neuron in the brain regions primarily involved with the symptoms seen, i.e., the limbic system and hypothalamus. This can be done by blocking enzymes involved in the degradation pathways or blocking the reuptake of the neurotransmitter, or altering the sensitivity of the postsynaptic receptor sites, thereby changing the sensitivity of the postsynaptic neuron to the neurotransmitter.

Drugs in the anxiolytic group (such as benzodiazepines) have some effect on the NE levels, but their hypnotic and tranquilizing effects are not clinically acceptable for most birds; in fact, the effects can be detrimental. If the bird becomes too uncoordinated and drowsy, the potential for injury from falling, etc., becomes greater than the benefit from sedation to stop the feather picking. Short-term use of diazepam (U.S.P., Valium®, Roche, Nutley, NJ), for example, may help with an acute mutilation episode, but its use in controlling chronic picking or preventing picking seems limited.

The other consideration with this group of medications facing the veterinarian is the potential for human (the owner) abuse of the medication. Drugs in this group are schedule drugs and may be addicting to humans.

The group of psychotropic drugs commonly classified as antidepressants has the potential to be effective for use in veterinary medicine. These drugs influence neurotransmitter function in the brain (Illustration 2).

Illustration 2. Biochemical events at brain synapse and sites of drug action



For purposes of discussion relative to potential use in veterinary medicine, particularly avian species, these drugs will be separated into four categories: lithium, monoamine oxidase inhibitors, tricyclic antidepressants, and non-tricyclic/non-MAO inhibitor antidepressants.

Table 1. Antidepressants: product list

Lithium		
Carbonate	Tablets	Generic
		Eskalith, Eskalith-CR Smith Kline & French Philadelphia, PA
		Lithane Miles Pharmaceuticals Elkhart, IN
		Lithotabs Rowell Baudette, MN
	Capsules	Generic
		Eskalith Smith Kline & French Philadelphia, PA
		Lithonate Rowell Baudette, MN
	Sustained-release tablets	**Lithobid** CIBA Summit, NJ
Citrate (syrup)		Generic
		Cibalith-S CIBA Summit, NJ

Monoamine oxidase inhibitors		
Isocarboxazid		**Marplan** Roche Nutley, NJ
Phenelzine		**Nardil** Parke-Davis Morris Plains, NJ
Tranylcypromine		**Parnate** Smith Kline & French Philadelphia, PA
Tricyclic antidepressants		
Amitriptyline	Tablets	Generic
		Elavil Merck, Sharp & Dohme West Point, PA
		Endep Roche Nutley, N J
	Injection	**Elavil** Merck, Sharp & Dohme West Point, PA
Desipramine	Tablets	**Norpramin** Merrell Dow Cincinnati, OH
	Capsules	**Pertofrane** USV Pharmaceutical Tarrytown, NJ
Doxepin	Capsules	Generic
		Adapin Pennwalt Rochester, NY
		Sinequan Roerig New York, NY
	Oral concentrate	**Sinequan** Roerig New York, NY
Imipramine	Tablets, capsules, injection	**Tofranil** Geigy Ardsley, NY
	Tablets	Generic
		Sk-Pramine Smith Kline & French Philadelphia, PA
		Janimine Filmtab, Abbott N. Chicago, IL
Nortriptyline	Capsules	**Pamelor** Sandoz Pharmaceutical Div E. Hanover, NJ
		Aventyl Lilly Indianapolis, IN
	Syrup	**Aventyl** Lilly Indianapolis, IN
Protriptyline	Tablets	**Vivactil** Merck Sharp & Dohme West Point, PA
Trimipramine	Tablets	**Surmontil** Ives New York, NY
Non-tricyclic, non-monoamine oxidase inhibitors antidepressants		
Monocyclic	Bupropion	**Wellbutrin** (Consult PDR)
Monomethylated tetracyclic	Maprotiline	**Ludiomil** CIBA Summit, NJ
Piperazine tricyclic	Amoxapine	**Asendin** Lederle Pearl River, NY
Triazolopyridine	Trazodone	Generic
		Desyrel Mead Johnson Pharmaceutical Evansville, IN

Sample listing of common products. Trade names bolded. Refer to current PDR for complete product availability, dispensing information, and manufacturers.

1. Lithium

Availability

Many forms, generic and brands (Table 1).

Mode of Action

The current hypothesis is that therapeutic action is from the ability to stabilize catecholamine receptors and prevent oscillation in receptor sensitivity between the hyposensitivity of depression and the hypersensitivity of mania (Illustration 2). Also acts to stimulate pluripotential stem cells in bone marrow.[1,3,23]

Use in Human Medicine

Acute mania, acute depression (may be in combination with a tricyclic antidepressant), prophylactic treatment for depression, treatment of uni and bipolar (mood swings) affected disorders, periodic psychosis, chronic maladaptive behavior patterns of children when combined with mood swings, chronic aggression, anorexia nervosa, and schizophrenia (in combination with neuroleptics). It has shown some value to some patients in the treatment of premenstrual tension, phobias, and general anxiety. Lithium has also been used with some success in the alleviation of chemotherapy-induced neutropenia, thrombocytopenia, and in idiopathic aplastic anemia.[2,17]

Use in Veterinary Medicine

Lithium has successfully been used in canines to alleviate severe cyclic granulopoiesis in grey collies and in cases of bone marrow hypoplasia from estrogen-induced toxicity. The decreased bactericidal capacity of the neutrophils and the decreased responsiveness of lymphocytes to antigens found in humans while on chronic lithium therapy have not been reported in dogs.[13,24,26]

Discussion

Psychologically effective therapeutic serum levels in humans have been well documented as 0.5 mcg/1–1.5 mcg/1; with levels above 1.5 mcg/1, levels of toxicities may occur.[1,2,3,17,23] Canine dosages of 21–25 mg/kg BID lithium carbonate, which were found adequate to achieve granulopoiesis, did not elevate canine serum levels into the therapeutic range.[13] No reports were found in the literature as to its use for psychological problems in dogs or of any behavioral changes noted at the doses used for granulopoiesis. Humans on prolonged lithium therapy are monitored routinely for serum lithium levels, thyroid function (lithium may induce mild, transient hypothyroidism), and kidney function (lithium-associated nephropathy). Polyuria and polydipsia are common side effects even at therapeutic dosage levels; the list of possible toxic and side effects will not be listed here for the sake of brevity but may be found in listed references.[1,3,17]

The author has used lithium carbonate at a dosage derived from the canine dose titrated to body weight in three cockatoos donated to the author as a possible aid to taming, "settling in," and to decrease the stress responses seen following shipment and introduction into a new environment. These were wild caught, untamed, and very nervous adult birds, but were not feather pickers. Following three weeks of therapy, all could be handled easily, were playing actively, were eating everything offered, and were displaying sexual activity. Serum uric acid, calcium, and phosphorus levels remained constant pre-, during, and post-treatment; however, all three exhibited marked polyuria and polydipsia even when the dosage was decreased to ¼ of the calculated dose midway through treatment. No discernable increase in the white blood cell count or changes in the hemogram, T_4, or other serum chemistries were noted in this trial. At ¼ the canine dose/weight, behavior changes were seen.

Lithium may be useful in avian medicine, but further work on establishing effective dosages and frequency of administration for psychological therapeutic benefits needs to be done. Long-term monitoring of other body functions also needs to be evaluated while on lithium therapy.

2. Monoamine Oxidase Inhibitors (MAOI)

Availability

Limited number of chemicals. No generics yet (Table 1).

Mode of Action

Inhibits enzyme responsible for intraneuronal breakdown of catecholamine and indoleamine neurotransmitters (e.g., NE and 5-HT, respectively) (Illustration 2). This allows the accumulation of neurotransmitters in presynaptic granules, which makes more of the neurotransmitter available to the postsynaptic neuron, such that the hyposensitive postsynaptic receptor sites return to the normal predisposition level of sensitivity.[17]

Use in Human Medicine

MAOIs are utilized for the management of many neuropsychiatric conditions, including reactive; neurotic; or atypical depression; phobic anxiety, e.g., agoraphobia, phobic depersonalization syndrome, refractory thought disorders, general anxiety, anxiety "panic" attacks, neurodermatitis, resistant narcoleptic states, bed-wetting, recalcitrant migraine headaches, and idiopathic orthostatic hypotension. Atypical depression is marked in part by diurnal mood variations, with evening rather than morning dysphoria, as well as some seasonal, apparently light-cycle-dependent mood patterns.[17,23]

Use in Veterinary Medicine

The author found no reports in the literature on the use of MAOIs in veterinary medicine. References to use in animal species were limited to pharmacologic research.

Discussion

It is the author's opinion that the MAOIs potentially could be very effective in dealing with avian feather picking and canine/feline psychodermatologic conditions, but due to potential hypertensive crisis and strict dietary restrictions needed (Table 2), use may be impractical at this time. New MAOIs are being developed that minimize these hazards in humans, and so eventually, this group of medications may be of great value to veterinarians.[23]

3. Tricyclic Antidepressants (TCA)

Availability

Many drugs and forms, generics, and brands (Table 1).

Mode of Action

TCA increases concentrations of 5-HT and/or NE in the CNS in the synaptic cleft between CNS neurons by blocking the reuptake of the neurotransmitter into the neuron (illustration 2). Long-term therapy seems to produce alterations of postsynaptic monoamine receptor sensitivity, suggesting that during depressive episodes, post-synaptic receptor site sensitivity is abnormal, in addition to deficiencies in concentrations of 5-HT and/or NE.[1,3,17]

Table 2. Monoamine Oxidase Inhibitors Dietary Restrictions

Tyramine-containing foods may precipitate a hypertensive crisis while taking an MAOI. Tyramine is the pressor amine produced by the breakdown of tyrosine. Tyramine exerts its pressor action by releasing NE from presynaptic storage sites. Its action is potentiated in patients on MAOIs because of the greater amount of NE present at the nerve ending due to

MAOI.

General rules: Any protein-containing food that has undergone degradation, aging, smoking, pickling, or fermenting may present a hazard. Alcohol must also be avoided—it is not recommended for birds/pets in any circumstance.

Specific Items to Avoid

- Cheeses (except non-matured cheese—cottage, ricotta, cream, American processed)
- Brewer's yeast, vitamin supplements containing such, yeast/protein extracts (like sometimes found in packet soups, etc.)
- Fava or broad beans (Italian green beans)
- Liver, pickled herring, any smoked fish, caviar, fermented sausages (bologna, pepperoni, salami, summer sausages, etc.), smoked ham, bacon, etc., i.e., any other smoked or pickled meat or fish
- Canned or overripe figs, stewed whole bananas/banana peel (pulp ok)
- Avocado, raisins (in large numbers)

Table 3. General information: aids for drug choice

Most sedating effects	Amitriptyline, doxepin, trimipramine, trazodone
Mild sedating effects	Imipramine, nortriptyline
Least sedating effects	Protriptyline, desipramine
Anti-Anxiety	Mild to moderate symptoms: TCA (especially doxepin, trimipramine) >MAOI >trazodone.
	Strong symptoms: imipramine, MAOI (especially phenelzine)

Use in Human Medicine

Acute and chronic major depressive disorders are characterized by one or more of the following symptoms: insidious onset, anorexia, weight loss, some insomnia, diurnal variation in mood, psychomotor retardation or agitation, panic/anxiety attacks, inability to cope with everyday problems, and alteration in normal social and sexual behavior patterns. TCA has been used simultaneously with lithium in the treatment of manic-depressive patients. Many require long-term therapy. The drug chosen to start treatment depends on the degree of sedation effect required, and the response of the patient within the first three to four weeks determines if an alternate drug should be tried. Generally, once the appropriate TCA has been found and a maintenance dose achieved that alleviates the symptoms, treatment is continued for at least six to 12 months beyond remission of symptoms.[1,3,17,23]

Serum therapeutic levels have been established and can be monitored, but most human patients are monitored by clinical observation of regression of symptoms and absence of side effects. The appearance of side effects may be indicative of a need for dosage adjustment or change of medication. Side effects may range from dry mouth, increased appetite, and drowsiness to severe anticholinergic systemic effects. Complete listings of adverse reactions and side effects may be found in the PDR and other references.[1,17]

Use in Veterinary Medicine

The author could find no references of clinical use of TCA in the veterinary literature. Animal usage was confined to laboratory animal trials for pharmacologic purposes.

Discussion

Based on the action of these drugs and their wide range of application, safety, and efficacy in human medicine for the treatment of symptoms that seem to be similar to problems seen in chronic feather pickers, the TCA group holds great promise for use in avians.

Studies in humans have indicated alteration in thyroid function may play a role both in the etiology and treatment of depression. Concurrent use of L-thyroxine and some TCA enhance the effects of both. Hypothyroidism and/or thyroid/reproductive hormone cyclic imbalances have been implicated as initiating factors for many chronic feather pickers. Many "pickers" are supplemented with L-thyroxine to stimulate feather growth. Dosages of L-thyroxine and TCA may need to be adjusted if given simultaneously.[17,19] Complete pharmacologic studies need to be done to fully determine if parallels of physiology, pharmacology, and clinical effectiveness for these drugs based on mammalian studies hold true for the psittacines. Preliminary trials using doxepin by the author on several chronic feather pickers are encouraging. Doxepin was chosen for trial because of its efficacy in treating anxiety and depression in humans, along with relative safety from toxic and side effects, palatability, and ease of administration.[1,17,23] Doxepin is one of the TCA drugs that provide the most sedating and calming effects, which may be advantageous in controlling feather picking and other behaviors commonly seen (Table 3).

Chronic feather pickers were chosen for trial with the consent of the owners. Species involved include African grey parrots and cockatoos (Moluccan, triton, citron). Dosages for trial were calculated by weight, and type of administration was dictated by the owner's ability to handle the bird. Details of a preliminary protocol are outlined in Supplement 1.

Birds are maintained at the calculated first maintenance dosage for one month. The owners report observations of behavior and any changes seen. A decision to continue/alter medication is then made.

Extensive client education about the medication, implications, possible side effects, duration of treatment, and experimental nature are covered before the bird is placed on the medication. A sample of a possible client information sheet is included with this report (Supplement 2). A sample of a human-patient TCA and MAOI information sheet is also included to acquaint the veterinarian with background information about the drug's use and presentation with humans (Supplement 3). It is important that the veterinarian prescribing the experimental protocol be familiar and comfortable with its application. Clients are counseled to report on any unusual behavior or problems encountered while their pet is on medication. The goal is to find the proper drug and dosage to alleviate symptoms. With Doxepin, dosage is slowly increased after the first month until symptoms of picking cease and/or the bird seems a little drowsy during the day. The dosage is then adjusted to that just below the slight daytime-drowsy point.

All the owners reported one or more of the following observation(s) about their bird at the 30-day report: less agitated, easier to handle, picking decreased, leaves collar on, less destructive, less aggressive to other birds, mating behavior (previously none), trying new food, increased appetite, less shaking and nervousness, friendly to people who previously seemed to trigger picking episodes, and playing and vocalizing (talking) more. At 60 days, two owners reported they had run out of medication and had not realized the changes in the bird until the birds were off medication for more than a week; both owners requested to start again. Comments from these owners included: "better pet on it than off," "he left the collar on when on medicated," "he's gotten picky about his food again," and "seems moody and unpredictable again." At 90 days, these two birds were refeathered, and the owners elected to stay on maintenance for at least six months. Two cockatoos in one household began serious mating activity after 60 days on medication and were withdrawn—both had ceased picking and were behaving normally for courtship.

The author has used doxepin on several cockatoos afflicted with psittacine beak and feather viral disease syndrome to decrease destructive preening and mutilation, as an aid to taming, handling, post-shipment stress, and in one apparently recovered bird who started picking to get his new owner's attention.

More work needs to be done to test the efficacy of doxepin and other TCA in other species, over time, in aviary vs. home situations, and in breeding situations. Currently, the author would recommend trying doxepin in a chronic feather picker, especially if self-mutilation is a problem and none of the conventional therapies are working. Most owners are willing to try rather than give up, as many of these birds are described as "having great personalities." Most feather-picker owners are also familiar with giving medications and taking observations, which makes monitoring therapy easier.

4. Non-Tricyclic/Non-MAOI Antidepressants

Availability

Relatively new, chemically distinct. Few brands (Table 1).

Mode of Action

Amoxapine: the primary effect is to restore postsynaptic receptor-site sensitivity of adrenergic neurons. Some blockage of reuptake NE and 5-HT (weak).

Maprotiline: restores postsynaptic adrenergic receptor site sensitivity and blocks reuptake NE.

Bupropion: unknown action at this time.

Trazodone: inhibits 5-HT reuptake. Decreases adrenergic receptor sensitivity and induces significant changes in 5-HT presynaptic receptors (illustration 2).[17]

Uses in Human Medicine

Amoxapine, maprotiline, and bupropion are used to treat the same problems as TCA and are apparently equivalent in effectiveness to TCA. Trazodone appears to be as effective an antidepressant as TCA without anticholinergic adverse effects. Sedative action is fairly strong and may be desirable with some ranges of symptoms. Patients that are poorly responsive to TCA with primarily NE action may respond to 5-HT primary action.[17,23]

Uses in Veterinary Medicine

The author found no reports of clinical use in veterinary medicine other than pharmacologic trials in laboratory animals.

Discussion

Trazodone may prove to be an alternative to tranquilization in feather pickers. It may also have benefits to those who do not respond to TCA that have primary action on the NE axis. The author would consider trying trazodone as a second choice to doxepin, especially in cases of self-mutilation and frantic or aggressive behavior. Controlled trials using trazodone need to be done to determine efficacy, dosage, species variability, and pharmacology of the drug itself in Aves. The author sees no apparent advantage of the other drugs in this category over the TCA, except in noting individual responses to different medications and the need to find the proper one may necessitate trying one with a different chemical compounding.

The possibilities for use of drugs presented in this paper for treating a variety of “psychologic” problems in birds as well as mammals should be investigated. In theory, and in very limited trials, these drugs may be an effective means to correct a physiologic problem that manifests in many species as a behavior or “psychological” problem. Psychodermatosis, such as acral lick granulomas in dogs and psychological alopecia (overgrooming) in cats, may be areas for psychotropic drug trials.[14,21] Other behavior problems currently treated with progestins may also be candidates for this alternative medical therapy.[16,25]

In conclusion, behavior-modifier drugs, such as lithium, tricyclic antidepressants, monoamine oxidase inhibitors, and non-tricyclic/non-monoamine oxidase inhibitor antidepressants, may be efficacious in treating behavioral or “psychological” disorders in birds and pet animals. These drugs act by correcting neurotransmitter dysfunctions in the brain that probably result from chronic stress. Previously classified “psychological” disorders should more accurately be considered a combination of real physiologic changes. Veterinary acceptance and use of these drugs require extensive testing and trials of these drugs in different animals for different conditions and the development of a means of monitoring and standardizing results.

Chronic feather pickers refractory to other traditional methods of treatment may benefit from the use of TCA or other drugs, as presented in this paper, as a way of treating the underlying neurologic dysfunction rather than just addressing the behavioral symptoms. Veterinarians’ and clients’ familiarity with the medication chosen for trial is essential for the safe use of the drug and the maximum beneficial effects to be realized for the pet.

Disclaimer

The nature of drug information is that it is constantly changing from research, clinical experience, and accepted medical practices. Decisions regarding any drug therapy are based on the independent judgment of the clinician. The author assumes no responsibility for and makes no warranty with respect to results obtained from uses, procedures, or dosages listed. The author shall not be liable to any person whatsoever for damage resulting from reliance on any information contained herein, whether with respect to drug identification, uses, procedures, dosages, or be the reason for any misstatement or error contained in this work.

Supplement 1

Suggested Guidelines for Clinical Trials of Doxepin 1987

Purpose

Alternative treatment for chronic feather pickers, especially if self-mutilating. **Chronic** is defined as recurrent (seasonal, patterns of stress-induced); daily neurotic (triggers ± identified); habitual regardless of surroundings or stimuli; collar ± effective; mate/other bird presence no difference or worsens. Unresponsive or minimally responsive to tranquilizers (benzodiazepines), progestins, and androgens. No parasitic involvement and no systemic infections, which are major contributors to the picking. Can grow feathers (endocrine dermatologic factors within normal—may need exogenous thyroid supplementation but is capable of replacing feathers). Not currently in active breeding program.

Species Suggested as Candidates for Trial

Cockatiel, African grey, cockatoo, conure, cockatiel

Methods to Monitor

Owner: Watch signs of overdose—ataxia, drowsiness, overeating/drinking, nausea, vomiting, increased anxiety/picking, polyuria, seizure, hyperactivity, and other behavior changes.

Veterinarian: Avian blood panel (at least CBC, UA, Bili, T_4) monthly, weight check, visual exam monthly. Communication with the owner at least monthly. Other clinical assessments as necessary. If the bird is exogenously supplemented with thyroxine, keep in mind TCA and thyroxine enhance the effects of each other; dosage reduction or modification of both may be necessary.

Sample Dosage and Method

Human dosing information as a basis for calculations. Upper limit of therapeutic dosage is not established but approximated from clinical experience.

Adult human dose: 75–400 mg daily. Start at 75 mg. Increase by 25–50 mg at weekly intervals until a maintenance dose is achieved. Average adult human therapeutic dose = 150 mg daily.

Veterinary application: dose somewhat weight dependent. Extrapolation and calculation from human doses = suggested dose of 1–5 mg/kg body weight daily. It is suggested that initially, dosage be divided daily until maintenance is established, then once daily may only be necessary.

Prefer the direct oral route. The time interval between doses may increase or decrease depending on the bird and owner. If a particular time of day is associated with intense picking behavior, may be advantageous to time dosage for 1–2 hours prior to this time. May increase dosage at 2–3 week intervals until slight daily drowsiness is seen, then back off slightly = maintenance. If side effects (undesirable) are seen prior to this point, determine if transient is associated with the initiation of therapy or if true side effects: dosage adjustment, timing, or discontinuing therapy are options.

Suggested Trial Doxepin

Example: African grey, weighing 454 gm. Start at 1 mg/kg divided daily. This equals 0.5 mg/454 gm. Doxepin (generic) capsules: 10, 25, 50, 75, 100, 150 mg. Oral suspension (Sinequan®, Roering, New York, NY) at 120 ml at 10 mg/ml. Considered good, refrigerated maximum 1 week. Better to divide powder into smaller bottles for use within 48–72 hours reconstituted. Divide powder into 16 ½ oz bottles (15 ml) = 75 mg/bottle at 5 mg/ml. Mix each with 15 ml milk, juices (orange, grapefruit, tomato, prune, or pineapple), Gatorade, Tang, lemonade, or sugar water at the time of use. Can mix powder from capsules with listed juices to achieve the same dose/ml but may be less palatable/dissolvable/stable.

For the bird cited needing 0.5 mg/ml, using liquid formulation = 5 mg/ml, dosage would be 0.05 ml orally BID. In 2 weeks, if tolerates that dosage, increase to 1.5–2.0 mg/kg/mg body weight divided BID or TID. Can continue increasing as needed, side until maintenance with absence of undesirable side effects reached and to the owner's and veterinarian's satisfaction.

Alternate dosing by water: not as desirable but may be necessary in some cases. Remember, dosing the water, not the bird. Helps to know approximately the average water intake daily of the particular bird. Will vary considerably between individuals; ambient temperatures, diet, and medication itself may alter consumption. Initially may take longer to achieve effects, and may be difficult to determine the true dosage for maintenance. Suggest flavor additives to water will be necessary. Those listed for use with the suspension formulation should be compatible but would avoid milk. Be sure the bird is used to the additive flavor and color of the water before adding medication. Medication may be hard to keep in a water-bowl suspension. Suggest remix, change 2× daily.

For the bird cited: assume 1 oz (30 ml) drinking water/day/454 gm bird. From calculations of direct dosing, want a drug intake of 0.5 mg/day. Converts to 0.5 mg/1 oz drinking water. Empty contents of a 10-mg capsule into 16–20 oz flavored drinking water. Mix thoroughly. Monitor actual water consumption closely while the bird is on medication and recalculate if necessary. Realistically, may need to double or triple the direct daily dose when added to water due to poor suspension, etc.

Caution! Do not use this drug if the bird has glaucoma, recent injury, cardiac, kidney or liver problems, history of bleeding, fainting, known systemic disorder, or systemic (infectious) disease. Avoid use in actively breeding birds.

SUPPLEMENT 2

Sample: Patient–Client Information—Non-Monoamine Oxidase Inhibitor Antidepressants

Client's Name:

Pet's Name:

This medication is currently licensed for use in humans. Usage of this drug, although not FDA approved, may be deemed necessary by your veterinarian for treatment of your pet's medical condition, based on drug use trials in animals and reported clinical use and efficacy in humans.

Drug:

Generic Name:

Trade Name:

Strength (mg):

Formulation (tablet, capsule, oral suspension):

Purpose (this medication is being used to treat):

Directions for Use

To ensure successful treatment, it is essential to follow these instructions.

Dose:

Route:

Number of times per day:

Medication should be given at the following time(s):

Important Information About the Medication

1. It is very important that this medication be given as directed by your veterinarian for best results. When taken regularly, this medication may require 2–4 weeks before full effects are noticed.

2. This medication does not usually produce euphoria and is not addictive.

3. This medication is usually well-tolerated, but any changes in your pet's behavior (play, sleep, vocalization, etc.), appetite, water consumption, urinary or bowel function, apparent dizziness or incoordination, daytime drowsiness, itching, or any other changes should be reported **immediately**.

4. Because response to medications varies tremendously between individuals, you and your veterinarian may have to go through a trying-out period for your pet before the drug and dose are found which seems to work best.

5. If your veterinarian prescribes other medication besides this one, it is important that directions for the administration of those medications be followed closely.

6. If you feel your pet is having problems with the medication, or you have problems giving the drug, or questions concerning the medication, please call us immediately.

7. As with all medications, store this in a cool, safe area away from the reach of small children.

SUPPLEMENT 3

Background Information: Drug Use—Patient/Client Education

Group Health Cooperative of Puget Sound Eastside Mental Health Service

PATIENT INFORMATION SHEET: TRICYCLIC ANTIDEPRESSANTS

Your medication:

I. Benefits

Although most people will feel better on some days and not on others, some people experience marked or prolonged depression. While depression is usually self-limiting and will end on its own, antidepressants act to elevate mood, increase energy, decrease anxiety, improve appetite and sleep, and help to alleviate the other symptoms of depression.

II. Course of Treatment

A. Once your doctor has prescribed an appropriate antidepressant, it is usually given all at bedtime unless otherwise instructed. A low dose of the medication is given initially, with an increase in the amount taken each night as directed by your doctor. These medications are not addicting and are not "tranquilizers," even though they may alleviate anxiety associated with depression. When the appropriate dosage is reached, you generally will sleep through the night without feeling unusually sedated in the morning. If you feel excessively drowsy, call the MHS consulting nurse for directions. The first week of treatment usually causes some **mild** drowsiness—this is to be expected and will disappear during the second week of treatment. If you are having difficulty falling asleep, you may wish to take your medication 2 hours before bedtime in order to absorb enough of it to aid sleep. Occasionally, an antidepressant will interfere with sleep. If this occurs, call the MHS consulting nurse for assistance. At times a change to a different antidepressant may occur to minimize side effects or to obtain more complete relief of depressive symptoms.

B. Generally, an antidepressant is needed for 9–12 months and, occasionally, longer. The length of treatment is to be determined by your doctor. Discontinuing the medication prematurely may increase the possibility of relapse of depression.

C. You should make an appointment to see the mental health consulting nurse 7–1- days after starting the use of an antidepressant and again in the fourth week and the twelfth week of taking the medication. You may be seen more frequently during this period, but not less. Refills will not be reordered for patients who are not being seen in the Mental Health Service Clinic. The consulting nurse will discuss the timing of further follow-up visits with you during your 4-week visit. Remember, the mental health consulting nurse is available for phone consultation M–F 8:30 a.m. through 5:00 p.m. (closed 1–2 pm for lunch).

D. It may take up to 3 weeks to obtain a good effect from an antidepressant. Generally, in the first week, a person starts to sleep and is calmer. In the second week, a person has more energy, and by the third week, a person feels less depressed and can again enjoy activities.

III. Cautions

A. Notify your doctor or MHS consulting nurse if you become pregnant or plan to become pregnant during therapy.

B. Be sure to tell your doctor or MHS consulting nurse if you are breastfeeding.

C. Until you are reasonably certain the antidepressant does not cause sedation or decrease in alertness; you should use caution when driving or operating hazardous machinery.

D. Tell your doctor or MSH consulting nurse if you have any allergies to medicines or have seizures, high blood pressure, heart disease, or glaucoma.

E. Tell your doctor or MHS consulting nurse if you are taking any medications, including over-the-counter medications.

F. Antidepressants have an additive effect with other sedative medications, such as antihistamines, tranquilizers, sleeping pills, and alcohol. We advise against using any alcohol at all during the first month of treatment with any antidepressant, and after that, small amounts of alcohol may usually be used safely. This should be discussed with your doctor or MHS consulting nurse.

G. Excessive use of caffeine may produce tremors or anxiety symptoms; use of **fewer than 5 cups/day** of caffeinated coffee is encouraged.

H. Keep this medication out of the reach of children since overdose is especially dangerous to young children. If you think you or anyone else has taken an overdose of this drug, seek medical attention immediately.

I. Do not abruptly stop the antidepressant—it may precipitate depression. Generally, these medications are tapered when it is time to stop them. Consult with your doctor or MHS consulting nurses before stopping the medication.

IV. Side Effects

A. You may experience mild dry mouth and constipation. Drinking fluids will help alleviate these problems, which lessen the longer you use the medication.

B. Dizziness when standing up quickly may occur. If this occurs, contact the consulting nurse.

C. Weight gain may occur with several of these medicines. This side effect can be countered with regular exercise and regulation of food intake.

D. Difficulty with close vision may occur, particularly in those over age 40. This does not mean you need glasses, but rather, is a side effect of your antidepressant. If this occurs, discuss it with the MHS consulting nurse.

E. Painful erections (priapism) may occur with the use of trazodone in men. If you note prolonged or painful erections, discontinue the medication immediately and contact the MHS consulting nurse.

F. Occasionally, nausea, headache, tiredness, confusion, fainting, irregular heartbeat, difficulties in urinating, shakiness, sore throat, fever, and skin rashes may occur. These should be reported to the MHS consulting nurse.

PATIENT INFORMATION SHEET: MONOAMINE OXIDASE INHIBITORS (MAOIS)

Your medication:

I. Benefits

Although most people will feel better on some days and not on others, some people experience marked or prolonged depression. Others will suffer panic attacks in which they will experience a sudden onset of extreme anxiety accompanied by physical symptoms, e.g., palpations, chest pain, and shortness of breath.

II. Course of Treatment

A. Once your doctor has prescribed an MAOI, it is usually given all in the morning unless otherwise instructed. A low dose of the medication is given initially, with an increase in the amount taken each morning as directed by your doctor. These medications are not addictive and are not "tranquilizers," even though they may alleviate anxiety associated with depression and panic disorder. When the proper dosage is reached, you generally will feel calmer, have more energy, and gradually note the disappearance of symptoms of depression and panic disorder. If you feel "jittery" or drowsy during the daytime, call the MHS consulting nurse for directions. If you take the medication late in the day, it may cause some difficulty falling asleep. If you are already having difficulty with insomnia, the insomnia subsides after 1–2 weeks of using MAOIs. Your doctor may decide to prescribe a sleeping pill for a short period of time if your insomnia is severe.

B. Generally, an MAOI is needed for 9–12 months and occasionally longer—the length of treatment is to be determined by your doctor. Discontinuing the medication prematurely may increase the possibility of relapse of depression or panic symptoms.

C. You should make an appointment to see the mental health consulting nurse 7–10 days after starting the use of an MAOI and again in the 4^{th} week and the 12^{th} week of taking the medication. You may be seen more frequently during this period but not less. Refills will not be reordered for patients who are not being seen in the Mental Health Service Clinic. The consulting nurse will discuss the timing of further follow-up visits with you during your 4-week visit. Remember, the mental health consulting nurse is available for phone consultation M–F 8:30 a.m. through 5:30 p.m. (closed 1–2 p.m. for lunch).

D. It may take up to 3 weeks to obtain good effect from an MAOI. Generally, in the first week, a person starts to feel calmer and notes increased energy. In the second week, a person no longer has panic attacks and sleep begins to improve. By the third week, a person generally feels much less depressed and can again enjoy activities.

III. Cautions

A. In combination with MAOIs, certain foods and medications can cause **serious high blood pressure reactions**. This can result in a severe headache, stiff neck, rapid heartbeat, nausea and vomiting, and chest pains. This reaction can be prevented by avoiding the foods and medications listed below.

Foods to Avoid

1. **All cheese**, except cottage and ricotta cheeses, cream cheese, and American cheese. Yogurt and sour cream may be used in moderation if fresh and refrigerated.

2. **Yeast extracts** are generally used in flavorings, e.g., Marmite or Bovril. The yeast used in baked goods is okay to use.

3. **Red wine, especially Chianti wine**. Alcohol should be used in moderation. Domestic beers, white wine, and clear spirits are okay—all other alcoholic beverages, including specialty and imported beers and liqueurs, are to be avoided.

4. **Liver, pickled herring, and fermented sausage**, e.g., salami, pepperoni, summer sausage, and bologna. Eat fresh meat, fish, and poultry only.

5. **Fava or broad bean pods (Italian green beans)**. The narrow green beans and lima beans are acceptable.

6. **Any ferments, overripe, unfresh, or aged food.**

7. Caffeine (e.g., coffee, tea) maybe be used in moderation, e.g., less than 5 cups of coffee perday. Decaffeinated coffee is acceptable.

Medications to Avoid

1. **Over-the-counter cough, cold, decongestant, and allergy products**. This includes nasal sprays and drops and cough syrups with dextromethorphan. If you need a decongestant or cough medicine, call the MHS consulting nurse for a prescription of an acceptable medicine.

2. **Hay fever, sinus, and asthma medicines**.

3. **Narcotics**, including those found in cough syrups. **Demerol (Meperidine)** especially should be avoided.

4. **Tricyclic antidepressants.**

5. **Appetite and weight suppressants**, including over-the-counter products.

6. **Stimulants**, e.g., Ritalin (methylphenidate) and Dexedrine (dextroamphetamine).

7. **Novocaine (procaine) with epinephrine** is used by dentists. It is safe to use cardiac xylocaine (lidocaine) without epinephrine. If your dentist has a question, he/she may call the MHS consulting nurse for assistance.

8. **Any prescription medicines** should be discussed with your doctor. This is especially important in the event of a medical or surgical procedure that involves the use of anesthetics, pain medications, and certain x-ray studies using dyes.

Rules of Caution

1. These dietary and medicine restrictions should be followed for at least two weeks after stopping treatments with MAOIs.

2. Tell your doctor or dentist that you are using MAOIs when seeing them for a medical or dental condition.

3. If you happen to use one of the items on the restricted list and nothing happened, do not assume it is safe to repeat this since foods, drinks, and medications vary greatly in their ability to cause a reaction.

4. Notify your doctor or MHS consulting nurse if you become pregnant or plan to become pregnant during therapy.

5. Be sure to tell your doctor or MHS consulting nurse if you are breastfeeding.

6. Until you are reasonably certain the MAOI does not cause sedation or a decrease in alertness, you should use caution when driving or operating hazardous machinery.

7. Tell your doctor or MSH consulting nurse if you have any allergies to medicines or have seizures, high blood pressure, heart disease, recent head injury, CVA (stroke), aneurysm, neurological problems, or glaucoma.

8. Inform your doctor or MHS consulting nurse if you are taking any medications, including over-the-counter medicines.

9. MAOIs have an additive effect with other sedative medications, such as antihistamines, tranquilizers, sleeping pills, and alcohol. We advise against using any alcohol at all during the first month of treatment with an antidepressant, and after that, small amounts of alcohol, as noted in the dietary restrictions, may usually be used safely. This should be discussed with your doctor or MHS consulting nurse.

10. Keep this medication out of the reach of children since overdose is especially dangerous to young children. If you think you or anyone else has taken an overdose of this drug, seek medical attention immediately.

11. Do not abruptly stop the MAOI. It may precipitate depression or panic symptoms. Generally, these medications are tapered when it is time to stop them. Consult with your doctor or the MHS consulting nurse before stopping the medication.

12. Your doctor may prescribe Thorazine (chlorpromazine) tablets to use if you experience a “hypertensive reaction” by using food or medicine on the restricted list. If you suffer severe headache, stiff neck, nausea and vomiting, chest pain, or rapid heart rate, take one of the Thorazine tablets every ½ hour until the symptoms start to subside. Go to your doctor’s office or the emergency department to have your blood pressure taken. **Don’t drive an automobile after taking a Thorazine tablet** since it may make you drowsy.

IV. Side Effects

A. Dizziness may occur when standing up quickly. If this happens, contact the MHS consulting nurse.

B. You may experience mild dry mouth and constipation. Drinking fluids will help alleviate these problems, which lessen the longer you use the medication.

C. Weight gain may occur. This side effect can be countered with regular exercise and regulation of food intake.

D. Occasionally tiredness, jitteriness, confusion, difficulties in urinating, impotence, lack of ability to have an orgasm, and occasionally other side effects may occur. These should be reported to the MSH consulting nurse.

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Compulsive Behavior: Recognition and Treatment
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Introduction

It has long been recognized that otherwise healthy animals, when kept in captivity, may develop strange behaviors. These behaviors appear abnormal because they are performed out of context, are often exaggerated, directed towards unnatural stimuli or objects, and are often performed repetitively in a constant manner. Well-known examples include pacing in polar bears[27,35] and other carnivores, tongue playing in giraffes and okapis, feather plucking in parrots, repetitive regurgitation and reingestion in primates,[1] and weaving in elephants.[31] Compulsive behavior is very common in domestic livestock. In these species such behavior, particularly when stereotypic, has always been considered to be confinement-induced conflict behavior, and has been linked to specific husbandry practices.[37] Compulsive behavior is also common in pets.[21] Stereotyped compulsive behavior is one of the most studied abnormal behaviors in domestic animals,[18] and much interest has been devoted to the topic in laboratory animals as well.[3] Although early progress has been made to validate the diagnosis of compulsive disorder,[10] further work is needed. The following working definition of compulsive disorder (CD) has been proposed: **"Behaviors that are usually brought on by conflict, but that are subsequently shown outside of the original context. The behaviors might share a similar pathophysiology (e.g., changes in serotonin, dopamine and beta-endorphin systems). Compulsive behaviors seem abnormal because they are displayed out of context and are often repetitive, exaggerated or sustained."**[11]

Causes of Compulsive Disorder

Compulsive behaviors are considered to be an expression of stress, frustration, and/or conflict.[37] Various forms of conflict behavior are caused by frustration or conflict and have been studied in a variety of species.[13] Prolonged and/or repetitive frustration and conflict may result in the conflict behaviors becoming generalized to other contexts (i.e., they emancipate from their original cause).[24,26] They are also believed to evolve gradually from more variable behavior to short sequences of a few simple behavioral elements.[4] Furthermore, it appears that the level of arousal necessary to trigger the performance of these behaviors diminishes as the behavior develops into a compulsive disorder.[11]

While the above outlined development of compulsive behavior may be typical for locomotory behavior, case histories of affected dogs indicate that self-directed oral behavior is displayed from the start in various contexts and does not increase in frequency. Also, these behaviors are typically shown in situations with little outside stimulation but presumably a high level of internal arousal. There is some evidence that locomotory and oral compulsive behaviors differ neurophysiologically as well.[2]

From clinical cases in dogs, it is obvious there may be genetic factors controlling the development of CD: some breeds may be particularly susceptible to developing a CD and others may develop a particular compulsive behavior if the environment is conducive to the development of CD. A genetic predisposition for certain compulsive behaviors has also been demonstrated in lines of Thoroughbred horses,[33] and breed has been shown to affect the likelihood of various compulsive behaviors being performed by horses.[22]

Any stressor, be it social, climatic, nutritional, or disease related, is likely to contribute to the performance of compulsive behavior. These factors may either be causal, or they may simply increase arousal levels and thus the likelihood that an already established compulsive behavior is performed (i.e., act as modulating factors).[25]

Pathophysiology of Compulsive Disorder

The pathophysiology of CD is not well understood. Most evidence stems from drug effects on the performance of compulsive behavior. Large doses of dopaminergic drugs such as amphetamine and apomorphine are effective in inducing stereotyped behavior in animals[3] or exaggerating spontaneous compulsive behavior,[2] while the dopamine antagonist haloperidol results in suppression of spontaneously occurring stereotyped behavior.[16]

Beta-endorphins have been implicated in stereotypy performance because beta-endorphin receptor blockers can be effective in reducing stereotypies.[5,6] However, the concept that performance of stereotypies is rewarded by endorphin release is no longer supported: cribbing in horses did not result in an increase in blood endorphin levels, and their pain sensitivity was actually increased during cribbing compared to when they were not cribbing.[19] Furthermore it has been suggested that beta-endorphins may play a significant role only early on in the development of stereotyped behavior.[16]

Because of similarities of animal CD and human obsessive-compulsive disorder, drugs inhibiting serotonin reuptake have been used to treat dogs with CD.[9] The effectiveness of such drugs implies that serotonin is involved in animal CD. Direct evidence of serotonin involvement has also been presented.[32] However, the role of serotonin in CD is not well understood.[15]

Treatment

Treatment consists of environmental modification and, where necessary, pharmacologic intervention. In the following, treatment is listed in order of implementation.

1. If possible, the cause of the problem should be identified and addressed. The environment should be changed to accommodate the most important species-typical behaviors. Environmental enrichment is not useful unless it specifically targets the behavior that is frustrated, and/or the behaviors most commonly performed by the species in question.

2. Stressors may be additive, and once a compulsive behavior is established, environmental stress may serve to perpetuate it. This includes situations where important releasing stimuli for species typical behavior are lacking, and situations in which an aversive stimulus such as inappropriate climatic conditions, an aggressive group member, or proximity of visitors cannot be avoided. It is therefore indicated to try to reduce environmental stress as much as possible.

3. In most cases, particularly in those that have been going on for a long time, drug therapy may prove necessary. Beta-endorphin antagonists such as naloxone, nalmefene and naltrexone have been suggested to be used for treatment. Beta-endorphin antagonists have high first-pass metabolism and a short half-life, and most are only effective as injectables. Only naltrexone is available as an oral formulation, because in humans its first metabolite, 6β-naltrexol, is an active beta-endorphin antagonist. However, this metabolite is not formed in some species such as dogs,[8] and clinical suppression of compulsive behavior in dogs is short-lasting.[7] In spite of a report supporting its effectiveness at 2.2 mg/kg PO SID–BID in dogs,[36] its use for the treatment of CD, at least in dogs, must be questioned.

Haloperidol has been used experimentally to reduce compulsive behavior in many species. It proved effective in suppressing stereotyped jumping in bank voles.[16] Haloperidol decanoate was used to reduce bar biting in sows at 250 mg IM per sow.[34] Haloperidol suppressed tongue playing in cattle.[30] A dose for haloperidol has not been established for companion animals. Landsberg *et al.*[17] list 1–4 mg per dog PO BID. This author has used it only in a few cases of dogs with compulsive disorder at 1–2 mg per dog, invariably without success. The use of haloperidol for treating feather picking in birds was reported.[20] In one case two African grey parrots were treated successfully with haloperidol at 0.4 mg/kg/day for 7 months.[14]

As is the case with human obsessive-compulsive disorder, pharmacologic intervention is most likely achieved with serotonin reuptake inhibitors. A clinical trial involving 51 dogs with a variety of compulsive behaviors has been performed for the tricyclic antidepressant, clomipramine.[12] Some success was reported for treatment of feather picking in psittacine

birds with clomipramine at 1 mg/kg PO SID or divided BID.[28] Clinical trials on cases of canine acral lick dermatitis have been performed for clomipramine, fluoxetine and sertraline.[29] Paroxetine has also been used clinically, but its effect has not been evaluated. Fluoxetine has been used successfully to suppress pacing in a polar bear at the Calgary Zoo.[27] Fluoxetine was given at 0.62 mg/kg SID for 77 days, then the dose was increased to 1 mg/kg SID. In companion animals we usually give a drug for 3 weeks after it appears to have an effect, then wean off gradually over 3 weeks to avoid a rebound effect.

4. Instead of modulating the brain serotonin system by inhibiting the reuptake and metabolism of serotonin in the presynaptic neuron, a tryptophan supplement can be fed. Tryptophan is a precursor of serotonin. Some success in the treatment of compulsive behavior in horses has been reported at a dose of 2 g/horse BID, or approximately 5 mg/kg BID.[23]

5. In persistent cases a program of counterconditioning (more correctly termed response substitution) might be considered. If this option is chosen, treatment has to be implemented with great consistency in order to be effective. It is very important that the animal be distracted **every time** it is about to perform the compulsive behavior, and an alternative behavior be solicited.

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Concerns and Prospects for Contraception in Carnivores
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Increasing awareness of the need to control reproduction for sound genetic management and to limit the production of surplus animals is focusing attention on current contraceptive choices.[40] In addition, concerns have been raised, particularly for felids[29,30] about the safety of long-term use of the melengestrol acetate (MGA) implants which are most heavily relied upon for contraception in zoo collections.

In 1990 a questionnaire designed to obtain data on past and current use of birth control methods in carnivores was distributed to 113 accredited North American zoos.[4] Fifty-three percent of the zoos responded, providing data on 38 species of carnivores in 20 genera. Data on reversible birth control methods were obtained for 28 species of carnivores; however, in only 6 species was there a sample size of 10 or more individuals.

Six methods were reported for carnivores. Three were reversible contraceptives containing synthetic progestins: MGA implants (Dr. U.S. Seal[a], VA Medical Center, Minneapolis, Minnesota 55417; 154 females, 27 species); medroxyprogesterone acetate (MPA) injections (Depo-Provera: Upjohn Co., Kalamazoo, Michigan 49001; 4 females, 3 species); and oral megestrol acetate (MA, Ovaban: Schering Corp., Kenilworth, New Jersey 07033, or Megace: no longer available; 10 females, 8 species). The synthetic androgen mibolerone (Cheque: Upjohn Co.) was administered to two female *P. onca*, and prostaglandin was used as an abortifacient in one canid.

Permanent sterilization was the second most common form of birth control: 80 males and 57 females. Most males (62.5%) were vasectomized, the remainder were castrated. In contrast, the majority of the females (98.2%) were ovariohysterectomized rather than having tubal ligations. The large number of males permanently sterilized clearly illustrates the need for a reversible male contraceptive. The data also suggest that the continued expression of sexual behavior may be judged to be more important for males than females.

Small sample sizes precluded meaningful evaluation of all but one reversible contraceptive, the MGA implant. Although 27 species were reported implanted, six species accounted for 75% of the data: *Felis concolor* (15), *Panthera pardus* (12), *P. onca* (20), *P. leo* (25), *P. tigris* (31), and *Ursus arctos* (12). Because the duration of efficacy has not been established, replacement every two years is suggested. The majority of respondents routinely replaced the implants between 20 and 26 months. However, four felids were implanted for 33 and two for 41 months without failure. Expiration of the implant was likely the cause of two carnivore pregnancies; a *P. onca* and *Ursus arctos* were implanted for 52 and 87 months, respectively, at the time of conception.

The actual failure rate of implants verified in place at conception was 1.9% when calculated per individual, but dropped to 1.4% when calculated per implant. An additional three pregnancies resulted when implant loss went undetected. Six percent of the implants were lost at varying times following insertion, undoubtedly an underestimation. Implant presence is not always monitored and can be difficult to verify visually. Furthermore, sexual behavior, including mounting and copulation, has been observed for individuals of all carnivore species for which an adequate sample size exists, thereby precluding behavior as a reliable indicator of contraceptive effectiveness.

Data on successful reversals are essential for the evaluation of any “reversible” contraceptive. The survey revealed that 21 females from nine species were allowed to mate following implant removal. Reversal rate was 100% when assessed per species, but 62% assessed per individual. However, the above data do not consider the reproductive history of the individual females. When only females parous prior to implant use were included, 12 of the 14 reversals (86%) were successful. Among the 12 females successfully reversed, duration of implant use ranged from five to 67 months; seven were implanted for over two years. The interval between implant removal and conception in non-seasonally breeding species (9) was two to nine months (mean, 4.8 months). Duration of implant use and latency to fertility were not correlated; indeed, two mountain lions implanted for 44 and 67 months conceived within 2 and 5 months, respectively, of implant removal.

Analysis of the potential health risks associated with long-term steroid contraceptives were beyond the scope of the survey. However, 64 individuals were implanted more than once, and 43 for 48 months or longer. A retrospective study including these chronically treated animals could provide important information on possible pathology.

Although we must await the results of studies directly addressing the safety of long-term MGA exposure, extensive literature on the treatment of domestic dogs and cats with natural and synthetic progestins and estrogens is available for review.[11,15] In addition to studies evaluating these steroids as contraceptives for the burgeoning pet population, dogs have been used extensively according to FDA directive for testing contraceptive formulations being considered for human application.

Steroid Hormone-Based Contraceptives

Synthetic progestins include, in addition to the MGA, MPA, and MA mentioned above, levonorgestrel (Norplant: Wyeth Laboratories, Philadelphia, Pennsylvania 19101), cyproterone acetate, chlormadinone, and proligestone (Delvosteron: Mycofarm, Essex, UK), all of which have been tested with dogs. Most reports for cats concern the use of MA, approved for use in cats in the United Kingdom, and MPA.

Controlled studies with lions and tigers[41,42] demonstrated slight suppression of cortisol with MPA and no deleterious effects with MGA treatment. However, investigations with domestic cats using MPA and MA, sometimes at higher doses or for longer duration, have documented more extensive side effects. In domestic cats, both MA and MPA stimulated appetite and weight gain.[24,26] More seriously, MA’s glucocorticoid-like activity can produce adrenocortical atrophy[9] and symptoms of diabetes mellitus[36]. Potential progestin-induced pathology includes stimulation of mammary gland hyperplasia and neoplasia[2,25,38] and induction of pyometra[31].

In dogs, deleterious effects of progestins on uterine and mammary tissue are similar to those described for the cat.[5,13,18,20,22,23,37] Unfortunately, the addition of estrogen to progestin therapy does not ameliorate but exacerbates the progestin-induced pathology.[20,45] For this reason, progestin administration should not be initiated during proestrus or estrus.[5] Various progestins have been documented to stimulate increased insulin[18] and diabetes symptoms[37]. Whether depressed adrenocortical function[10,16] and adrenal weight[13] are accompanied by changes in ACTH is unclear.[14,16] Pathological changes of the liver and gall bladder,[23,37] as well as elevated growth hormone associated with acromegalic symptoms,[10] may result at higher doses.

In contrast to these deleterious effects, female fetuses conceived during treatment with MGA showed no signs of virilization,[12] nor did MGA administration during the last 30 days of pregnancy adversely affect parturition or survival of pups[54]. However, other progestins or higher doses may delay parturition and jeopardize fetuses.[46] Females bred after cessation of treatment with MPA gave birth to normal pups.[73]

Not surprisingly, the more numerous studies conducted on dogs using a wider variety of progestins have revealed some differences among the compounds, doses, and routes of administration. It is important to point out, first, that most studies used doses higher than necessary to block conception and, secondly, that at lower doses many of the changes noted are similar to those which occur naturally during estrus and pregnancy or infertile luteal phase.[13] In addition, especially at lower doses, apparently pathologic effects may be transient.[7,37,52] Trials with yet another synthetic progestin, proligestone, show it to be more specific in suppressing pituitary function for blocking ovulation but less progestogenic, which should moderate side-effects.[47,48]

The other two major classes of gonadal steroids, estrogens and androgens, also have been tested for contraceptive application in dogs. Although estrogens (diethylstilbestrol, estradiol cypionate) have been used to block implantation following mismating in dogs and cats, their ability to stimulate uterine disease, bone marrow suppression, aplastic anemia, and ovarian neoplasms makes them inappropriate contraceptive compounds.[4,20,27] Both testosterone (dogs[43]) and the synthetic androgen mibolerone (dog;[44] cat;[8] wolf (*Canis lupus*), *Panthera pardus*, *P. onca*, and *P. leo*[18]) have proven effective contraceptives. However, masculinizing effects included clitoral hypertrophy, vulval discharge, mane

growth (female lion), mounting, and increased aggression. Mibolerone treatment is not recommended for cats and administration to dogs is contraindicated for females that have impaired liver function, are lactating or pregnant (female fetuses are virilized).

Species differences in response to both natural and synthetic steroids must be emphasized. For example, in contrast to their stimulation of uterine hyperplasia in canids and felids, progestins are prescribed to prevent endometrial hyperplasia in human females.[1] In rats, MA decreases and estrogen increases the incidence of mammary neoplasms,[20,35] whereas in dogs and cats progestins but not estrogens stimulate mammary tumor formation. Administration of progestin-only or progestin plus estrogen oral contraceptives to rhesus monkeys resulted in no mammary hyperplasia.[2] In cattle, MGA causes an increase rather than a decrease in adrenal weight.[55] In fact, many scientists have argued against the use of dogs for human steroid contraceptive testing because of these differences.[17,39]

Alternatives to Steroid Hormones

Analogues of luteinizing-hormone releasing hormone (LHRH), also called gonadotrophin releasing hormone (GnRH), are being tested with dogs. Although LHRH antagonists (e.g., detirelix) were expected to find contraceptive application, their high doses and expense have relegated them to acute treatments such as pregnancy termination.[51] In contrast, an extremely potent LHRH agonist (nafarelin), stimulated estrus within six days of treatment initiation, but suppressed estrus during the ensuing year of administration.[50] Normal cycles and fertility resumed after treatment ceased.

LHRH agonists are also effective at suppressing testosterone production and spermatogenesis in male dogs. As with females, there was an initial period of testosterone stimulation followed by gradual decline over 30 days, and no ejaculates were obtained after 3 weeks. Spermatozoa were collected by 8 weeks after cessation of treatment.[49,51]

LHRH agonists and antagonists, by suppressing gonadal hormone production, also suppress behaviors supported by these hormones. Reductions in male aggression may be welcome in some species or individuals. However, especially in canids where pack cohesion may be maintained by sexual bonds and the parental behavior shown by subordinates, such treatment might create new problems. Androgen implants can be used in cases where maintenance of male-type behavior or secondary sex characteristics (e.g., antlers, mane) is desired.

Long-term delivery is currently a problem with agonists. Because they are not orally active and don't follow the same diffusion dynamics as steroids, traditional delivery methods have not been effective. Both a silicone elastomer matrix and a reservoir system are being tested.[51]

Immunization against hormones such as LHRH show promise for both male and female contraception. Trials have been conducted with dogs, but have not yet been completely successful.[21] Vaccines have also been developed against the zona pellucida (ZP), the glycoprotein layer coating the oocyte and pre-implantation embryo. Theoretically, immunization should block oocyte penetration by sperm without affecting ovulation and the expression of estrous behavior. However, studies with dogs have revealed additional, more generalized, ovarian effects,[32,33,34] and it is feared that long-term treatment might result in infertility. Recent work with rabbits, which also had shown ovarian pathology following ZP vaccination, suggests that further purification of the antigen may minimize such effects.[28] Other problems common to vaccines include skin lesions from the adjuvant at the injection site, individual differences in response, and variable duration of efficacy.

Vas plugs, both preformed[53] and injectable silicone, are another alternative now under investigation with exotic felids. Preliminary results with a variety of species, though promising, have been variable, primarily due to species differences in vas size and distensibility (unpublished). It is hoped that recent modifications in the injectable plug technique will be more successful.

A class of compounds which were tested in dogs for potential human application may still be appropriate for exotic canids and perhaps other species. Bisdiamines reversibly inhibit spermatogenesis without affecting hormone levels.[3] They were withdrawn from human clinical trials because they inhibited alcohol dehydrogenase, a side-effect which presents no problem in the absence of alcohol consumption.

Endnotes

a. Currently available from Dr. E. D. Plotka, Marshfield Medical Research Foundation, 1000 North Oak Avenue, Marshfield, WI 54449.

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Contraception in Zoo Mammals: Rumors and Realities
American Association of Zoo Veterinarians Conference 2007

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ABSTRACT

Contraception is the deliberate prevention of production of offspring. The simplest or most permanent methods of contraception can include housing males and females separately, or surgical alteration of anatomy such that sperm and ova cannot combine (vasectomy, ovarian or uterine removal, testicular removal, or tubal ligation). Temporary contraception is commonly employed in zoological species, retaining the ability to resume reproduction of genetically valuable individuals if management conditions change over time. Choices between the various available contraceptive techniques all involve assessment of risks, benefits, financial costs, behavioral costs, ethical considerations, practical limitations, technical abilities, and resources. An additional, very real component of contraceptive decision-making is the anecdotal or databased information that colleagues provide to the discussion. Each situation generates a different set of considerations when deciding upon the most appropriate contraceptive.

Contraceptive data summaries and recommendations are available via internet[2] and in affordable published texts,[1] but rumors contrary to the data still abound. Examples of the concerns and questions posed to the AZA Wildlife Contraception Center include: Are melengestrol acetate (MGA) implants now contraindicated for use? Are porcine zona pellucida vaccines effective for contraception? Can an animal that is administered a gonadotropin-releasing hormone (GnRH) agonist for contraception (leuprolide or deslorelin) be housed immediately and safely back with other animals? Can any male mammal be given a GnRH agonist for contraception or aggression control? Temporary contraception might be expensive; is it worth it?

Decades of available data and expertise should be incorporated into responsible decisions regarding contraceptive usage.

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Effect of Melengestrol Acetate on Male Muntjac (*Muntiacus reevesi*)
American Association of Zoo Veterinarians Conference 1987

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Melengestrol acetate (MGA) (Snycropells, Agway) is a progestational compound that can prevent pregnancy in some species of hoofed stock. When provided orally on a daily basis, studies in cattle show cessation of estrus and/or ovulation depending on the dose.[1-3] It has been used successfully in domestic cattle, sheep, and white-tailed deer when added daily to the ration at a total dose per animal of 0.3 to 1.0 mg per day.[4,5] Young male white-tailed deer treated with MGA showed no adverse side effects nor changes in subsequent fertility.[5]

Fecundity reduction could be useful in zoo Artiodactyla in preventing the overpopulation of limited space or seasonally, in preventing births during cold winter months. This would be particularly appropriate in species, such as deer and some antelope, with multiple males in a structured hierarchy. In these cases, temporarily removing males can upset the hierarchy and result in serious fighting.

This report describes a pilot study of the effects of MGA on male muntjac (*Muntiacus reevesi*) reproductive status and general health.

Five male muntjacs, ranging in age from six months to four years, were evaluated for semen analysis, testicular measurements, secondary sex characteristics, body weight, and blood profiles before, during, and after treatment with MGA. The males were examined under ketamine (10 mg/kg IV), diazepam (0.2 mg/kg IV), and halothane (1.5%) anesthesia; semen was collected by electroejaculation and examined by standard methods.[6] Evaluations were performed at day 0, 15, and 30 to establish control data. MGA was then added to the concentrate ration at 0.2 mg/animal for 60 days, then increased to 0.3 mg/animal for an additional 30 days. The animals were reevaluated at day 60, 90, and 120 (during treatment) and day 180 (60 days after withdrawal).

Results showed a statistically significant decrease in sperm concentration (48%) and total sperm (23%) during treatment with recovery to control levels post-withdrawal. There was no effect on complete blood counts, serum chemistries, or general health. There was a subjective decrease in aggressive behavior and in preorbital and frontal gland secretions. The six-month-old male showed continued maturation, testicular growth, and secondary sex characteristic development during MGA treatment.

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Effects of a GnRH Vaccine on the Estrous Cycle of an Asian Elephant (*Elephas maximus*)
American Association of Zoo Veterinarians Conference 2009

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ABSTRACT

Repro-BLOC® gonadotropin-releasing hormone (GnRH) vaccine (Amplicon Vaccine LLC, Pullman, WA) is effective at suppressing estrous cyclicity in heifers.[3,8] The production of antibodies to a GnRH fusion protein neutralizes GnRH, thereby preventing follicle-stimulating hormone and luteinizing hormone (LH) release from the anterior pituitary, leading to sterility in both genders. GnRH vaccines have been evaluated as a management tool in horses, ruminants, cervids, swine, dogs, and cats.[2,5-7,9] GnRH vaccination has been used in male African[4] and Asian (Thomas Hildebrandt, personal communication) elephants to decrease aggression.

Repro-BLOC® was administered to a geriatric female Asian elephant for management of suspected uterine leiomyomas associated with anemia and hemorrhage, although leiomyomas are not uncommon in this species and typically benign.[1] We speculated that GnRH vaccination would be effective at suppressing ovarian activity in female elephants and would thereby reduce the size of the leiomyomas and minimize the risk of further hemorrhage. Five vaccinations in increasing doses from 3 to 30 mg were administered over 20 months before efficacy was documented. Serial serum analyses showed estrous cycle suppression in association with a rise in GnRH antibody binding and a decrease in progesterone and LH. Ultrasonographic examinations were performed to evaluate uterine changes. The hematocrit normalized soon after the initial hemorrhage with no recurrence of anemia. To the authors' knowledge, this is the first reported use of a GnRH vaccine in a female elephant. GnRH vaccination in elephants shows great potential for reversible contraception and management of uterine pathology in older females and warrants further investigation.

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 Effects of Fluphenazine Decanoate on Reproductive Cyclicity and Cortisol Levels in Central Chinese Goral (*Naemorhedus goral*)

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Effects of Fluphenazine Decanoate on Reproductive Cyclicity and Cortisol Levels in Central Chinese Goral (*Naemorhedus goral*)
American Association of Zoo Veterinarians Conference 2007

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Abstract

Long-acting neuroleptics (LANs) have been used for behavioral management of ungulates in captivity and for translocation for many years.[1,3,5] With half-lives ranging from hours to days, LANs can aid behavioral management by decreasing aversive and aggressive behaviors and, potentially, stress responses in ungulates under intensive management conditions. Theoretically, their use could augment breeding situations in species prone to stress or intraspecific aggression. However, their mechanism of action is competitive antagonism of dopamine, which is associated with alteration of prolactin and gonadotropin release.[2,4,6] Little is known about LAN effects on the luteinizing hormone (LH) surge and ovulation in artiodactylids. This study was designed to assess the effects of fluphenazine decanoate on ovulation and stress in a small antelope species undergoing intensive handling by measuring serum LH, progestin and cortisol, and monitoring daily follicular development by ultrasound. Seven central Chinese goral (*Naemorhedus goral*) were randomly assigned to two groups: A) treatment with 1 mg/kg fluphenazine decanoate IM (n=4), or B) control, saline injection IM (n=3). Reproductive cyclicity in both groups was synchronized using 7-day controlled internal drug release devices (CIDR-G; Pfizer AG, Karlsruhe, Germany) containing 330 mg progesterone, combined with 8 mg IM prostaglandin $F_{2\alpha}$ at CIDR insertion. Beginning 24 h following CIDR removal, blood was collected from each animal every 6 h for 96 h, and ultrasound examinations were performed every 24 h. Serum cortisol concentrations were lower in the treatment group ($p<0.05$), however, fluphenazine decanoate appears to affect ovarian response to synchronization in this species.

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Enrichment of Captive Non-Human Primate Environments, One Clinical Veterinarian's Perspective
American Association of Zoo Veterinarians Conference 1994
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Introduction

Over the past decade zoo staff, visitors, and federal regulators have been changing how they envision their responsibilities toward those members of the order primates that zoos house for public education, SSP research, and propagation.

These concerns are reflected in the geometric increase in the number of articles in scientific and lay publications as well as entire books devoted to this issue.[1] This abstract does not pretend to present a complete summary of all the data and opinions expressed to date. Zoos house species of primates that are behaviorally, biologically, and ecologically diverse. Some examples of successful strategies will be given in hopes of stimulating new innovations that will fit your setting.

Methods

First, define the parameters that best assess the psychological and physiological well-being of each species in the collection. No universal definition of well-being exists.[2,3,4,5,6] List what is known about wild environment, social behavior, and diet when planning a program. Second, objectively and subjectively document the effect of any change. Controlled studies with comparisons between individual or groups held in different settings or of the same individual/groups before and after a change will do much to avoid criticism of zoos for change based on public pressure or unsupported opinion. Appropriate enrichment will vary with different species, age, sex, group composition, and individual temperament.[7] Re-evaluation of established procedures is the final step in providing "optimal enrichment" for a setting. Limit the number of assessment parameters that will be evaluated. Too few may bias the results but too many make other results uninterpretable (given the way parameters may interact).[5]

The following is a list of categories of enrichment, methods to monitor success and costs to consider when formulating a plan. Some examples of each category are also given.

1. Categories of enrichment

- a. Social
  - i. Companionship
    - a) Same species
      - (1) Pair
      - (2) Single sex/age group
      - (3) Family mixed age and mixed family groups—as appropriate to this species in the wild
      - (4) Changes in other pairs or groups (proximity to estrus females may affect stability or fight incidence)
      - (5) Part or full-time
    - b) Other species—mixed exhibit or dog as surrogate
  - ii. Training to alter behavioral repertoire
  - iii. Visual, auditory, olfactory exposure to animals/humans
    - a) Direct
    - b) Indirect—video of another exhibit of same species in main exhibit by holding area
- b. Physical features
  - i. Cage—size vertical and horizontal complexity
    Plantings, vine tangles, grapevines, bamboo, honeysuckle, kudzu, maple, pine, oak, cedar branches
    Rotate primates out of outdoor exhibit periodically to allow plantings to regrow.
    Windows to other animals/exhibits/outdoors
    Visual barriers to allow escape from view
    Tunnels to connect cages and allow migration or escape interactions with other species in exhibit.
    Indoor/outdoor components
    Bedding material
    Perch, rope, garden hose, branches of various sizes and flexibility
    Nest areas—places to hide or sleep away from viewing
  - ii. Diet—variability of composition, when and how offered
    Broadcast to allow foraging in hay or wood chips
    Crickets, mealworms, lizard, mice from murine viral free research vendors (or extras from local university).
    Seasonally rotating available fruit and vegetables, including beans, corn on cob
    Feed at differing locations within cage at heights suitable for species housed
  - iii. Occupational—within and outside cage
    Objects to manipulate, (i.e., toys, foraging, mirrors, TV, tires, innertubes, radio, fishing in bowl of water or pool for food or toys)
    Stick retrieval of food outside cage, food puzzles in many shapes Games played against the public
    Freezing food or toy in block of ice
    Burlap sacks, cardboard boxes placed inside one another, rolls of paper to spread around an exhibit.
  - iv. Physical—temperature, humidity, light
    How often changed—daily vs. seasonal
    Rain inside the exhibit
- c. Ultimate Goals
  - i. Give control over some part of their environment, (i.e., ability to alter whether in a group, on exhibit or off, when and what eaten, etc.)
  - ii. To engage the primates most complex cognitive and affective skills, so that they will be free of distress most of the time, be in good physical health, and exhibit a substantial range of species typical behaviors.

2. Examples of methods to monitor success of enrichment:

a. Serial recording of physical characteristics: hair/skin, eyes, gait, posture, facial expressions, presence of diarrhea/constipation
b. Non-invasive:
   i. Weight gain/growth
   ii. Number of births/deaths/year
   iii. Disease patterns
   iv. Incidence of wounding
      Self
      Interactions with others
   v. Vocalizations
      Number and type
      Percent of distress calls
   vi. Behaviors, species-specific, quantification, percent of aggressive/affiliative, other, quality of parental care.
   vii. Keeper/public interactions (we cannot ignore opinions)
   viii. Ability to deal with stress
   ix. Incidence of stereotypic of other abnormal behaviors
c. Invasive:
   i. Telemetry
      Circadian temp and ECG
   ii. Sequential hormone analysis
      Fecal/plasma
   iii. Responses to behavioral training
   iv. Immune function
      Globulin subsets and quant
   v. T cell % and response to mitogens
   vi. Cortisol response to dexamethasone suppression test

3. Costs of Enrichment:

a. Additional staff trained to implement and monitor program—monitoring health of staff/volunteer working with non-human primates
b. Added stress on some primates not accustomed to communal living
c. May increase morbidity and mortality while changing environment or due to falls from trees or fights
d. Exhibit and holding area redesign
e. Purchase costs of toys and other apparatus

Results—Some Changes That Have Been Noted in an Enriched Setting

Appropriate enrichment clearly provides increased opportunity to minimize boredom, obesity, and pathologic behavior. Pair or group formation is frequently not a simple task. Short- or long-term group incompatibility is always possible. Adult female *Macaca* in an established group with resident males may have a xenophobic reaction to newly introduced females. The males rarely intervene but the group of established females frequently injure new arrivals. New arrivals seldom are seen to defend themselves against these group attacks.

Same sex adult pairing is more difficult than infant/adult pairing in many species of *Macaca*.[8]

Placement of a radio and feeder with levers that allowed *Macaca mulatta* to turn a radio on/off and eat when they desired, decreased cortisol levels and decreased abnormal behaviors.[9]

Stable pairing or group-housing old *Macaca* with juveniles leads to decreased NK cell and lymphocyte proliferation in the old *Macaca* two months after group formation versus that of single housed old *Macaca*.[10] This unexpected finding has been noted repeatedly and shows another cost of social housing even though the older *Macaca* were more active and appeared to interact well with the juveniles.

Increased time is spent foraging and aggression and regurgitation are decreased when great apes are offered multiple small meals and supplemented with seeds, fruit, or browse each day.

All male langur groups have few fights if they are composed of an even number of members. They form affiliative pairs. An odd man (out) is unlikely to be accepted by a group.

Ruffed lemur or *Saimiri sciureus* group-housed males: Only dominants of group will show an increase in testicle size and serum testosterone during breeding season. Aggression toward submissive males increases if a female is introduced during breeding season.

S. oedipus female: Only the dominant female will cycle and conceive.[11] Young endocrine-suppressed female *S. oedipus* are more likely to leave an extended family group to enter plastic tunnels and migrate to empty cages. Perhaps tunnels could be used to determine when they are ready to leave their family and establish a new group.[12]

Cage design for arboreal primates requires structures of differing diameter elasticity and texture arranged at various heights and angles to facilitate movement via indirect routes. This maintains eye-limb coordination as well as providing "enrichment." Non-sanitizable structures may need to be replaced at regular intervals, but they should not all be replaced at one time which would remove all territorial markings. Changing placement of structures within the cage at regular intervals also provides novelty.

Captive born primates must learn how to interact with other species in a mixed exhibit. I have handled multiple arm wounds from yearling marmosets learning not to steal food from the mouth of sloths.

Unlike marmosets, galago neonatal mortality increases if mothers are not caged alone. In the wild, pregnant females have been noted to leave the group prior to parturition and do not return for several weeks.[13]

Summary

"Distress must be separated from eustress or innocuous stress with which animals effectively cope and might even seek and enjoy. Most animals, including humans, seek some form of stress to relieve an otherwise sedentary life."[14]

"Psychological well-being is a subjective phenomenon related to the quality of one's life experiences."[6] Soumi has shown that major differences exist between individuals of comparable species, age, sex and in some cases rearing experience in terms of their response to stress. Some monkeys respond to mild environmental stressors with a marked behavioral catecholamine, steroid, and immune response while other individuals have minimal response to the same stimuli. This further adds to the difficulty of designing enrichment plans that will suit all members of a group without boring most to avoid stressing some. To quote Soumi and Novak, "The wisdom of Solomon was not sufficient to provide an optimal environment for all of his subjects. It may also be insufficient to create an optimal environment for all captive non-human primates."[5]

None of the parameters listed directly assess well-being. When in doubt, listen to the animals. Try different combinations to see which work. Accept some risk/cost as an unavoidable part of increased social and physical complexity. This was not designed to be comprehensive review. Many of the authors or texts cited can provide additional suggestions.

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GnRH Vaccine Reaction in Large Flying Foxes (*Pteropus vampyrus*)

2018 Joint EAZWV/AAZV/Leibniz-IZW Conference

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Abstract

Free-ranging large flying fox (*Pteropus vampyrus*) colonies are normally harems with one male to multiple females. All-male colonies are common in the population under managed care with adverse interactions occurring between males due to significant sexual conflict; resulting in trauma. These behaviors correlate with seasonal variations in hormones (i.e., testosterone, cortisol).[2] Thus, hormone suppression was expected to decrease agonistic behaviors[4] and improve welfare. One ml of GnRH vaccine[a] was administered subcutaneously to 12 male bats in an effort to suppress seasonal hormonal change. Eleven bats received the injection in the interscapular region and all developed vaccine reactions with one or more clinical presentations that included localized irritation, swelling, and pruritus that progressed to skin ulceration and necrosis with sloughing, and facial edema. One individual received the injection in the leg and did not develop any reaction. The nature of this species to behaviorally focus on areas of irritation escalated the extent of the wounds, with some cases requiring intense medical, surgical, and behavioral intervention. While this vaccine has been used widely in many species with few adverse effects,[3] large flying foxes appear to be particularly sensitive. Proposed contributing factors include: injection site location, severe inflammatory reaction associated with stimulation of the volatile compounds made by shoulder scent glands[7], stimulation of the androgen sensitive sebaceous glands,[1,5] focal interaction with innate bacteria in the skin,[6] and a complex sensitivity/hyper-response to the adjuvant. Ongoing data collection suggests successful hormonal suppressive effects, therefore the administration of this GnRH vaccine in large flying foxes warrants further investigation.

a. Improvest: gonadotropin releasing factor analog-diphtheria toxoid conjugate

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Histologic Analysis of Testicular Development and Sexual Maturation in Rehabilitated Northern Sea Otters (*Enhydra lutris kenyoni*)
American Association of Zoo Veterinarians Conference 2022

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Abstract

Northern sea otters (*Enhydra lutris kenyoni*) that strand at a young age in Alaska are considered non-releasable and are thus placed in zoological institutions for long-term care. As part of the routine captive management of this species, males are often castrated to prevent reproduction, preserve limited spaces for future non-releasable stranded individuals, and minimize potential aggression among cohorts. To determine their relative stage of development, testicles from 13 castrated, rehabilitated Northern sea otters were submitted for histologic examination. Five of the otters (aged 187, 304, 373, 401, and 1423 d) had evidence of sexual maturity to varying degrees. Histologic findings ranged from spermatocytes with some maturation of spermatogenic precursors to fully active spermatogenesis. Spermatozoa were seen in the otters that were 401 and 1423 d (1.1 and 3.9 y). Sexual maturity for wild male sea otters in Alaska has been previously reported to be from as old as 5–6 y to as young as 3 y.[2,3] Social maturity, or the ability to breed and reproduce, may occur a few years later than the onset of physiologic maturity with age, weight, territory quality, and the length of time holding a territory influencing a male otter's mating success.[1,3] Early testicular development in the case of rehabilitated sea otters may be related to abundant resources, lack of competition, and decreased environmental pressures. Additionally, these findings have implications for husbandry practices in both short- and long-term care facilities.

Acknowledgments

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Hormonal Implants to Control Aggression in Bachelor Herds of Scimitar Horned Oryx (*Oryx dammah*): A Progress Report
American Association of Zoo Veterinarians Conference 1992

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In recent years, a number of regional breeding programs (SSP, EEP, ASMP, etc.) have been established to manage small populations of captive endangered and threatened species. Through the use of elaborate computer modeling systems, these programs have been designed to minimize the loss of genetic variability that is inherent in small populations via genetic drift. In addition to minimizing the loss of founder genetic lines, captive-breeding programs must regulate family sizes and sex ratios to maximize the effective size of the population (N_c).[1]

Although the maintenance of a balanced sex ratio would appear to be straightforward, consideration of the social structure of the species further complicates matters. In those species that exhibit either a "harem-forming" or "territorial male" social structure, maintenance of an appropriate ratio of males to females may be difficult in a traditional zoological setting. Typically, these species are held in single-male/multi-female groupings, and adolescent males are removed from the group before male–male aggression develops. However, as these populations grow, a large number of unpaired males accumulate and must be housed individually. Attempts have been made with several species to establish bachelor herds at some of the zoological institutions with larger holding facilities (Bamberger Ranch, Fossil Rim Wildlife Center, etc.), but male–male aggression still develops and substantial injuries are commonplace.

In an attempt to develop tools for the management of bachelor herds of some non-domestic species, a study was initiated that will attempt to evaluate the effects of several hormonal products on male aggressive behavior.

PROGESTINS

Synthetic progestins have been used as aids in fertility control in females of numerous species for many years.[4,5] However, the use of these compounds in males, has been limited primarily to the use of megestrol acetate to control inappropriate sexual behavior in domestic dogs. Stover, *et al.*[6] attempted to evaluate the effects of melengestrol acetate (MGA) on the fertility of male muntjac (*Muntiacus reevesi*). Their results showed a significant decrease in total sperm (23%) and sperm concentration (48%), and complete post-treatment recovery. Additionally, they reported a subjective decrease in aggressive behavior during treatment.

The mechanism by which progestins affect male reproduction and behavior is not well understood. The effect that they have in females through negative feedback, and subsequent inhibition of LH secretion from the pituitary, may also occur in males. Decreased secretion of LH would result in both reduced production of testosterone and a subsequent reduction in spermatogenesis. It has also been suggested (Seal, pers. comm.) that progestins may have a direct antiandrogen effect.

Regardless of the mechanism, the use of progestins in males results in loss of libido and socio-sexual behavior. It is precisely this effect, that is considered desirable for controlling male–male aggression.

GNRH (OR LHRH) AGONISTS

Gonadal function is directly controlled by LH and FSH secreted by the pituitary. Since release of these hormones is directly controlled by GnRH (also known as LHRH), manipulation of this releasing factor can profoundly affect the reproductive functioning of both males and females.[2] In recent years, the production of potent, synthetic GnRH agonists and antagonists has allowed for the development of new approaches to contraception and hormone therapy.

GnRH agonists have been shown to effectively reduce sperm production in males of a number of species.[3] As with other methods that interfere with LH secretion, the effect of GnRH agonists on spermatogenesis is mediated through a reduction in the production of testosterone. Although this proved to be undesirable for contraceptive purposes as it resulted in a loss of libido and secondary sex characteristics, the use of GnRH agonists has been frequently utilized to treat testosterone-dependent diseases such as prostatic hyperplasia and neoplasia. In these applications, GnRH agonists have been shown to reduce testosterone levels far enough to be comparable to surgical castration.

The effects of GnRH agonists on libido and sexual behavior, while undesirable for most contraceptive applications, may prove useful in controlling male–male aggressive behavior.

Method

Because of their aggressive nature when confined to all-male groups, and the large number of males who are being managed individually by the SSP, scimitar-horned oryx (*Oryx dammah*) were chosen for the study. Two bachelor groups of adult male scimitar-horned oryx (body weights=123–170 kg; mean=147.4 kg) were established at the Fossil Rim Wildlife Center. Each group was held in a large pasture (>100 acres) which contained other animals of several species. In the spring of 1991, each animal was immobilized with a combination of carfentanil (14–18 mcg/kg; mean=15.9 mcg/kg) and either xylazine (0.12–0.16 mg/kg; mean=0.13 mg/kg) or acepromazine (0.06 mg/kg) administered via a projectile dart. Time from dart to recumbency ranged from 2:10 to 12:00 minutes (mean=4:45 minutes). Following immobilization, the animals were transported to the veterinary hospital for semen and blood collection and surgical placement of the hormonal implants. Following the placement of the implants, the animals were transported to holding pens where the carfentanil was antagonized with either naloxone (1.4–1.8 mg/kg; mean=1.7 mg/kg) or diprenorphine (0.14–0.16 mg/kg; mean=0.15 mg/kg). When xylazine was included in the anesthetic mixture, it was antagonized with yohimbine (0.12–0.16 mg/kg; mean=0.14 mg/kg). Following antagonism of the anesthetic(s), the animals were ambulatory in 2:05–6:45 minutes (mean=3:40 min). Specific procedures for each group of animals were as follows:

Melengesterol acetate group—Homogeneous silastic implants containing 12.6–13.8 g of melengestrol acetate (MGA, Upjohn Corp., Kalamazoo, Michigan 49001, USA) were prepared as described previously. A 10×10-cm area on the left lateral aspect of the neck was clipped and scrubbed with chlorhexidine scrub. A 3-cm incision was made through the skin, and a pocket slightly larger than the implant (2-cm diameter × 7-cm length) was opened in the musculature via blunt dissection. The implant was placed into the pocket and the incision was closed with several simple interrupted sutures of 2-0 Maxon™ (Davis and Geck Inc., Manati, PR, 00701, USA). Each animal was given 4.5×10^6 I.U. of penicillin G benzathine and penicillin G procaine intramuscularly following the procedure. Individuals in this group were held in isolation pens for one week prior to being placed into a group situation to allow blood levels of MGA to become established.

GnRH agonist group—Homogeneous silastic implants containing 0.12–0.16 g of the GnRH Agonist **$_D$Trp^{6}Pro^{9}NHEt GnRH-HOAc** (provided to E. Plotka by investigators at NIH) were prepared in a similar fashion to that described for MGA implants.[5] A 5×5-cm area on the dorsal aspect of the left pinna was clipped and scrubbed with chlorhexidine scrub (**Note—this site was selected due to the small size of this implant, and the need for reliable palpation and successful removal at later stages of the study**). A 1.5-cm incision was made through the skin, and a pocket slightly larger than the implant (1-cm diameter × 0.3-cm thick) was opened subcutaneously via blunt dissection. The implant was placed into the pocket and the incision was closed with several simple interrupted sutures of 2-0 Maxon™ (Davis and Geck Inc., Manati, PR, 00701, USA). Each animal was given 4.5×10^6 I.U. of penicillin G benzathine and penicillin G procaine intramuscularly following the procedure. Individuals in this group were held in isolation pens for one month prior to being placed into a group situation to allow blood levels of **$_D$Trp^{6}Pro^{9}NHEt GnRH-HOAc** to become established, and to allow for regression of the transient rise in serum testosterone that occurs following the use of GnRH agonists. Prior to placement in a group, serum was collected from each of these animals for future assays of testosterone suppression.

Although the remaining phases of the study have yet to be completed, it is our intention to re-immobilize each animal in the summer of 1992 (1 year) for semen and blood collection,

and removal of the hormone implants. These samples will be compared with the samples collected prior to placement of the hormone implants to assess the effectiveness of each treatment in suppressing testosterone levels and sperm production. In the summer of 1993, another immobilization will be performed on each animal so that semen and blood can be collected to assess the return of normal reproductive function.

Behavioral observations will be conducted during the project in an attempt to quantify changes and differences in male socio-sexual behavior and aggression.

Results

At the time of this writing, assays as to the physiological effects of the hormone implants and complete behavioral assessments have not been completed. However, a number of empirical observations are worthy of discussion.

MGA group—When the animals in this group were taken out of their individual holding pens and placed into a group, a number of threat and dominance-related behaviors were noted. All of the individuals in this group exhibited “horning behavior” (using the horns to thrash small trees and shrubs—considered a displacement behavior) and circling (dominance behavior); however, no actual fighting occurred. By the end of the first day, all aggression seemed to have stopped, and all of the males were seen lying together. In the months since their introduction, there has been no serious fighting although minor dominance displays, and occasional chasing does occur. There have been no serious injuries resulting from intraspecific aggression among these animals.

GnRH agonist group—Prior to the initiation of this study, the animals in this group were maintained in a large pasture (>100 acres) that contained among its multi-species population 2 adult male addax (*Addax nasomasculatus*). The male scimitar-horned oryx regularly chased the addax males and were completely dominant over them at feeding stations. When the oryx in this group were returned to the pasture after one month in the holding pens, their behavior changed substantially. There were no signs of aggression or dominance behavior and all of the animals stayed tightly grouped at all times. Additionally, the addax males who previously were subordinate to the oryx were now very dominant and chased individual oryx on a regular basis. The behavior of these animals remained relatively unchanged, with no intraspecific aggression or dominance behaviors seen, for approximately 8 months. In February 1992, the behavior of the oryx began to revert back to normal male patterns. Circling, horn wrestling, and other dominance behaviors were regularly seen, and several of the oryx began to chase the addax males again. In a 5-week period beginning in February 1992, both of the addax males were seriously gored by oryx males resulting in the death of one animal and major reconstructive surgery in the other. The behavior of the animals in this group appears to have returned to baseline patterns.

Discussion

While both the GnRH agonist and the MGA implants appear to have modified male socio-sexual behavior and reduced levels of intraspecific aggression, the effect was much more pronounced for the GnRH agonist. The short duration of effect for the GnRH agonist implant was most likely due to poor estimations of the dose required to maintain adequate blood levels for one year. As this was the first attempt by these investigators to incorporate this substance into a silastic implant, improper estimation of doses was likely. Additionally, the high costs of synthetic GnRH agonists may make them less applicable to conservation-oriented activities where financial resources are often quite limited. Further evaluations of the MGA implant may show that its lower-level effect on male aggressive behavior may be acceptable, especially when costs are considered.

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Hysterosalpingographic and Laparoscopic Findings in an Adult Female Chimpanzee (*Pan troglodytes troglodytes*)
American Association of Zoo Veterinarians Conference 2002

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Abstract

Due to development and implementation of a chimpanzee reproduction program at the National Zoo in Havana, Cuba, uterine morphology was evaluated in an adult female chimpanzee (*Pan troglodytes troglodytes*). Uterine evaluations were performed using the techniques of hysterosalpingography and laparoscopy. The hysterosalpingography revealed a normal uterus with a longitudinal diameter of 3 cm, cervix 2 cm in diameter, a channel cervix of 1.5 cm diameter, and the fallopian tubes were permeable. The laparoscopic examination revealed a subserosal uterine leiomyoma with external alterations in form and dimension. The lesions observed neither deteriorated the uterine endometrium, obstructed the fallopian tubes, or affected the internal capacity of the uterus. These results allowed the authors to consider this female chimpanzee potentially fertile.

Introduction

From the early 20th century there has been improvement in the use of endoscopic techniques in veterinary medicine.[7] The first laparoscopic procedure in veterinary medicine, performed in 1985, involved uterine horn ties in a dog.[9]

A laparoscopy is an endoscopic procedure for the visual examination of the peritoneal cavity and its contents. It has been of great value in the diagnosis of the gynecological affections, the monitoring of reproductive cycles in domestic cats and wild animals[8] in endosalpinx studies, the mobility and permeability of ducts, the fimbrio-ovarian relationship, and the characteristics of the peritoneum[3]. Other diverse uses such as, monitoring ovarian cycles, detection of anomalies of the abdominal organs, extractions of leiomyomas, and ovarian biopsies have been described.[1,7,9]

A hysterosalpingography is the radiologic visualization of the uterine cavity through the introduction of a contrast agent into the cervix. The principal indication for this type of diagnostic examination is the study of sterility and infertility. The hysterosalpingography tests tubule permeability and is also indicated for the determination of the size and form of the uterus. This technique may also be applied to the detection of fallopian obstruction, channel narrowing, or dilatation. Although a hysterosalpingography can suggest the presence of adhesions, the specificity of this test is only 83%.[3]

A hysterosalpingography can be helpful in the diagnosis of uterus septate or bicorne, however, it is necessary to carry out a laparoscopy to establish the definitive diagnosis. A hysterosalpingography can be used to evaluate the size and thickness of the fallopian conduct, as well as the characteristic of the endosalpinx.[5,6] Hysterosalpingography and laparoscopy are important diagnostic tools in infertility studies to evaluate the general aspect of the internal genital.[4]

The present work describes the procedures used to carry out the gynecological evaluation of the genital apparatus in one captive female chimpanzee that had a previous history of infertility and stereotypic behavior, such as aggressiveness, indifference to the male, homosexuality, and hypermenorrhea.

Methods

A 33-year-old female chimpanzee housed at the National Zoological Park of Cuba was studied. The animal was anesthetized using xylazine (6 mg/kg IM) followed by ketamine (5 mg/kg IM). In addition to the gynecological examination, a complete physical examination and blood sampling for diagnostics and baseline serum sample banking was performed.

Following aseptic preparation of the vulvo-perineal region, the hypersalpingography was performed. With the cervix fixed and visualized, a metallic catheter was introduced through the cervix and 10 ml of a contrast agent (meglumine diatrizoate) was introduced prior to obtaining the radiographic film.

For the laparoscopic procedure, the point of insertion was half-line at navel level. A telescope degree O, rigid rectilinear vision scope was inserted, 4 mm in diameter and 25 cm long.

Results

The hysterosalpingography revealed a normal uterus with a 3 cm longitudinal diameter, a cervical diameter of 2 cm, a channel cervical diameter of 1.5 cm, and the fallopian tubes were permeable. The uterus appeared normal uterus (cavity free) without internal form alterations and fallopian conduct was permeable.

Laparoscopic examination of the uterus revealed the presence of leiomyomas and external alterations in uterine form and dimension. The leiomyomas appeared as a prominence in the peritoneal cavity in the form of a polypoid. Similar pathologies have been reported in humans.[2] Inflammatory lesions were also observed, characterized by multiple adherences from the uterus to the abdominal wall, which appeared to impede the appropriate mobility of the uterus. The existence of this pathology, in association with infectious agents, causes infertility.[5] A microbial analysis performed prior the laparoscopy was negative. The inflammatory lesions observed may indicate previous infection.

Conclusions

A leiomyoma is a benign tumor composed of smooth muscle and conjunctive tissue. Classified by location, they may arise from one of the three uterine layers, endometrium, myometrium, and serosa.[8] The initiating cause of leiomyomas is not known. In a few cases, leiomyomas can cause infertility, abortions, deterioration of the uterine endometrium, obstruction of the fallopian tube, or alter the position of the cervix, preventing correct sperm deposition.[8] Leiomyomas may interfere with the capacity of uterine distension.[10]

The majority of leiomyomas cause few to no symptoms, but if observed, the most common symptoms are prolonged and intense hemorrhage during menstruation. The hypermenorrhea observed in the animal from this report may be a result of the leiomyomas detected during laparoscopic examination.

Although some alterations in the reproductive tract were detected in the female chimpanzee from this report, the internal capacity of the uterus was found to be unaffected. The external lesions observed in the uterus are compatible with previous uterine infections that were not present at the time of gynecological evaluation. Based upon the hypersalpingography and laparoscopic examination techniques utilized in the report, the authors consider this female chimpanzee to be potentially fertile.

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Importation of Unapproved Drugs: How to Order Azaperone and Concentrated Medetomidine
American Association of Zoo Veterinarians Conference 2003
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ABSTRACT

Azaperone is a tranquilizer with multiple applications in zoo medicine.[1] It is used as a part of sedative combinations in elephants, giraffes, and rhinoceros. It has also been used to decrease aggression during introductions in a number of species. Concentrated (10 mg/ml) medetomidine facilitates immobilization of large carnivores and great apes.[2] The medetomidine available in the United States comes as 1 mg/ml. This more dilute formula means that large volumes of drug must be delivered if it is to be used on large animals. This is frequently not practical when anesthetic agents must be delivered via dart or hand injection.

These drugs are not manufactured in the United States and permits are required to import them. There is variable information available on how to apply for and receive permits. The purpose of this presentation is to clarify and streamline the process.

Stresnil (azaperone 50 mg/ml) is currently manufactured by Midwest Veterinary Distribution, 1600 Inkster Blvd., Winnipeg, Manitoba, Canada (800-356-4799).

The product Zalpoine (medetomidine 10 mg/ml) is manufactured by Orion Pharmaceuticals, PO Box 425, Fin-20101 Turku, Finland. They can be contacted via www.orionpharma.com.

The permit required is a letter allowing "Medically Necessary Personal Veterinary Imports". It is issued by the Department of Health and Human Services, Food and Drug Administration, Office of Surveillance and Compliance. The permit application is submitted to:

Toni Wooten
Division of Compliance, HFV-236
Center for Veterinary Food and Drug Administration
Metro Park North
7500 Standish Place
Rockville, Maryland 20855
FAX 301-594-1812
Phone 301-827-1168

The supervisory person in the office is Kim Young. He can be contacted at: 301-827-3353.

The following information must be submitted to apply for the permit:

1. Veterinarian's name, address and phone number
2. Clinic name and address
3. Client's name and address
4. Patient name and nonfood species
5. Name of drug
6. Drug family or class
7. Name and address of drug supplier
8. Legal status of the drug in the foreign country
9. Amount of drug to be imported—must be small noncommercial quantities
10. Disease condition to be treated
11. Reason why an approved human or animal drug will not treat the disease condition
12. A statement that:
    a. You will notify the animal owner that the drug is not approved
    b. That the drug will not be used in any food animal
    c. And that you agree to notify the FDA if there are any adverse reactions
13. How did you learn of the existence of this drug?
    a. The FDA wants to verify that foreign drugs are not actively promoted in U.S. markets.
14. The veterinarian must sign at the end of the submitted information.

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Improvement in the Health and Well-Being of a Bonobo (*Pan paniscus*) Troop Through a Dynamic Operant Conditioning Program
American Association of Zoo Veterinarians Conference 2002
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ABSTRACT

The ultimate goal of an operant conditioning program is to create trust between animals and caregivers. The development of trust allows for a richer quality of life for both animals and zoo staff. Trust is built through clear communication, respect for individuals and their idiosyncrasies, and consistently positive experiences. As trust develops, animals become more relaxed, stress levels lessen, and animals display more normal social interactions. Immense health benefits are reaped from decreased daily stress levels and from the development of close and trusting social bonds. Lowered stress levels promote cardiovascular and metabolic health directly through decreased production and release of stress hormones.[2] Improved social interaction leads to natural enrichment between troop members, and a cascade of other benefits. Trust allows the animals to display more natural behaviors, and allows for better observation of animals and interactions by staff. Improved evaluation of medical problems leads to more appropriate interventions and treatment, often without the need for chemical immobilization. Observation of more natural behaviors allows species managers to better understand life stages and social development of a species, which allows for improved management decisions at individual, troop, and population levels.

These dynamic changes were observed after initiation of an operant conditioning program with the bonobo troop in 1993. Prior to training, the bonobos were difficult to manage and exhibited hostile behaviors such as aggressively grabbing at and routinely urinating on care staff, spitting, screaming, and throwing feces. Medical care was complicated by the inability to separate animals and their fear of the veterinarians. The bonobos were distressed by novel situations and any variation in their routine induced intense panic and aggressive behaviors. The care staff often relied on trickery or bribery to manage the animals, which intensified their mistrust and fear. The staff elected to begin an operant conditioning program utilizing positive reinforcement in order to develop a safer working environment and a less stressful existence for the bonobos.

Keepers worked hard to establish safe, positive working relationships with the animals by rewarding desirable and non-aggressive behaviors. Undesirable behaviors were ignored and most were extinguished in 4–6 weeks. Initial concepts were simple and included name recognition, targeting, stationing, separations, and proper shifting. These early behaviors provided the necessary building blocks for more complex behaviors. Over the 2nd and 3rd year of the program, animals learned to present body parts for examination, the concept of left and right, and were desensitized to medical equipment such as syringes and stethoscopes. An early challenge of the program was to extend the trust that had built up between the animals and their keepers to the veterinary staff. Veterinarians and veterinary technicians visited the troop frequently and handed out treats in order to overcome the fear and negative history associated with past veterinary experiences. Keepers projected a strong positive attitude at the arrival of the veterinary staff in order to model a trusting behavior for the animals. In the same way, the bonobos were taught to accept unfamiliar people by introducing new people as often as possible. Acceptance of strangers is necessary for the successful use of medical consultants when needed.

After 3 years of consistent training, the level of trust between the bonobos and care staff increased, and the previous stress-related behaviors were markedly decreased. The bonobos demonstrated better listening skills, had more patience and did not become frustrated as easily. Most importantly, staff developed a deeper understanding of each animal's personality and unique learning pattern. The bonobos evolved from animals that were fearful, guarded, and extremely dangerous into relaxed, interactive, inquisitive, caring, and gentle animals. The bonobos appear to enjoy their training intensely and become excited whenever they master a new behavior. Their intelligence and quick learning speed pushes the care staff to create a dynamic program that continues to stress more complex and multitask behaviors.

All behaviors are trained first by keepers. Once an animal is comfortable with a new behavior, the veterinary staff first observes, often suggesting variations that will be needed. Constant dialog is necessary between the veterinary staff and the keeper to develop functional behaviors. Next, veterinary staff participates in the behavior by shadowing the keeper movements. The keeper cues both the animal and the veterinary staff member during a behavior, with the animal focusing its attention on the keeper, even while the veterinarian or technician observes or touches it. In this fashion, the veterinarian can complete a fairly thorough physical examination, including ophthalmic, aural, and dental evaluations, thoracic auscultation, and mammary gland and lymph node palpation. Throat swabs, rectal cultures, and rectal temperatures are easily obtained.

Blood collection is facilitated by a polyvinyl chloride (PVC) sleeve that attaches to the front wall of an animal holding area (Fig. 1). The bonobos place their arm inside the PVC sleeve, and grasp an adjustable bar at the far end. Veterinary technicians collect blood through slits cut into the wall of the sleeve on a regular basis from approximately half of the adult bonobos. While juveniles often mimic adult behavior and willingly place their arms in the blood sleeve, they rarely have the attention span, patience, and ability to hold still that is needed for successful venipuncture. Many bonobos also accept the placement of a blood pressure cuff on their arm while stationed in the blood collection sleeve. Radiographs of arms and legs of unanesthetized animals have been accomplished using this PVC sleeve, as have skin tests to screen for mycobacterial infections. Currently, cage modifications are underway to allow for thoracic or abdominal radiographs with animals positioned by operant conditioning.

Figure 1

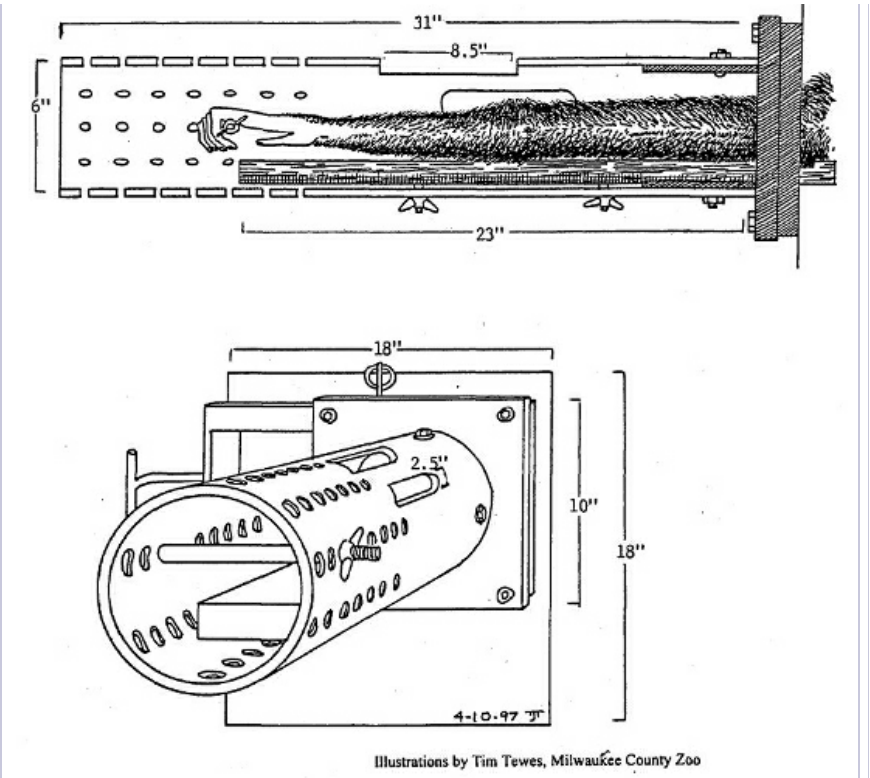

Illustration of “blood sleeve” used at Milwaukee County Zoo bonobo facility.

Cardiac and reproduction ultrasound examinations are performed in non-anesthetized animals stationed in an overhead chute of 5 × 5 cm metal mesh. The overhead chute connects two play areas and animals frequently relax in this chute. For ultrasonography, the bonobos assume sternal recumbency with their arms extended over their head. Animals with barrel-shaped chests must learn to twist onto the left hip in order to lower their left chest wall closer to the mesh for echocardiography. A 10 × 10 cm sliding door was designed to allow better access with the ultrasound probe but most measurements are taken with the probe inserted through the mesh. Initially, keepers acclimatized the animals to equipment below the chute by starting with an old black and white television and an extension cord attached to a syringe case.

The trust and training developed by this operant conditioning program has improved the level of veterinary care for the bonobos. Routine problems such as bite wounds can be evaluated thoroughly without the need for immobilization because the animals are quick to display their wounds to the keepers and veterinary staff, and allow minor wound cleaning with disinfectant solutions on a daily basis. Chronic medical conditions and the effects of therapy can be monitored over time through physical examination and sample collection. Species reference ranges for blood values, vital signs, cardiac parameters, fetal development, and gestational stages can be developed in awake, non-immobilized animals.

A major accomplishment of the operant condition program was a non-invasive artificial insemination that resulted in an offspring from a Species Survival Plan (SSP) recommended pairing. Bonobos show a preference towards mating with novel individuals,[1] and an inhibition to breeding between individuals that have lived together for several years has been observed in several captive collections (Gay Reinartz, Bonobo SSP Coordinator, personal communication). In the wild, bonobos live in multimale, multifemale troops and this inhibition may represent a natural barrier to inbreeding. Two founder bonobos living at the Milwaukee County Zoo had reproduced naturally many times, but only one male offspring had survived to adulthood. While the SSP desired more offspring from this pair, no natural breeding had occurred between these individuals for several years. Through operant conditioning, the keeper was able to collect and test urine from the female to time ovulation, to collect an ejaculate from the male, and then insert the sperm coagulum deeply into the female’s vagina using a speculum. The female was then allowed to breed with sterile, vas clipped males to induce normal vaginal stimulation. The female tested urine-positive for pregnancy after 2 months, and paternity testing of the resultant offspring verified that the semen donor was the father.

In the spring of 2002, most of our eight male and eight female bonobos developed a severe respiratory infection shortly after a wave of respiratory illness passed through the local human population. Throat cultures of three bonobos also grew *Streptococcus pneumonia*, which can cause fatal pneumonia in this species. Daily medical evaluations of all animals and successful medication of extremely ill bonobos was only accomplished due to the advanced operant conditioning program. Sick animals needed to be shifted into safe groups to allow oral medication or darting as needed. Remarkably, the alpha male watched calmly while the veterinarians darted severely ill troop members, and even allowed immobilization of females for removal of infants with lobar pneumonia with a minimum of aggressive responses. Three infants were temporarily hospitalized for intensive care, then reunited with the troop 1 week later. The animals appear to recognize that interventions result in positive outcomes, and trust that troop members removed for medical care will return. Even after 2 weeks of intervention, the bonobos reacted positively to the presence of the veterinary staff.

The ongoing, dynamic operant conditioning program for the bonobo troop at the Milwaukee County Zoo has forever changed the way we care for our closest living relative. Our caregiving style is shaped by concern for both the physical and psychologic needs of the bonobo. The operant conditioning program has given the care staff much patience, empathy, humor, and a deep connection with the animals. The trust built by this program has allowed the animals to display far more natural behaviors and interactions than previously observed. The ability to manage the animals safely and with decreased stress has allowed for a significant increase in troop size to 16 animals. The larger troop size provides for more of the fission-fusion interactions normal to bonobo troops, and has allowed the care staff to understand natural behavior, social interaction, and developmental stages far more deeply. The increase in troop size and the operant conditioning program also allows for better collection of baseline medical data in this endangered species, which we hope will benefit bonobos in the wild and in captivity.

ACKNOWLEDGMENTS

The operant conditioning program could not have been successful without the time and assistance of the entire keeper staff of the Stearns Family Apes of Africa and Primates of the World, veterinary technicians Margaret Michaels and Joan Maurer, previous veterinarian J. Andrew Teare, DVM, and training consultants Shelly Ballman of Oceans of Fun, Inc. and Beth Trczinko. The illustration was provided by Tim Tews, and has been previously published in the Bonobo SSP Husbandry Manual *The Care and Management of Bonobos in Captive Environments*” and in the conference proceedings from “The Apes: Challenges for the 21st Century,” Brookfield, IL, USA.

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 # Is There Any Rhyme or Reason to Rhinoceros Reproduction? A Summary of Reproductive Characteristics, Species-Specificities, and Challenges for the Future

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Is There Any Rhyme or Reason to Rhinoceros Reproduction? A Summary of Reproductive Characteristics, Species-Specificities, and Challenges for the Future
American Association of Zoo Veterinarians Conference 1999

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ABSTRACT

Progress in characterizing the reproductive physiology of all four captive rhinoceros species has revealed interesting variation among species within this taxon and also has been useful in defining future challenges for ensuring the long-term stability of captive breeding programs. Our goal was to combine information from our large-scale study in which the reproductive cycles of Sumatran (n=2) and African black (n=15) and white (n=11) rhinoceroses were monitored, with previous reports from other investigators to produce a concise summary of what is known today about rhinoceros reproductive physiology. Noninvasive fecal hormone metabolite monitoring has been the primary method used for characterizing reproductive cycles, and resulting data have provided a foundation of basic knowledge upon which we now can build by employing additional research tools. For example, ultrasonography already has proven useful for identifying reproductive characteristics that otherwise might have remained undetected.

The African black rhinoceros (*Diceros bicornis*) has been the most prolific and best studied of the captive rhinos.[1,2,9] Most female black rhinos are exhibiting reproductive activity. Their reproductive cycles average about 25 days; however, variable cycle lengths are common with approximately 50% of cycles <20 or >30 days. Although reproductive success has been relatively high, there are several animals that appear to be healthy and reproductively active but continue to breed without becoming pregnant. Identifying the cause of this apparent infertility is the primary challenge ahead for black rhinoceros reproductive research. However, the greatest threat to the captive black rhinoceros population is their unusual susceptibility to several uncommon diseases.

Similar fecal progesterone metabolite monitoring studies in the African southern white rhinoceros (*Ceratotherium simum*) have proven more difficult to interpret,[5,6,10] and reproductive success in this species is inferior to that in its close relative, the black rhinoceros. Approximately 50% of captive female white rhinos appear acyclic. The remaining female white rhinos can be categorized as exhibiting one of three different types of reproductive cycles: 1) 60–70-day cycles; 2) 30–35-day cycles; or 3) a mixture of long (60–70-day) and short (30–35-day) cycles. Several females with 70-day cycles are breeding without producing calves. These long cycles are characterized by an extended luteal phase, and fertility is questionable since no successful pregnancies have been documented in animals exhibiting long cycles exclusively. Determining the causes of both acyclicity and extended cycles is a research priority for the southern white rhinoceros. Additionally, early pregnancy loss and uterine pathology have been documented by ultrasound,[6] and further examinations of additional animals are necessary to determine their prevalence and potential association with reduced fertility.

The reproductive cycle of the Indian rhinoceros (*Rhinoceros unicornis*) has been characterized by both behavioral observations and urinary hormone metabolite monitoring.[3,4] The reproductive cycle appears to vary, ranging from 39–64 days. In this rhinoceros species, increases in urinary estrone conjugates are associated with estrous behavior and breeding. Recent research using serial ultrasound examinations in a regularly cycling female has revealed the development of extremely large follicles (>10-cm diameter) several days before ovulation, which might explain the high levels of estrone produced by this species during estrus. Captive breeding of the Indian rhinoceros has been relatively successful; however, aggressive interactions between some male–female pairings, even during the female's estrus, have interfered with breeding success on several occasions. These behavioral incompatibilities between specific pairs limit our ability to genetically manage the captive population, and the development of artificial insemination may provide a useful method for overcoming this hurdle in the Indian rhinoceros captive breeding program.

The other Asian rhinoceros in captivity, the Sumatran rhinoceros (*Dicerorhinus sumatrensis*), has been studied intensively during the last few years. In the last century, captive breeding efforts with this species have been unsuccessful, in part, due to difficulties detecting estrous behavior and aggressive interactions between pairs when animals are introduced during the female's nonreceptive period. Long-term, serial ultrasound examinations and serum hormone analyses have revealed that the Sumatran rhinoceros experiences a 21-day reproductive cycle[7] and appears to be an induced ovulator, a characteristic not previously reported within the Perissodactyla family. Early pregnancy loss has been detected in one animal on three occasions,[7] and uterine pathology has been reported in several other animals.[8] The reason for this uterine pathology is unknown and warrants investigation. Similarly, the cause of early pregnancy loss is a mystery, and determining why it is occurring and how to overcome it will be research priorities as efforts to produce offspring in the captive Sumatran rhinoceros continue.

In summary, the reproductive cycle of each rhinoceros species differs, ranging from 21 days in the Sumatran rhinoceros to 70 days in some white rhinos. Similarly, ovarian activity differs among species. For example, preovulatory follicles in the Sumatran rhinoceros are ~25 mm in diameter, and breeding appears to induce ovulation. In contrast, preovulatory follicles in the Indian rhinoceros may grow to >10 cm in diameter and spontaneously ovulate. Challenges for the future include understanding the reasons for and overcoming the challenges of 1) repeated copulations without pregnancy; 2) early pregnancy loss; 3) uterine pathology; 4) extended luteal phase cycles and acyclicity in the white rhinoceros; and 5) aggressive interactions between pairs of Indian and Sumatran rhinos introduced for breeding.

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Long-Acting Deslorelin Implants to Control Aggression in Male Lion-Tailed Macaques (*Macaca silenus*)
American Association of Zoo Veterinarians Conference 2000

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Abstract

All male groupings are problematic for most mammalian species housed in zoological institutions. Aggression between males often necessitates housing them individually without visual contact with each other for long periods of time.[1] This can lead to behavioral problems and also takes up valuable holding space. Control of aggression between males is highly desirable since it allows males to be housed together.[1]

St. Catherines Island Wildlife Survival Center (WSC) maintained a free ranging troop of lion-tailed macaques (LTMs) for 6 years. During that time, several males were born, matured in the troop, and eventually migrated out of the troop. In 1997, it was decided to discontinue the project and the existing troop was sent to another institution. Two surplus males were sent to a second institution, leaving three males at WSC. One male was a retired breeder and the other two were his mature offspring. Aggression through the mesh cagework had been noted between all three males over the years. A variety of traumatic injuries have required veterinary attention.

Deslorelin, an experimental GnRH agonist implant, has shown promise in reducing male aggression and is currently under investigation for this purpose in a number of species (Jochle W, personal communication). The objective of this study was to evaluate the effectiveness and safety of long-acting deslorelin implants to control undesirable aggression in intact, mature male lion-tailed macaques. The study is still ongoing at the time of this abstract being written; thus, the results are preliminary.

Three mature male LTMs, a 10-year-old, a 12-year-old, and a 32-year-old, were utilized in this study. The animals were initially housed individually with limited visual contact in indoor/outdoor enclosures. They were fed a complete diet of monkey chow, fruit, and vegetables. The animals were handled only under anesthesia. Ketamine (Ketaset, 100 mg/ml, Fort Dodge Laboratories Inc., Fort Dodge, IA) at 5 mg/kg and medetomidine (Domitor, 1 mg/ml, Pfizer Animal Health, New York, NY) at 0.05 mg/kg were utilized throughout the study and the animals were intubated and maintained on isoflurane (IsoFlo, Abbott Laboratories, North Chicago, IL) anesthesia when electroejaculation was performed for semen collection. The health status of each animal was determined prior to the study by a physical examination, complete blood count (CBC), serum biochemistry panel, serum viral antibody panel including herpes B virus, TB testing, fecal examination for parasites and enteric bacterial pathogens, and radiographs. The oldest LTM had only one testicle, severe dental disease, possible calcified seminal vesicles, mild osteoporosis, and degenerative joint disease. Treatment consisted of daily glucosamine HCl and chondroitin sulfate (Nutramax Laboratories Inc, Baltimore, MD), a vitamin D/calcium supplement, and occasional buffered aspirin. The other two LTMs were considered to be healthy. A physical examination, CBC, and serum biochemistry profile were performed during every immobilization. Reproductive evaluations included testicular measurements (i.e., testes length and width, volume, and firmness), subjective prostate size evaluation, semen evaluation (i.e., semen volume, total sperm count, pH, semen concentration, percent motility, and progressive motility) and were conducted prior to implant injection and at 3-month intervals throughout the study. Fresh feces and serum were collected and frozen at -70°C on a weekly and monthly basis, respectively. Behavioral observations were made throughout the study and were most intense when the animals were initially placed together. The behaviors were divided into three categories: aggressive behavior non-contact, aggressive behavior contact, and facial or vocal aggression. A plexiglass shift door was used prior to placing the animals together so that visual contact aggression behavioral data could be collected.

Serum testosterone levels were considered to be within normal range[2] for the three LTM at the beginning of the study. The two younger animals were producing large volumes of normal sperm, while the older male was producing only small numbers of sperm. Each animal received a 6 mg long-acting deslorelin implant by SC injection between the shoulder blades on 18 September 1998. The older LTM had negligible serum testosterone levels after the first month and was producing no sperm at 3-months post-deslorelin injection. This remained unchanged throughout the remainder of the study. The younger two males were still producing normal levels of serum testosterone at the 3-month evaluation and large volumes of normal sperm were being produced. Fecal testosterone levels were more difficult to interpret and did not seem to correlate well with the serum levels. The 12-year-old animal's weight had decreased significantly, while the other two LTMs maintained their body weights (Table 1). Another 6 mg of deslorelin was administered SC to the two younger males on 18 December 1998.

Table 1. Serum testosterone (T) levels (ng/ml) and body weights (wt) of three lion-tailed macaques (Macaca silenus)

Date	32-year-old (T/wt)	12-year-old (T/wt)	10-year-old (T/wt)
22 Sept 1998	16.1/9.7	5.6/8.7	7.0/10.5
15 Oct 1998	1.0/9.4	6.6/8.6	7.6/10.9
17 Nov 1998	1.0/9.4	6.4/8.2	8.0/10.8
18 Dec 1998	0.6/9.3	8.6/7.8	8.8/10.5
19 Jan 1999	0.7/9.0	5.6/7.5	7.9/9.9
19 Feb 1999	0.5/8.9	4.2/7.5	4.6/10.0
19 Mar 1999	0.3/8.9	2.4/7.2	0.8/9.7
29 Apr 1999	0.3/9.0	2.0/7.4	0.8/9.0
5 June 1999	0.3/9.6	0.9/7.2	0.7/9.0
13 July 1999	0.2/9.8	1.3/7.2	0.5/8.8
20 Aug 1999	0.2/9.6	1.7/7.1	0.2/8.8
17 Sept 1999	NA/9.8	NA/6.9	NA/8.6
22 Oct 1999	NA/9.4	NA/7.2	NA/8.8
16 Nov 1999	NA	NA/7.1	NA/8.6
21 Jan 2000	NA	NA/7.1	NA/8.8

NA = not available

Over the next 3 months, serum testosterone levels slowly decreased in both young animals and the 12-year-old's weight continued to decrease while the 10-year-old maintained his

weight. Semen evaluation at 6 months (19 March 1999) revealed that both young animals had larger numbers of motile sperm when compared to the two previous evaluations. One week prior to this evaluation, behavioral observations revealed that all three LTMs were much less aggressive towards each other through the plexiglass window. The LTMs were then slowly introduced to each other for short periods of time each day.

Serum testosterone levels and body weights continued to drop over the next 3 months. All three LTMs were left together for a few hours while being observed. Initially there was a lot of mounting behavior and minor aggression. Grooming behavior became more common over time and less mounting and aggressive behaviors were noted. The prostate of all three animals measured ~1 × 0.5 cm before deslorelin treatment but was barely detectable 3 months following deslorelin treatment. Also, a coagulum fraction present in ejaculates from the two younger animals collected on 22 September 1998 and 18 December 1998 was absent in subsequent ejaculates. An increase in testes size and morphologically normal spermatozoa on the 18 December 1998 and an increase in total spermatozoa produced on 18 March 1999 for the two younger animals was noted. This is attributable to the short-term increase in circulating testosterone concentrations (Table 1; 18 December 1998) following treatment with a second implant. The 10-month evaluation revealed significant reduction in motile sperm and numerous spermatocytes in the 10-year-old's semen and still large numbers of motile sperm in the 12-year-old's semen. By 20 August 1999, 11 months into the study, the three animals were together most of the time and showing very little aggressive behavior.

On 19 September 1999, the 32-year-old was worked up for unusual respiratory sounds and deemed to have megaesophagus and possible aspiration pneumonia based on plain radiograph evaluation. Treatment consisted of clindamycin (150 mg, Greenstone Ltd., Portage, MI) 10 mg/kg BID and enrofloxacin (Baytril, Bayer Corp., Animal Health, Shawnee Mission, KS) 2.5 mg/kg BID, both drugs were given orally for 14 days. The unusual respiratory sounds improved, and regurgitation was never observed. On 22 October 1999, endoscopy was used to confirm the megaesophagus. The LTM died while recovering from anesthesia. Gross necropsy revealed an enlarged esophagus and gas filled gastrointestinal tract, spondylosis, calcified seminal vesicles, cysts in the renal cortex bilaterally, severely worn dentition, and severe degenerative joint disease in a variety of sites. Histopathology revealed a mild plasma lymphocytic esophagitis and enteritis, coagulative necrosis of pancreatic acinar tissue and adjacent fat, renal tubular cysts within the renal cortex, and diffuse atrophy of seminiferous tubules with thickening of the wall with fibrous connective tissue. Although unlikely, it could not be definitely stated that the deslorelin did not play a role in some of these changes. Despite this animal's death, the study was continued with the other two individuals.

During the 14-month evaluation, the 12-year-old's semen evaluation revealed significantly reduced numbers of motile sperm, while no sperm was noted on the 10-year-old's ejaculate (Table 2). Reevaluation 2 months later revealed similar findings. Results of serum testosterone levels from 21 September 1999 to April 2000 are pending. The two LTMs are currently housed together 24 hours per day. Reproductive exams, physical exam, and serum testosterone levels are currently being performed every 3 months.

Table 2. Morphometric measurements and sperm traits of three lion-tailed macaques (Macaca silenus) before and after deslorelin treatment (6 mg long-acting implant by SC injection on 18 September 1998)

	Date	Testes volume (cm^3)	Total sperm/ejaculate (× 10^6)	Sperm motility (%)	Normal sperm morphology (%)
32-year-old[a]	22 Sept 1998	8.4	0.2	40.0	-
	18 Sept 1998	5.7	0.0	-	-
	19 Mar 1999	5.8	0.0	-	-
	13 July 1999	10.3	0.0	-	-
10-year-old	22 Sept 1998	36.0	226.0	56.7	32.0
	18 Dec 1998b	48.3	60.2	30.0	64.0
	19 Mar 1999	30.1	313.8	61.7	35.0
	13 July 1999	20.0	0.1	0.0	2.0
	16 Nov 1999	15.6	0.0	-	-
	21 Jan 2000	13.7	0.0	-	-
12-year-old	22 Sept 1998	35.3	20.2	56.7	32.0
	18 Dec 1998[b]	34.8	9.4	50.0	68.0
	19 Mar 1999	26.2	61.4	55.0	66.0
	13 July 1999	17.5	327.5	55.0	10.0
	16 Nov 1999	17.0	60.4	25.0	4.0
	21 Jan 2000	17.3	55.6	20.0	12.0

[a]No right testis
[b]Additional 6 mg deslorelin

Preliminary results from this study suggest that deslorelin implants may be useful in creating bachelor groups of LTMs with significant reduction in aggression. Side effects include loss of weight and muscle condition, similar to a castrated animal.

Acknowledgments

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Long-Term Administration of Haloperidol in an African Elephant (*Loxodonta africana*), Supporting the Therapy of Self-Destructive Stereotypic Behavior
2016 Joint AAZV, EAZWV, IZW Conference
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Abstract

Haloperidol has been used for behavior modification in several species.[2,3,5] In the African elephant (*Loxodonta africana*), single administration dosages are described,[1,4] but an extended oral regimen has not been published. A 29-year-old female African elephant, kept for 23 years alone, showed stereotypic behavior, following a translocation into a newly established group of conspecifics. The lack of socialization, abnormal eruption of the tusks, inflammation of the tusk sheaths, and anxiety appeared in the medical history of the animal. The behavioral anomalies worsened in over the next 2 years in the winter period, when the confinement in the closed barn increased. Knocking of the head, chip fractures of the tusk, traumatic lesions and persistent inflammation of the facial area fulminated. In the second year a complex treatment begun, including pain management, several episodes of wound debridement in standing sedation, X-ray assisted shaping of the tusks, modification of the handling techniques, behavioral enrichment, and the oral administration of 120 mg haloperidol (Haloperidol-Richter 1.5 mg Tablet, Richter Gedeon Nyrt., Budapest, 1103 Hungary) daily for 20 weeks. The prescribed dosage produced anxiolysis without profound sedation and adverse effects. The self-destructive behavior stopped, the elephant became more receptive for the stimuli of the environment and the conspecifics, developing appropriate responses. Further deterioration of the tusks and possible exposure of the pulp cavity was avoided and complete recovery of the soft tissues could be achieved. The neuroleptic therapy efficiently supported the complex management of this behavior problem.

Acknowledgments

The authors acknowledge the Nyíregyházi Állatpark Nonprofit Kft. (Sosto Zoo) staff for all their husbandry efforts, Dr. Debbie Young, Dr. Ellen Wiedner, Dr. Gerhard Steenkamp, and the Észak-magyarországi Lógyógyászati Kft. for their contribution to this work.

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Lupron (Leuprolide Acetate) Depot Use in African Crested Porcupines (*Hystrix africaeaustralis*) to Control Intermale Aggression
American Association of Zoo Veterinarians Conference 2010
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ABSTRACT

Leuprolide acetate is a long-acting gonadotropin-releasing hormone (GnRH) agonist. Administration initially results in an increase in follicle-stimulating hormone (FSH) and luteinizing hormone (LH) causing transiently elevated testosterone.[5] In mammals, testosterone suppression usually follows, often approaching zero. Lupron has been used to suppress testosterone and testicular function in Atlantic bottlenose dolphins (*Tursiops truncatus*),[2,3] to prevent breeding and control aggressive behavior in California sea otters (*Enhydra lutris*),[1,5-7] to control undesirable male-associated behaviors in California Sea Lions (*Zalophus californianus*),[3,5] to control mating aggression in pelagic stingrays (*Pteroplatytrygon violacea*),[12] and for aggression and birth control in lion-tailed macaques (*Macaca silenus*).[10] It has been shown to lower testosterone levels in black-faced, gray kangaroos (*Macropus giganteus*), African wild dogs (*Lycaon pictus*) and spectacled bears (*Tremarctos ornatus*).[4] It has also been effective in controlling intermale aggression among gray seals (*Halichoerus grypus*) and harbor seals (*Phoca vitulina*) housed together in the same colony (Stremme, unpublished).

Two newly acquired, 2-year-old, unrelated, male African crested porcupines (*Hystrix africaeaustralis*) began to exhibit aggressive behavior causing wounds requiring veterinary care. Castration was ruled out due to the possibility of future breeding. The monthly form of Lupron was administered intramuscularly to both animals at 0.075 mg/kg every 28 days in an attempt to control the aggression. The animals were anesthetized every 4 weeks with isoflurane, USP to obtain blood to monitor testosterone levels and in some instances to also give the Lupron injections. Serum was sent to the University of Cornell Animal Health Diagnostic Center Endocrinology Laboratory, Ithaca, NY, USA.

Testosterone levels did not drop near zero as expected, and aggressive behavior continued. There was no consistent drop in testosterone levels even when the dose was increased to twice the initial dose (0.150 mg/kg) and three times the initial dose (0.225 mg/kg). In fact, it seemed to rebound and actually increased with the increased dose of Lupron. Leuprolide acetate appears to be ineffective in lowering testosterone levels and in controlling intermale aggressive behavior in African crested porcupines.

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Management of Norwegian Lemmings (*Lemmus lemmus*) at Helsinki Zoo
American Association of Zoo Veterinarians Conference 1988
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Arctic lemmings have been kept successfully at Helsinki Zoo since 1970. The founder population came from the University of Helsinki and originated from Kilpisjärvi area in Northern Finland. New genetic material was obtained in 1978 when 40 lemmings were captured from the wild. Basic feeding and management has been described by others[1] and forms the basis of this report.

Management and Feeding

The exhibit terrarium measures 250 cm x 200 cm. Interior materials are natural: sand, stones, moss, grass-mats, and pieces of wood that are placed on a concrete floor. Lighting is provided by ordinary low-intensity bulbs. The optimum ambient temperature seems to be 10°C, at which animals do well and breed year round. Overheating has been a problem during summer months. Additional breeding boxes measure 80 cm x 40 cm and are 25 cm high and covered with wire-mesh. The bottoms of the boxes are covered with a 10 cm layer of peat, dry grass, and moss. The bedding material is moistened when necessary and it is changed 1 to 3 times weekly.

Feeding is very critical. Helsinki Zoo uses a powder which contains: 1 part of wheatgerm; 2 parts of green meal; 3 parts of milk powder. There is always free access to moss. Lemmings are very selective and use preferably feather moss (*Pleurozium schreberi*), while fork mosses (*Dicranum* spp.), peat mosses (*Sphagnum* spp.), and hair mosses (*Polytrichum* spp.) are not readily accepted. Apples are provided, as is water from a droplet bottle. Multivitamin drops are periodically added to the drinking water.

Breeding

There is one male and two or three females in every breeding box. Females breed approximately every three months, sometimes even more often. The gestation period is about 24–27 days, litter size is 4 to 6 (max 8). The offspring are weaned at the age of six weeks. Both sexes are kept together, which seems to reduce aggressive behavior between young males. Overcrowding seems to induce nervous behavior, and surplus animals are removed from the box/exhibit.

Diseases

Pathology on individual deaths is not available as autolysis is very rapid. Disease “outbreaks” have been caused by *Bordetella bronchiseptica* (purulent pneumonia), *Salmonella typhimurium*, and *Listeria monocytogenes*. Tetracyclines in the drinking water has been used with limited success to control disease problems.

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Medical Management of Curassows
American Association of Zoo Veterinarians Conference 1999
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ABSTRACT

To provide better medical care and improve husbandry techniques, a brief review of curassow ecology,[1] husbandry,[2] and screening of curassow medical and necropsy records from the Houston Zoological Gardens (HZG) was conducted. The Houston Zoo has housed over 230 curassows of 10 various species since 1973 from which the records were reviewed.

Curassows are in the family Cracidae, a primitive bird group in the order Galliformes. It is a long-lived (20+ yr), arboreal gallinaceous bird group found in the Central and South American tropics and subtropics. The family Cracidae contains approximately 13 curassow species (Table 1), Chachalacas, and Guans. Curassows are fowl-like with strong legs and feet, ample tail and wings, and a well-developed hind toe used to grasp branches. They are primarily vegetarians with a muscular gizzard which can grind hard seeds and nuts as well as fruit, greens, insects, and invertebrates. Due to the muscularity of the ventriculus, curassows tend to swallow large amounts of small pebbles or gravel. Curassows are the only group of the Cracidae family that have a developed crop. Male birds are usually larger than the females and both sexes are vocal with a well-developed syrinx. Certain species of male curassows: *Nothocrax urumutum*, *Crax globulosa*, *C. pauxi*, and *C. mitu* have an elongated trachea, used in vocalization for increased loudness or low pitch sounds. The trachea extends under the skin, and in some species overlays the abdomen, then curves back around and enters the thoracic inlet. Some curassow species have a feathered crest on the top of the head. Curassows' natural enemies include predatory birds, mammals, and man.

Table 1. Curassow taxonomy (genus and species vary slightly with different authorities)[3]

Genus/species	Common name	Genus/species	Common name
Crax alberti	Blue-knobbed	*Crax pauxi*	Northern-helmeted
Crax alector	Black	*Crax rubra*	Great
Crax blumenbachii	Red-billed	*Crax salvini*	Salvin's
Crax daubentoni	Yellow-knobbed	*Crax tormentosa*	Crestless razor-billed
Crax fasciolata	Bare-faced	*Crax unicornis*	Southern-helmeted
Crax globulosa	Wattled	*Nothocrax urumutum*	Nocturnal
Crax mitu	Razor-billed		

Table 2. Representative hematology and plasma biochemistry values of the curassow (Crax globulosa) from International Species Information System (ISIS)[3] and the Houston Zoological Gardens (HZG) in-house analysis

Parameter	Units	ISIS			HZG		
		x	1 S.D.	N	x	1 S.D.	N
WBC	10^3/µl	22.4	13.8	48	20.9	14.3	36
RBC	10^6/µl	3.25	0.35	31	3.23	0.35	34
HGB	g/dl	15.5	2.5	34	15.2	2.0	34
HCT	%	43.5	5.5	47	42.0	4.4	37
MCV	fl	131.8	13.7	31	131.9	13.1	34
MCH	pg	47.3	5.2	30	47.4	5.3	33
MCHC	g/dl	36.6	4.6	33	36.0	3.8	34
Heterophils	10^3/µl	5.1	5.7	47	4.5	4.1	36
Lymphocytes	10^3/µl	14.5	12.2	47	12.6	11.9	36
Monocytes	10^3/µl	1.6	1.8	39	1.7	1.8	34
Eosinophils	10^3/µl	0.7	0.7	37	0.5	0.4	28
Basophils	10^3/µl	0.9	0.6	41	1.0	0.6	34
Plasma protein	g/dl				4.8	1.2	22
Glucose	mg/dl	306	45	46	309	47	34
BUN	mg/dl	3	1.0	40	3.5	0.9	31
Creatinine	mg/dl	0.3	0.1	9	0.3	0.1	10

Uric acid	mg/dl	9.8	3.2	46	10.0	3.6	33
Calcium	mg/dl	11.6	1.2	46	11.8	1.2	32
Phosphorus	mg/dl	6.9	1.6	14	9.0		1
Sodium	mEq/L	162	8	21	161	5	5
Potassium	mEq/L	4.0	1.2	21	4.3	1.5	5
Chloride	mEq/L	117	4	15			
Iron	µg/dl	229	36	4			
Cholesterol	mg/dl	179	34	42	170	31	32
Triglyceride	mg/dl	120	66	34	132	71	32
Total protein	g/dl	4.0	0.5	45	4.0	0.7	32
Albumin	g/dl	1.7	0.4	16	1.5		1
Globulin	g/dl	3.9	5.6	16	3.1		1
AST (SGOT)	IU/L	35	15	43	34	13.6	32
ALT (SGPT)	IU/L	13	7	41	14	6.5	30
T. bilirubin	mg/dl	0.3	0.2	25	0.3	0.1	19
Alk. Phos	IU/L	263	214	44	214	153	33
LDH	IU/L	378	158	8			
CPK	IU/L	1718	694	14	1026	321	3
CO_2	mmol/L	13.7	3.2	6			
GGT	IU/L	5	5	4			

Curassows are generally monogamous and occur in pairs, although trios (cock and two hens) or family groups can be found. Males have an intromittent organ, which can be used to sex young birds. Adult birds are sexually dimorphic, with the males being larger in size than females and in many species the males have a large knob or wattle on the cere. The female lays and broods two eggs, incubation lasts approximately 29–32 days. Females can produce four clutches per year if the eggs are pulled for artificial incubation or domestic chicken brooding after the clutch is laid. Chicks are precocial, grasping and perching as soon as they are hatched, thus smaller perching should be provided. They are fed by both parents by offering foods in the beak, curassow parents do not regurgitate for their young.

Certain normal mannerisms of the curassow, if one is not aware of them, can lead to misdiagnosis of neurologic disease. Curassows have a tendency to flick their heads and present with a head tilt when anxious or nervous. They also will flick their tails up and down as well as pass the head over the shoulders and back.

Curassow pens should be fairly large and contain several perches for roosting due to the birds' body size and their arboreal nature. It is thought that curassows spend approximately one-half of their time perching above the ground. An enclosed section for protection from the cold and frostbite should be included. Males are territorial and two or more housed together tend to fight. The birds can be excessively aggressive during the breeding season and may even attack zoo visitors. Curassows may also be aggressive towards and can kill smaller birds and generally do not make a good species for free-flight pens.

In general, curassows are hardy birds and are not prone to disease. Because they are classified in the order Galliformes, it is felt that curassows are susceptible to most of the diseases affecting poultry such as reticuloendothelial virus, *Salmonella* spp., *Mycoplasma* spp., and *Chlamydia*. Very few infectious diseases have been diagnosed in live curassows at the HZG. Bacterial pododermatitis has affected some birds. Low numbers of endoparasites have been found and included ascarids, *Capillaria*, strongyles, *Strongyloides*, *Dispharynx*, *Heterakis*, and coccidia. Feather lice and mites have also been found on several birds.

Non-infectious diseases predominated in curassows presented for medical attention at the HZG. The birds often are found to have general clinical signs such as debilitation, emaciation, weight loss, abnormal behavior, lethargy, lameness, and occasionally moribund. Trauma was the medical problem most commonly diagnosed for the following reasons: cagemate aggression, parental trauma to young, self-mutilation (rubbing), restraint, and incompatible neighboring species. Fractures, of toes, legs, and wings, and integument lacerations and tears were common. Other integument problems consisted of overgrown beak, toenail trauma, and uropygial impaction. Curassows are susceptible to frostbite when temperatures approach the low 40s (Fahrenheit) or lower. Curassows also have a tendency to pick objects off the ground, thus there have been several cases of zinc toxicosis in captive zoo birds but only rare instances of intestinal obstruction. Reproduction problems were also commonly found in curassow hens due to their large egg size and included eggshell retention, egg binding, and cloacal prolapse. Intromittent organ prolapse and infection was seen in one adult male. Curassow chicks greater than 1 day of age generally have few problems at HZG, but rotational leg deformities were found in chicks that did not have good perching material supplied after hatching. Many chicks had problems with poor or abnormal hatching.

Diagnoses of necropsies performed at the HZG reflected the clinical signs and diagnoses found in live birds. Forty-two complete necropsy reports of approximately 60 available were reviewed and diagnoses recorded. Necropsy results not included were those that were incomplete or the diagnoses were not confirmed by histologic review. Diseases affecting multiple organs were peritonitis, primarily due to egg yolk contamination, and septicemia. Digestive tract diagnoses included enteritis, colitis, and hepatitis. Respiratory lesions found were pneumonia and aspiration (especially in newly hatched or pre-hatched chicks), bronchitis, and aspergillosis. Reproductive diseases of hens were similar to those in the live birds such as egg binding, salpingitis, metritis; one ovarian granuloma was found. Histologic lesions often were not found in chicks, many appeared to die during hatching, sometimes associated with abnormal positioning. Histologically, omphalitis and yolk sacculitis predominated. The HZG has seen necropsy lesions in several curassows that are typically found in birds infected with reticuloendothelial virus (REV) such as lymphoid leukosis, lymphoma, and lymphoreticular disease. Reticuloendothelial virus infection was not confirmed in any of these cases, as most were diagnosed histologically before REV PCR testing was available. Other neoplasias found were intestinal carcinoma and adenocarcinoma. Non-infectious, gross necropsy lesions from birds that were euthanatized due to poor prognosis or had died included hypothermia, frostbite, trauma, and musculoskeletal deformities and malformations (rotational deformities, fractures, scoliosis, slipped tendons, bumblefoot, myopathy).

In conclusion, curassows are large, unusual tropical gallinaceous birds that are not hard to keep and maintain in a zoological setting. The species is susceptible to many diseases, but with good quarantine, disease screening protocols and husbandry procedures, most diseases found can be prevented or treated.

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 # Moderation of Alarm and Flight Responses in Pronghorn (*Antilocapra americana*) Administered Zuclopenthixol Acetate

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Moderation of Alarm and Flight Responses in Pronghorn (*Antilocapra americana*) Administered Zuclopenthixol Acetate
American Association of Zoo Veterinarians Conference 2005

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Abstract

Zuclopenthixol acetate (ZA) was administered to hand-raised and trained pronghorn (*Antilocapra americana*) to evaluate the effect of ZA on flight and alarm behavior. Baseline observations were made when the pronghorn were 7–9 mo (30–34 kg) to rank their level of sedation, food and water consumption, locomotion, fearfulness, tendency to approach people, tendency to approach novel items, and tendency to associate with other pronghorn (social reinstatement). Pronghorn were administered ZA 1 mg/kg i.m. using the “Z” technique. The “Z” technique entails applying tension to the skin prior to injection, and subsequently releasing this tension after injection. This results in intact skin covering the i.m. injection site, such that drug cannot leak from the injection site. After administration of ZA, pronghorn were regularly re-evaluated over a 5-day period. In addition, the pronghorn’s responses were evaluated once daily during the 5-day period when they were exposed to novel objects that were intended to incite a mild flight and alarm response. Mild sedation, changes in locomotion, and decreases in food consumption were initially observed, but soon resolved. Treated animals had decreased flight distances and alarm responses. This trial suggests that ZA has some potential for moderating flight and fear responses for some purposes, but there was variability among individuals, and ZA was not a replacement for training or basic management procedures. Further work is needed to evaluate alternate dosages, age-specific variations in dosages, long-acting decanoate formulations of ZA, the efficacy of ZA combined with other neuroleptics, and the potential for moderating undesirable aggression, sexual, and self-mutilation behaviors.

Multiceps Cyst in a Domestic Born Chimpanzee
American Association of Zoo Veterinarians Conference 1987

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Multiceps serialis and other larval cestode cysts have regularly been reported in many species of wild caught monkeys and apes, but no cysts have been documented in USA born non-human primates. Carnivores are the final host for *Multiceps serialis*. A coenurus (cyst) is acquired by ingestion of fecal contaminated material by an intermediate host such as a rodent, lagomorph, or primate. Intramuscular cysts are most commonly found and they pose little risk to the infected individual. The rare coenurus in the eye, brain, liver, or peritoneum can, however, pose a significant health risk.

A four-year-old male chimpanzee was noted to have a swelling in the mid-thigh region. Aseptic aspiration of the lesion produced a clear liquid with no growth on aerobic or anaerobic cultures and no cellular debris in the stained centrifuged sediment. Surgical exploration revealed a two centimeter cyst which was removed. The histopathologic diagnosis was larval cestode coenurus most consistent with *Taenia* (*Multiceps*) *serialis*. No other cysts were noted at the time of surgery and none have developed in this male during a five year follow-up period.

This chimpanzee was born in an indoor breeding colony where animals are housed in large pens with cement floors. Carnivores did not have access to this indoor facility. A variety of fruits, vegetables, and grains were utilized in the diet depending on seasonal availability. These foods were acquired from local supermarkets and feed dealers. Fruits and vegetables were washed and peeled prior to use but were not cooked. Popcorn and grain were broadcast on the floor to encourage foraging. Portions of other foods were also retrieved from the floor after being removed from the feed pens and dropped. Local straw was used as bedding. Dirty bedding material was removed multiple times a day. Bedding was not disinfected prior to use because autoclaving and other methods were not considered practical. Baled straw is not a homogeneous product. Many bits of debris may be commonly noted. It is likely that the cestode ovum was ingested while the animal was foraging in the straw. This is the only instance where a cestode cyst was documented in this colony of more than 50 individuals during its eighteen-year existence.

A number of institutions feed local produce and use straw or similar bedding material for non-human primates and other animals. The psychological benefits of an enriched environment are clear. Time spent foraging decreases aggression. This one incident serves as a reminder that there is a small risk associated with the use of unprocessed foods and non-sterilized bedding material. To date the benefits of stimulating normal foraging or nesting behavior far outweigh the slight risk of acquiring a cestode cyst.

Operant Conditioning of Diabetic Primates to Accept Insulin Injections
American Association of Zoo Veterinarians Conference 1998
Cynthia E. Stringfield, DVM; Jennifer K. McNary
Los Angeles Zoo, Los Angeles, CA, USA

Introduction

Diabetes can affect a wide variety of primates.[1] At the Los Angeles Zoo, we currently have two cases of diabetic primates that have been or are in the process of being trained, using operant conditioning methods, to accept insulin injections without any type of manual restraint.

Case Reports

“David,” a red-tailed moustached guenon (*Cercopithecus cephus cephus*), was found to be diabetic in May of 1997 after a routine preventive medicine exam. This animal was wild caught and estimated to be 24 years of age. The animal lived with two other animals, and when its diet was evaluated, it was determined that this guenon was eating primarily the grapes and bananas. The diet was altered; however, the keeper had difficulty getting the animal to eat other items in the exhibit environment. After three months of no improvement on an oral hypoglycemic agent, the guenon was brought to the health center to live in a large squeeze cage and undergo intensive training. According to its keepers, the guenon was very aggressive to people and other animals and “didn’t like anybody.” This monkey was high-strung, suspicious, cautious, and reacted quickly and instinctually. Operant conditioning was started, and the animal worked with one person for two sessions a day. A clicker and colored target were used with food rewards being given for the proper response. Diet was drastically altered to increase fiber and eliminate sugar and was accepted readily. This diet was used during training, then the remainder given after the training session. This initial training allowed the animal to become comfortable with the trainer and learn what was expected and how to successfully respond. Within two months it was expert at stationing and putting its arm through the bars to touch the target. The animal never became comfortable having its arm held or manipulated and would retreat when its arm was handled. However, when it would approach in a less formal manner, it became apparent that the animal liked to present by laying down with its back facing its trainer in a submissive manner. The animal would allow its back and other parts of its body to be scratched. Training was then altered to have the animal present in this manner. The animal was moved to a double dog run-type chain-link outdoor enclosure. Training rapidly progressed within another two months, from scratching its back, to pinching the skin, to poking with a needle, to administering a small amount of cold saline SC, to administering insulin. The animal is currently in the process of being regulated and since the animal does not allow blood collection, it is monitored via urine analysis for glucose. The next step will be to return the animal to the exhibit and work with it in the back holding area there.

“Tule,” an 18-year-old DeBrazza guenon, was being treated with prednisone for inflammatory bowel disease. Glucose and ketones were present in the animal’s urine; it was taken off the prednisone and then re-evaluated in November of 1997. The animal was severely compromised and diagnosed as a diabetic that needed immediate insulin therapy. (The animal was later diagnosed with Cushing’s disease as well.) The guenon was brought to the health center, housed in a large squeeze cage and given twice-daily insulin injections in the tail or rump by veterinary personnel with the use of the squeeze. Training was instituted in a similar manner as outlined above with the red-tailed moustached guenon; however, the initial goal was solely to get the animal to relax and provide it a positive experience with a person. The training was done at a separate time and by a different person so as not to associate the negative experience of being squeezed and getting injections with training. Initially, this animal was very ill and stressed but as it began to relax and its health improved, the training progressed to involve more touching and handling. The next step was to incorporate the injections. Progress was made very rapidly at this point; to date the animal allows injections with minimal squeezing and much less stress. This was an especially challenging case due to the animal’s medical condition necessitating treatment with restraint while simultaneously undergoing training.

Conclusions

These cases demonstrate that diabetic primates can be managed successfully and without stress with injectable insulin therapy long-term. The training required differs depending on the species and temperament of the animal. The animal gives the trainer cues as to what is the most comfortable and least threatening way to give the injections, and the manner of treatment and monitoring can then be tailor fit for the animal and its living environment.

Acknowledgments

The author would like to thank and commend the animal care and veterinary staff involved for their intense efforts, patience and perseverance that resulted in such positive outcomes for these animals.

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Ostrich Castration for Behavioral Control
American Association of Zoo Veterinarians Conference 1987
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ABSTRACT

A surgical technique was developed to caponize or castrate aggressive male ostriches whose territorial behavior was dangerous to keepers and the viewing public. The anesthetic management involved manual capture using physical and behavioral (darkness) restraint while inducing with ketamine at approximately 5 mg/lb. Maintenance of these patients, whose weights varied from 150 to 400 pounds was accomplished with high flow rates of oxygen and concentrations of Halothane ranging from 4 to over 6 percent.

On large mature birds a surgical approach through an incision behind the last rib allowed removal of one testicle from either side. Later a technique was developed to remove both testicles from a single left lateral approach on young birds whose sex was not yet apparent from plumage differences. Small hands facilitated the surgery, especially when removing both gonads from one side. Castration in early spring is recommended as the onset of the breeding season increases testicular size making location easier. Waiting until peak gonadal development may increase the risk of hemorrhage as the testicular blood supply is not ligated in this procedure. The gonads can be palpated and removed using blunt dissection with the fingers although use of a fiberoptics unit would assure visualization and removal of the appropriate tissue. The incision is closed in three layers using 0 or 00 absorbable suture. Some minor problems such as subcutaneous emphysema around the site of the skin incision were experienced and one bird tore out most of the sutures during a rough anesthetic recovery and later died of peritonitis. The majority of birds castrated recovered uneventfully.

The procedure permanently reversed the aggressive behavioral changes brought on by the breeding season. There were no negative long-term side effects related to castration. This procedure appears to be a reasonably safe means of creating a compatible and safe non-breeding exhibit.

 # Pharmacokinetics of Deslorelin Acetate Implants and Fecal Hormone Monitoring in the Domestic Goat (*Capra hircus*)

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Pharmacokinetics of Deslorelin Acetate Implants and Fecal Hormone Monitoring in the Domestic Goat (*Capra hircus*)
American Association of Zoo Veterinarians Conference 2022

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Abstract

Management of zoological species relies on effective and reliable contraception. Deslorelin acetate implants[a] are routinely used as a contraceptive tool and to mitigate hormonally-based undesirable behaviors. Since this product was designed for use in dogs, the minimal effective dose and duration of action must be extrapolated to other taxa. Current dose recommendations are based on clinical effect and accumulated data on usage in various taxa.[1–6] The authors developed and validated a novel liquid chromatography-tandem mass spectrometry assay to measure deslorelin in serum. A pilot study evaluated the pharmacokinetics of deslorelin implants *in vivo* in domestic goats (*Capra hircus*). A single 9.4 mg deslorelin acetate implant was placed subcutaneously in three adult, intact female goats. Serum samples were analyzed at baseline and 16 designated timepoints (15 minutes to 14 days) following implantation. Preliminary results indicate that the maximum plasma concentration (C_{max}) for deslorelin was 365.9 ppb (ng/ml), time to C_{max} (t_{max}) at 1 hour, and a plateau phase extended from 24 hours (mean 23.2 ppb) through 14 days; the lowest concentration was at 14 days (mean 4.2 ppb). The minimum effective concentration for contraception is unknown. Fecal samples are being assayed for estrogen and progestagen to determine whether production of gonadal steroid decreased after deslorelin placement. This study demonstrated successful measurement of deslorelin *in vivo* to the level of ppb. These results provide initial data that may be extrapolated to other ruminants. Our novel assay will lay the foundation for future studies regarding dosage and frequency of deslorelin implants in other species.

[a]Suprelorin12, Virbac (Australia) Pty Limited, 361 Horsley Road, Milperra NSW 2214, Australia

Acknowledgments

This study was funded by the AZA Reproductive Management Center at the Saint Louis Zoo, which provided the deslorelin acetate implants and performed the fecal hormone testing. The Diagnostic Laboratory at Michigan State University College of Veterinary Medicine developed the assay and performed subsequent testing. The authors thank the zookeepers and veterinary technicians at the Binder Park Zoo and the Potter Park Zoo for their assistance in sample collection and processing.

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Search Result #38: **Pharmacokinetics of Oral Carprofen in the California Sea Lion (*Zalophus californianus*)**

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Author(s): Christopher Dold, DVM; Martin Haulena, DVM, MsSc; Frances M.D. Gulland, VetMB, PhD
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Pharmacokinetics of Oral Carprofen in the California Sea Lion (*Zalophus californianus*)
American Association of Zoo Veterinarians Conference 2004
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ABSTRACT

Racemic carprofen (Rimadyl™ Pfizer) is a veterinary non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class that includes ibuprofen, naproxen, ketoprofen, and vedaprofen.[9] It is licensed in the United States for use in dogs to help control inflammation and pain associated with surgery and osteoarthritis.[5,12] Forms of the drug have been used in other domestic species, including cattle,[7] horses,[6] cats,[11] and rats[10]. Ketoprofen has been used to good effect in Asian elephants (*Elephas maximus*),[4] llamas,[8] and camels[1]. There is a growing precedent for the off-label use of carprofen in California sea lions (*Zalophus californianus*; W. Van Bonn, personal communication),[2] and sea otters (*Enhydra lutris*)[3]. However, little is known about the use of carprofen in California sea lions and no controlled study that describes the pharmacokinetics or clinical effectiveness of analgesics and/or NSAIDs in pinnipeds has been performed to date. Understanding the pharmacokinetics of a drug can improve the likelihood of establishing dose parameters that will allow the practitioner to alleviate pain and reduce inflammation, while minimizing untoward side effects. Improved pain control is necessary as we continue to develop and improve the comprehensive medical and surgical care of sea lions in rehabilitation and display facilities.

California sea lions (n=10) with traumatic injuries, osteoarthritis, pneumonia, or keratitis resulting in blepharospasm that were eating on their own, appeared to be of normal hydration status, and that during rehabilitation would have received analgesic/anti-inflammatory therapy for their disease, were entered into the study. Study animals received an admit examination including a comprehensive physical exam, complete blood count (CBC) and serum chemistry analysis, and a pre-drug heparinized plasma sample. Those animals were then started on a treatment course of carprofen at the recommended canine dose of 3–4 mg/kg orally once daily for 5 days. Study animals were randomly assigned to two of ten possible time points (0.25 and 0.5, 1, 1.5, 2, 3, 4, 5, 8, 12 h) for post-drug heparinized plasma collection on the first day of carprofen treatment. These time points were then summarized to reconstruct a drug elimination curve. Heparinized plasma, a CBC and serum chemistries were also collected on day five of treatment and again five days later. Plasma concentrations of carprofen were determined by high-performance liquid chromatography. Hematology and serum chemistries were assessed for significant changes during and after treatment. Daily clinical assessments (SOAPs) were made to document any improvement (or lack thereof) in the animals' condition. Specific attention was paid to lameness exams, mobility and activity, appetite, and interaction with pen mates, to subjectively determine analgesic efficacy.

The maximum plasma concentration, elimination half-life, and systemic availability of carprofen were determined. No adverse changes that could be correlated with carprofen administration were found on hematology or serum chemistries. There were no documented clinical deleterious side effects associated with drug administration. All study animals continued to eat and interact with pen mates. Animals with trauma or osteoarthritis-associated lameness showed improved mobility and there was documented reduction in blepharospasm in those study animals with corneal disease.

These data suggest that racemic carprofen is an acceptable drug to use for the alleviation of pain and inflammation associated with trauma, osteoarthritis, and corneal disease in California sea lions. The authors caution that the use of this drug in sea lions is considered “off-label”, and while there were no deleterious side effects seen in this study, some have been reported in other species.[11]

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Pituitary Neoplastic Disease in Nine Budgies
American Association of Zoo Veterinarians Conference 1987
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The pituitary adenoma is a relatively common tumour in the budgie and may cause a wide variety of interesting clinical signs. Behavior changes, endocrine disorders, and signs directly related to a space-occupying lesion have all been reported. Unfortunately, this neoplasm tends to affect young budgies, and little is known about treatment. Findings in a group of recently affected birds are documented here to assist the avian practitioner with early diagnosis.

Records from the Airdrie Veterinary Laboratory (Agricultural Regional Center) and the Calgary Caged Pet Clinic were searched for examples of pituitary neoplasia. Nine cases from 1986 are detailed in the following case report and summary.

Case Report

A three-year-old male budgie was presented to the clinic for dyspnea and “diarrhea.” The owner reported that both signs had been present for about one week. At the time of presentation, the droppings consisted of a liquid stool and a large volume of urine. Water consumption was estimated by the owner to be over 30 ml per day. Respiratory rate was increased, and the bird was inactive and fluffed. No nasal discharge was present, and the eyes were only partially open. Upon touching the bird (tame), loud prolonged vocalization occurred. Physical exam showed a bird in moderate condition (32 grams) with mild asymmetrical exophthalmos and pupils fixed and dilated (little or no response to light). Feathers were in poor condition with some hypopigmentation on the chest. CBC revealed a marked leukocytosis (WBC) 110,000: 77% heterophils, 22% lymphs. The bird died shortly after being admitted to the hospital.

Gross necropsy found that the bird was actually a female (despite blue cere) and that thyroids and liver were enlarged; the liver contained diffuse pale areas. Lungs and pituitary were not obviously abnormal on gross. *E. coli* and *Pseudomonas* were recovered from the liver on culture, and histology showed a focal hepatitis with bacterial colonies. Thyroid dysplasia and hyperplasia were seen in addition to a partially encapsulated mass in the region of the pituitary. Cells with large nuclei and abundant pale eosinophilic cytoplasm were found arranged in nests, with some smaller basophilic cells also present and a few mitotic figures. The mass was well vascularized, and the diagnosis was pituitary adenoma (plus thyroid and liver abnormalities).

Nine (consecutive) cases were studied in total. Two were from one household (unrelated cage mates). Mean age was 2.0 years. The range was six months to four years, and six of the nine birds were male. Presenting complaints included dyspnea (two birds), abnormal droppings (three birds), and depression/somnolence (four birds). All were found to have mydriasis, most of the birds showing no pupillary light response. Owners were usually not aware that the birds had a visual deficit. Polyuria was frequently confused with diarrhea. Polyuria was seen in four of the nine birds, and exophthalmos was also in four of the nine birds. Almost all of these budgies “over-reacted” to handling, with much squawking and struggling. Reactions were often so characteristic as to make us immediately look for mydriasis. Typical nervous signs such as head tilt/circling, head pressing, and seizures were seen in less than half the birds. Some may have been euthanized before the disease progressed that far. Clinical pathology wasn’t particularly helpful, except for the budgie that was described in the case report. White counts ranged from 8,000 to 14,000. None of the birds looked at in this study were obese, but this has been documented in other reports.[1] At least two of the budgies showed thyroid abnormalities, but this is relatively common in our area, and the exact significance is unknown.

Some of the birds undoubtedly had clinical signs for several months before presentation. Polyuria seemed to be the most consistent early sign. Budgies manage so well in their own cage even when visually impaired that it would probably be hard for the owner to be sure when blindness occurred. However, none of the birds survived long after diagnosis; three weeks being the maximum.

Gross and histopathologic appearance of the tumours varied, and four of the neoplasms were not even visible on gross examination. The brains were either fixed in formalin after the dorsal cranium was removed, or the palate was cut away to reach the sella turcica. In any event, the brains were sometimes not disturbed too much before histological examination to avoid destroying any tissue. However, a few of the tumours were quite large, one being 7×5 mm (large can be a relative thing in the budgie). At least two of the masses had a high mitotic index and must technically be called adenocarcinomas. These masses had an invasive perimeter and were very vascular. Traditionally, veterinary literature on this disease will refer to it as pituitary adenoma or pituitary chromophobe adenoma. No metastases were found in these nine budgies.

Discussion

The pituitary gland sits in a critical location and is responsible for a number of complex endocrine functions, so it is not surprising that a wide range of clinical signs may be seen when dysfunction occurs. The avian pituitary produces LH; FSH; TSH; a growth hormone, prolactin (pigeons); as well as ACTH and melanin-secreting hormone.[2]

The case history mentioned here showed a variety of endocrine abnormalities that may have been related to the neoplastic condition. Signs that might be seen in Cushing’s disease (polyuria), sex hormonal alterations (cere colour inappropriate), and hypothyroidism (feather changes) were all noted. Blindness was also an important component of the disease in these nine budgies (blindness is to pituitary adenoma what lameness is to renal adenoma). Partial or complete loss of vision results when the mass either invades or puts pressure on the optic chiasma. Blindness probably produced the pronounced startle reaction that was typical. True behavioral changes are also possible with an invasive brain tumour; somnolence could be related to this, to thyroid dysfunction, or simply to depression as seen in any serious illness.

Pituitary neoplasms in the dog may produce changes in mental state that include aggression, rage, hyperexcitability, disorientation, coma, and abnormal appetite.[2] Blindness is not as common. Like the budgie, they also tend to have polyuria. This is produced by one of two mechanisms: insufficient ADH release or increased GFR due to high glucocorticoid levels. Only one bird in this study showed actual feather loss that might be expected with classical Cushing’s disease. The use of op’DDD (Lysodren, a distant relative of DDT) is not recommended as it affects only the adrenal cortex, and the space-occupying or invasive effects of these tumours in the budgie are more serious than the hormonal problems. Steroidal chemotherapeutic agents, such as prednisolone, are also not helpful because glucocorticoid levels are already high. Hypophysectomy in the budgie is not practical because of small size and limited access.

Young budgies presented for polyuria/diarrhea that show unexpected or unusual behavior should have a careful eye examination. Early diagnosis can at least avoid inappropriate drug usage, prevent unnecessary suffering, and provide a realistic prognosis.

Acknowledgments

The author would like to thank the Airdrie Veterinary Laboratory for their interest in caged bird pathology and help with these cases, and Dr. Kerry Korber of the Calgary Caged Pet Clinic for valuable follow-up.

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Preliminary Results of a Cabergoline Trial in Captive Elephants with Hyperprolactinemia
American Association of Zoo Veterinarians Conference 2006
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Abstract Introduction

An Asian elephant (*Elephas maximus*) at Busch Gardens Tampa Bay (BGT) was diagnosed with hyperprolactinemia with a persistently elevated serum prolactin concentration greater than 15 ng/ml, by the Conservation and Research Center (CRC) laboratory in January 1996. She also had a number of other problems including uterine disorders, that resulted in consistently elevated progesterone. In March 2002 she was given cabergoline orally at a dose of 1 mg twice weekly PO for six months. Cabergoline is a long-acting dopamine receptor agonist with a high affinity for D2 receptors. It exerts a direct inhibitory effect on the secretion of prolactin. Cabergoline (Dostinex®, Pfizer Inc. Kalamazoo, MI) was purchased from a local pharmacy. Serum prolactin concentrations declined almost immediately after treatment initiation, followed about one month later by a drop in progesterone to baseline. Progesterone secretion remained low until November 2002 when she resumed cycling based on the observation of a normal luteal phase based on serum progesterone profile. From November 2002 through January 2004, she exhibited four normal estrous cycles. Prolactin secretion also remained within the normal range for elephants[1] over one year after treatment withdrawal. This female suffered no adverse effects due to the cabergoline treatment. There were no behavioral changes noted or changes in appetite. Given the need to increase reproductive rates of African elephants (*Loxodonta africana*) to prevent captive extinction, it might be efficacious to treat genetically valuable females with cabergoline in the hope it will reinitiate reproductive cyclicity. Nearly 1/3 of African elephants with hormone data are not cycling normally, and in an earlier study 1/3 of these (11 of 30) were found to have increased serum prolactin levels.[1]

Methods and Materials

A clinical trial was undertaken with six captive African elephant females that were identified as good candidates for a cabergoline treatment study (i.e., they are acyclic and had mean prolactin concentrations of >15 ng/ml). The treatment consisted of 1 mg cabergoline given twice weekly PO for six months. Serum was banked and then analyzed at the CRC for progesterone and prolactin.[1] All elephants were thought to be otherwise healthy. Because prolactin is known to be an inflammatory marker,[4] all candidates were required to have a negative lateral flow immunochromatography (rapid test) and multiple antigen immunoassay (MAPIA) for *Mycobacteria tuberculosis*.[5]

Results

A summary of the results is given in Table 1. The treatment period is complete for three elephants, all of which showed a decrease in prolactin levels. Elephant 1 showed a good response while on treatment but did not cycle and serum prolactin has subsequently risen to pretreatment levels. Increasing the dose in elephant 2 and 3 reduced prolactin to baseline levels but again, did not result in a return to ovarian cyclicity. Elephant 4 was taken off the study after only a few doses due to increased aggressive behaviors. This is believed to be due to changes in the group social dynamics and not related to the cabergoline, as this behavior has continued after withdrawal of the drug. Based on these findings, the two newest candidates (elephant 5 and 6) with very high prolactin concentrations, have been placed on 2 mg/twice weekly for one year pending continuation of this project.

Table 1. Treatment dates, doses, and responses to cabergoline treatment in captive elephants

Elephant number	Dates of treatment	Dose	Response
1	2/2005–1/2006	1 mg (2x/week)	Prl[a] averaged ~15 ng/ml. After treatment prl declined to normal baseline (~6 ng/ml) until 9/05 and now has returned to slightly elevated concentrations (~13 ng/ml). No change in cyclicity status.
2	6/2004–2/2005	1 mg (2x/week)	Prl averaged ~30 ng/ml but had started to decline before treatment. During treatment, prl averaged ~10 ng/ml, with occasional spikes of 20–50 ng/ml. No resumption in cyclicity. Decided to increase dose.
	2/2005–Current	2 mg (2x/wk)	Prl decreased further to ~5 ng/ml from 2/17–4/27, but then surged for three weeks in May 2005, followed by now baseline levels (<10 ng/ml). No change in cyclicity status.
3	8/2004-12/16/2004	1 mg (2x/week)	Prl averaged ~40 ng/ml pretreatment, decreased to ~25 ng/ml, but still considered elevated and no change in cyclicity status, so increased the dose.
	12/17/2004–4/14/2005	2 mg (2x/week)	Within two weeks prl declined to normal baseline (<10 ng/ml) and remained low until treatment withdrawal. After two weeks prl started to rise, peaked at 70 ng/ml, and now remains elevated at ~30 ng/ml. No change in cyclicity status.
4	5/28/2005–6/14/2005	1 mg (2x/week)	Stopped after a couple of weeks due to aggressive behavioral change.
5	Pending		Variable prl, ranges from 20–80 ng/ml. Recommend 2 mg twice weekly for one year.
6	Pending		Very high average prl (off curve) >80 ng/ml. Recommend 2 mg twice weekly for one year.

[a]Serum prolactin.

Discussion

Normalization of prolactin levels facilitated the return of normal cycles in an Asian elephant, but none of the African elephants have resumed cycling so far. Thus, while the use of cabergoline shows promise in reducing elevated prolactin levels in both Asian and African elephants, other factors may need to be considered or a longer course at higher doses may be required, for treatment to be successful in reinitiating ovarian activity. The latter suggestion is supported by two of the animals (elephants 2 and 3) in this limited trial, in which a decline in prolactin occurred after the dose was increased. Understanding the etiology of hyperprolactinemia in elephants may also help in returning females to normal cycling. Relapse of hyperprolactinemia is more common in humans with micro- or macroprolactinomas.[2] Chronic estrogen stimulation is also known to increase prolactin levels.[3] A proposed pathophysiology is that elevated estrogen levels from persistent cycling will lead to elevated prolactin levels and acyclicity. A difference between the two species in the causes of and potential treatment options for hyperprolactinemia should also be evaluated more closely.

Acknowledgments

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Proactive Development of an Integrated Behavioral Husbandry Program in a Large Zoological Setting
American Association of Zoo Veterinarians Conference 2002

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Abstract

Introduction

Behavioral husbandry programs have become an essential part of animal management in zoos and aquaria. Enrichment and training are used to help meet the needs of the animals and improve animal care.[1,5,7] Training is useful in achieving daily husbandry tasks and has been applied to allow certain veterinary procedures. Since the early 1990s, a number of publications have outlined the use and benefits of enrichment on animal health and training for specific diagnostic and therapeutic purposes.[2-4,6-8] In many cases, these programs are created in response to a particular problem that has already occurred. When specific behavioral husbandry programs are instituted after the need arises, there is a delay in correcting the problem or the ability to perform the required procedures using operant conditioning and other training techniques.

Background Information

In April 1998, Disney's Animal Kingdom opened to the public. The creation of this new zoological park provided a unique opportunity to proactively design and implement a behavioral husbandry program along with the development of traditional animal care protocols. Hiring of keepers, animal managers/curators, veterinary, science, and behavioral husbandry staff began approximately 2 years before the opening of the park and arrival of many of the animals. The goal was to develop and implement a training and enrichment plan, in conjunction with husbandry and medical programs, for every animal in the collection. Due to the challenges of managing mixed species in large exhibits, training techniques (e.g., operant conditioning) are considered essential tools for moving, separating, introducing, and acclimating the animals to each other and their exhibit and holding areas. In addition, the goals include the ability to perform a wide range of husbandry and veterinary procedures identified for each species, and meet the physical, social, psychologic, and physiologic needs of the animals through appropriate enrichment and care methods.

Program Framework

In creating the behavioral husbandry program at Disney's Animal Kingdom, the expectation is that all teams (animal care, veterinary, education, and science) use a framework or process for developing and maintaining both enrichment and training plans for the animals. The program framework includes the following components: setting goals, planning, implementation, documentation, evaluation, and readjustment.[6,9] To focus time and resources, a list of behavioral priorities have been developed for each species. Identification of training goals and development of animal-specific plans are based on the following criteria: daily management needs, medical needs, natural history of the species, and individual's history. In addition, enrichment goals and plans incorporate knowledge of the species' and individual's physical, psychologic, and social needs.

Enrichment Program

Enrichment plans are proactively designed. Rather than identify a specific item or enrichment technique first, the enrichment program framework requires setting the goal of encouraging or providing opportunities to exhibit specific species-appropriate behaviors and then identifying enrichment initiatives that can be used to achieve those goals.[6] After planning, approval is required by the zoological manager and behavioral husbandry staff along with input from the veterinary and animal nutrition staff before implementation occurs. An enrichment calendar is created and responses to the specific enrichment initiatives are recorded and reviewed to determine if the goals have been reached (see www.csew.com/enrich/ for examples of forms used). (VIN editor: Original link not accessible 2–16–2021). Adjustments are made on a routine basis. Food items used for enrichment are considered part of the animals' regular diet and evaluated for their nutritional contribution as well as their enrichment value.

Training Program

Although a training plan is designed for each species in the collection, selected species or groups are identified by the veterinary, animal care, and behavioral husbandry staff as high priority species for training to minimize the requirement for immobilization. At Disney's Animal Kingdom, these species are elephants, rhinoceros, giraffe, hippopotamus, and okapi. Veterinary procedures are identified that could be performed using training techniques with or without the use of restraint devices. Examples include physical examination, blood collection, ultrasonography, injections (for drug or vaccine administration), minor wound treatment, and foot/hoof care.

Keepers and managers use the same framework (i.e., setting goals, planning, implementation, documentation, evaluation, and readjustment) with regard to creating training plans. Successful planning and implementation requires active participation and support by all teams (Table 1). When training for a veterinary procedure, the veterinary staff begins by explaining the procedure and describing each step to be performed (i.e., equipment used, requirements for positioning, area of animal that will be touched, potentially stressful, or painful stimuli). Veterinarians help prioritize the behaviors included in the plan for the species. In addition, veterinarians and veterinary technicians attend training sessions on a regular basis to provide feedback during the shaping of the behaviors and allow the animal to acclimate to the presence of less familiar staff members.

Table 1. Disney's Animal Kingdom animal training: philosophy and expectations

1	Safety is always our first consideration in any training initiative (i.e., animal safe, keeper safe, equipment safe, process safe).
2	All keepers and zoological managers are expected to understand and articulate the animal training philosophy that was taught in training methods class. All keepers are expected to be able to articulate and apply animal training techniques to achieve training goals as outlined by their area team.
3	There is no separation between animal training and animal management. All keepers/zoological managers are trainers; all trainers are keepers/zoological managers.
4	Training is one of the many animal management tools that we use to facilitate good animal care. Many of the behaviors trained are meant specifically to facilitate medical care, often allowing us to avoid immobilizing/physically restraining an animal for treatment. The choice of immobilization/restraint versus training will be based upon the amount of time needed to train, the severity/urgency of the illness/injury, and the benefit to the animal. Sometimes it will not be possible to use training techniques during a particular husbandry/medical procedure and various levels of restraint or immobilization will be necessary.
5	A successful training program should be proactive, not reactive. In other words, planning is an important part of a successful training program.
6	Keepers should routinely review past training records for patterns. For example, training records can be used to assess routine causes of periodic aggression, or identify differences in relative success in training various behaviors. Keepers can use these past records to predict situations that may be precursors to breakdown in trained behaviors. Zoological managers should periodically ask keepers if these reviews have been completed.
7	All keepers are expected to learn about the natural and individual history of the animals that they care for and train. When training, keepers need to assess and understand how the animal's natural history and individual history affect that animal during the training process. Zoological managers should make sure that keepers have and use this knowledge.

To ensure consistency among the animal care staff, the behavioral husbandry team provides an Introductory Training Methods class and on-the-job training. Currently that team is in

the process of developing additional opportunities to develop technical skills using other species. Specifically, a colony of rats will be maintained for staff to use in practicing a variety of training techniques. Dedicated behavioral husbandry managers and specially trained zoological managers oversee the implementation and provide one-on-one mentoring.

As with enrichment, documentation is essential to evaluation and readjustment of a training plan. Records are written after every training session. Tracking of progress on trained behaviors are reviewed using the "Procedure Status Forms" for high priority species. Examples can be found on the training website (www.csew.com/training/). (VIN editor: Original link not accessible 2–19–2021). Husbandry training has routinely been applied to mammals, especially marine mammals, primates, and other megavertebrates.[5,8] However, the same techniques are readily applicable to ungulates, birds, reptiles, fish, and even some invertebrates. Realistic expectations for training species-appropriate behaviors should be created during the goal-setting step using knowledge of that animal's natural history, physical capabilities and temperament, and management logistics. A few examples of successful training include: training waterfowl to voluntarily enter crates, stationing of the Komodo dragons on a scale, shifting of crocodilians to holding areas using an audible cue, desensitization of white and black rhinoceros to rectal ultrasonography (either in a stall or chute), physical examination and blood collection from tigers and giraffe, open mouth behavior in multiple species for examination and drug administration (e.g., lions, hippos, primates), presentation for injection by hand (e.g., primates), and storks entering holding areas from exhibit on cue.

Additional information on training and enrichment programs is available at www.csew.com/training/ (VIN editor: Original link not accessible 2–19–2021). and www.csew.com/enrich/. (VIN editor: Original link not accessible 2–19–2021).

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Psychotropic Drug Use in Captive Wild Animals
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ABSTRACT

While a limited amount of data has been published regarding the use of the psychotropic drugs in animals commonly kept in zoo environments, that does not mean that the enormous amount of data that does exist regarding these drugs cannot be cautiously extrapolated to help improve the lives of zoo animals. The mammalian brain in particular is remarkably similar from taxon to taxon, so with a knowledge of the neurotransmitters that most affect behaviors and the drugs that most affect those neurotransmitters, appropriate drug choices can be made to assist in improving the welfare of some individuals. While drugs should never be expected to make up for a poor or inappropriate environment, they can be very helpful for animals that are exhibiting maladaptive or malfunctional behaviors regardless of the inciting cause.

INTRODUCTION

A minimal amount of peer-reviewed research data has been published on the use of psychotropic drugs in wild animals, and what has been published is mostly in the form of occasional case reports. However, many of these drugs have been in development for decades, and much research exists on their use in a variety of different species, including non-human primates. Veterinary behaviorists have used many of these drugs successfully in pets over the past 20 years by extrapolating what information we do have about their use in humans and laboratory animals. While much remains to be learned about the exact mechanism of these medications, the fact is that they do help improve the quality of life for many animals when used in a rational manner.

What is the most rational manner in which to use these medications? The first and probably most important thing we can do is to change our “mindset” about psychotropic drugs. We need to stop thinking of psychotropic drugs as something that we will use to “change behavior” but rather as a tool that can be used to help put an animal in a state of mind where it can learn. Most animals with problem behaviors are, for a variety of different reasons, experiencing some degree of anxiety or fear. The ability to learn can be seriously impaired when an animal is in a constant state of anxiety. Decreasing anxiety with medication gives us the opportunity to use behavior modification to teach animals alternative behavioral responses or use desensitization and/or classical conditioning to change their response to a particular fear, anxiety, or stress-inducing stimuli.

To ensure the greatest safety for an animal being prescribed a psychotropic drug, a complete blood count and serum chemistry profile should always be performed first. While evidence of the drugs causing organ dysfunction is rare, if an animal had a pre-existing condition that was not yet diagnosed, administration of the drugs could potentially exacerbate it.

NEUROTRANSMITTERS

Psychotropic drugs are believed to produce their behavioral effects due to their actions on different neurotransmitters in the central nervous system. The neurotransmitters that are particularly pertinent to behavior and behavioral problems are gamma-aminobutyric acid (GABA), glutamate, acetylcholine, norepinephrine (noradrenaline), dopamine, and serotonin.

GABA is an amino acid neurotransmitter that is synthesized from glutamate. GABA neurons are the major inhibitory neurotransmitter in the brain and are widely distributed throughout the central nervous system where they serve important regulatory functions associated with vigilance, anxiety, muscle tension, memory and epileptogenic activity. Benzodiazepines and barbiturates are examples of drugs that act on GABA neurons.

Acetylcholine is the most widely distributed neurotransmitter. Cholinergic neurons are excitatory neurons with pathways distributed throughout the central and peripheral nervous system. Muscarinic cholinergic synapses are found in smooth muscle, cardiac muscle, peripheral autonomic ganglia, and parasympathetic post-ganglionic synapses. Nicotinic cholinergic synapses are found at the neuromuscular junction. Blockade of muscarinic cholinergic receptors is responsible for atropine-like side effects of the antipsychotics and tricyclic antidepressants: dry mouth and eyes, urine retention, constipation, mydriasis, cardiogenic effects (tachycardia), and increased intraocular pressure.

The monoamine neurotransmitters (catecholamines and indoleamines) are related by their chemical structure. These neurotransmitters are concentrated within the hypothalamus, midbrain and limbic system and are stored within vesicles in the axons and nerve terminals. They are primarily inactivated by reuptake at the synaptic cleft, so drugs that block or inhibit their reuptake increase their availability and activity.

The catecholamine neurotransmitters include norepinephrine, epinephrine and dopamine. These neurotransmitters generally produce CNS stimulation. A large portion of the brain’s dopamine is located in the corpus striatum where it modulates the part of the extrapyramidal pathways concerned with coordinated motor activities. Dopamine levels are also high in some regions of the limbic system. Dopamine depletion or inactivation occurs as a result of administration of tranquilizers, neuroleptics or antipsychotics and leads to behavioral quieting, depression and extrapyramidal signs. Excess dopamine release is caused by administration of amphetamines, apomorphine or methylphenidate and has been associated with the development of stereotypies.

Norepinephrine is formed by the hydroxylation of dopamine. Centrally, norepinephrine is stimulating and is postulated to affect mood, the functional reward system and arousal. Peripherally, norepinephrine is the post-ganglionic neurotransmitter of the sympathetic nervous system. Excess noradrenergic activity has been associated with mania, while norepinephrine depletion is associated with depression.

The indoleamine neurotransmitters include serotonin, and melatonin. These neurotransmitters are synthesized from dietary tryptophan. Serotonin (also known as 5-hydroxytryptamine [5-HT]) receptors are found predominantly in the brain and act primarily in an inhibitory manner both pre- and post-synaptically. Different receptor subclasses are responsible for modulation of sleep/wake cycles, mood, and impulse control. 5-HT receptors are widely distributed throughout the brain, and much is still being learned about the far-reaching effects of this important neurotransmitter. There is growing supporting evidence for the role of serotonin in aggression. Impaired synthesis or metabolism of serotonin has repeatedly been found to be associated with increased aggression.[1,11,15] Dogs diagnosed with aggression have lower levels of 5-HIAA (a serotonin metabolite) in their cerebrospinal fluid than control dogs.[14] An inverse correlation between levels of 5-HIAA in the CSF and a history of aggression has been found repeatedly in human, primate and laboratory studies.[7,10,19]

Monoamine oxidase is an enzyme that metabolizes norepinephrine, dopamine, and serotonin. Monoamine oxidase inhibitors such as selegiline cause elevation in monoamine neurotransmitters by inhibiting this enzyme.

Once you have a general understanding of the neurotransmitters and their basic effects, it is simplest to speak of the psychotropic drugs by class, as most classes are defined by the neurotransmitters they affect. Knowledge of the general effects of the different neurotransmitters, then helps you to understand the drug effects and why we use them as we do, as well as why the drugs have the side effects they do.

BENZODIAZEPINES

Benzodiazepines are one of the most widely prescribed drugs in the world. They work by facilitating the transmission of GABA in the central nervous system. The primary functions for which we use benzodiazepines in veterinary medicine are reducing muscle movement and anxiety and controlling seizure activity.

Generally speaking, benzodiazepines have a rapid onset of action with effects that can last a variable period of time, generally under a day. Clinicians should use caution when giving benzodiazepines to animals that may be aggressive as they have the potential to lead to disinhibition of aggression.[3] To confound matters, however, in laboratory studies, they have

been shown to increase affiliative behaviors in some species such as rhesus macaques and they have been found to have a taming effect in some species.[5,6,16] At low doses, benzodiazepines have a calming, anti-anxiety effect, and at higher doses they may be sedating. Paradoxical excitation seems to be a relatively common problem noted when prescribing benzodiazepines in dogs, but we haven't documented the use of these drugs enough in other species to know how common that may or may not be in other species. If it occurs, generally, we recommend increasing the dose by 25–50% and giving another test dose after the excitation of the first dose wears off. If excitation occurs again, then switching to a different benzodiazepine can be tried before abandoning use of the class completely in that individual. Due to the possibility for paradoxical excitation, it is ideal for a "test dose" of a benzodiazepine to be given at a time when a caretaker can observe the patient for a few hours and when the animal can be separated from its social group for a while, if it is safe to do so. Obviously, depending on the individual you are treating, the problem and the particular environment, it may be safer to switch drugs immediately if you have a paradoxical reaction. This is a decision that must be made by the clinician on a case-by-case basis.

There are many different kinds of benzodiazepines, ranging in duration of action from 3 hours (alprazolam) to 10 hours (clorazepate). When treating pets, benzodiazepines are often just given 30–60 minutes prior to the occurrence of a fear-inducing event. When the events that are disturbing to a particular patient cannot be predicted, a regular dosing regimen should be established.

Benzodiazepines do have the potential to produce addiction, so after long-term use in an animal, the dose should be decreased slowly (25–30% per week) in order to prevent problems when stopping the drug. Tolerance to the drug is also common, so clinicians should be prepared to increase the dose when the animal must be on it for an extended period of time.

Benzodiazepines are highly protein bound, and hypoproteinemia will lead to an increased volume of distribution. They are metabolized in the liver and excreted by the kidneys, so their use should be avoided if liver or kidney disease exists. Idiopathic hepatic necrosis has been documented in cats receiving diazepam, so you may wish to avoid its use completely in felids. However, there is limited evidence to suggest other benzodiazepines are particularly dangerous to cats and many of them are used safely in practice on a regular basis. In laboratory studies, clonazepam specifically has been found to be substantially less toxic to cats than chlordiazepoxide, diazepam or flurazepam.[3] Other side effects of the benzodiazepines include ataxia, muscle relaxation, increased appetite, anxiety, hallucinations, muscle spasticity and insomnia. Contraindications for the use of most benzodiazepines also include glaucoma, pregnancy and lactation.

Benzodiazepines can be very useful when employing multimodal drug therapies, as they can be safely used with other maintenance medications such as SSRIs and SNRIs.

Table 1. Commonly used benzodiazepines and oral dosage information in dogs and cats

Medication	Dog dose	Cat dose	Useful information
Alprazolam (Xanax)	0.02–0.1 mg/kg q 4 h	0.0125–0.25 mg/kg q 8 h	Minimal active metabolites Rapid onset of action
Clonazepam (Klonopin)	0.1–0.5 mg/kg q 8–12 h	0.015–0.2 mg/kg q 8 h	Extensive liver metabolism but less toxic to cats
Diazepam (Valium)	0.5–2.0 mg/kg q 4 h	0.1–1.0 mg/kg q 4 h	Multiple active metabolites Short half-life May potentiate organophosphates
Oxazepam (Serax)	0.04–0.5 mg/kg q 6 h	0.2–1.0 mg/kg q 12–24 h	No active metabolites Slower onset but longer duration of action

GABA Analogues

These drugs work on voltage-gated calcium channels to prevent calcium influx which inhibits the release of excitatory neurotransmitters such as glutamate. This action helps to block pain, increase the seizure threshold and decrease anxiety. Gabapentin is the drug most often used in veterinary medicine. Pregabalin is also available but is still on patent and therefore much more costly. Side effects are infrequent. Withdrawal-associated seizures are reported in humans, so taper use of this medication as a precautionary measure. Avoid the use of the commercial liquid human formulation as it contains xylitol.

Selective Serotonin Reuptake Inhibitors (SSRIs)

Selective serotonin reuptake inhibitors (SSRIs) work by blocking the serotonin transport system (SERT) and as the name implies, this lead to increased levels of serotonin in the synaptic cleft while having minimal effects on other neurotransmitters. With prolonged administration, downregulation of post-synaptic autoreceptors also occurs. The SSRIs are classified as antidepressants; however, they have anxiolytic, anticompulsive and some antiaggressive effects as well. They contribute to mood elevation and calming, with minimal sedation and no impairment of learning.

When pet owners report side effects of the SSRIs, anorexia and sedation are the most common. In most cases, the side effects decrease with time and they almost always disappear completely if the medication is discontinued. Other side effects that have been noted in a variety of species are constipation, diarrhea, urinary retention, anxiety, irritability, agitation, tremors, insomnia, and decreased libido. Again, these virtually always disappear with discontinuation of the drug.

Serotonin syndrome is a condition that has been reported in humans taking excessive quantities of medications that increase serotonin levels, or other medications that are incompatible with the SSRIs at the same time as SSRIs. Signs may include tachycardia, tremors, ataxia, restlessness, seizures, vomiting, nausea, hypotension or hypertension and sudden death. At this time, no case of serotonin syndrome in a pet being treated with psychotropic drugs has been documented, so it is very difficult to say how problematic it may be in any nondomestic species. To avoid serotonin syndrome, medical records need to carefully document **all** medications **and** nutraceuticals or supplements being given to an animal. For example, supplements such as St. John's wort and L-tryptophan work by increasing levels of serotonin, so these types of products could potentially lead to serotonin syndrome if their use goes unnoticed.

The SSRIs should not be used on an as-needed basis. They should be given for at least 6–8 weeks to take effect before considering stopping the drug. At that point, if there are no negative side effects, adding an adjunctive drug may be more practical than stopping the SSRI and restarting another drug that may take 6–8 weeks to take effect. The SSRIs should not be given to animals receiving selegiline, amitraz dips (or Certifect) or thioridazine. While the use of these products may be uncommon in the zoological setting, an awareness of these contraindications could be important. Treatment with fluoxetine should not be started until 2 weeks after discontinuation of selegiline or amitraz treatment. Due to the long half-life of fluoxetine, treatment with selegiline should not be started until 5 weeks after the discontinuation of fluoxetine. The use of SSRIs should also be avoided in geriatric patients or those with kidney or liver disease, diabetes, glaucoma and in pregnant or lactating females. Caution should be used in prescribing them to breeding animals because of the potential for decreased libido. The SSRIs are strongly bound to plasma proteins so their use when prescribing other drugs that bind to plasma proteins should be avoided. Care should be used if administering SSRIs with tricyclic antidepressants (TCAs), carbamazepine, haloperidol and benzodiazepines as lower doses of these medications will be required.

The SSRIs are not addictive, but gradual withdrawal is recommended. In case of overdose with an SSRI, treatment is supportive.

Table 2. Typical oral doses of two of the more commonly used SSRIs

Drug	Dog dose	Cat dose
Fluoxetine (Prozac)	1.0–2.0 mg/kg once daily	0.5–1.5 mg/kg once daily
Paroxetine (Paxil)	1.0–1.5 mg/kg once daily	0.5–1.5 mg/kg once daily

Serotonin and Noradrenaline Reuptake Inhibitors (SNRIs)

These drugs increase the amounts of both serotonin and noradrenaline available at the synaptic cleft by inhibiting reuptake. As with SSRIs, down regulations of autoreceptors will occur with prolonged administration, thereby increasing efficacy. These drugs also have anticholinergic and antihistaminic effects and act as α-1 adrenergic agonists. TCAs are the most commonly used SNRIs in veterinary medicine and include amitriptyline, clomipramine, desipramine, doxepin and imipramine. Clomipramine is available in a veterinary formulation (Clomicalm®) approved for the treatment of separation anxiety in dogs, so it has received much use in the veterinary field in the last 10 years.

SNRIs are used for the same behavior problems as SSRIs, should be administered long term as a maintenance medication and are given orally once or twice daily. Because of their anticholinergic, antihistaminic and α-1 adrenergic agonistic effects, there can be pronounced side effects which include cardiac arrhythmias, decreased blood pressure, constipation, urine retention, gastrointestinal signs and sedation. As with SSRIs, SNRIs should be used with caution in animals already receiving other medications that affect serotonin levels. TCAs and SSRIs have been shown to artificially lower laboratory thyroid values, so these should be interpreted with caution if evaluated in an animal that has been receiving these medications for more than a few weeks.

Although not addictive, gradual withdrawal is recommended when using these medications.

Serotonin Antagonist-Reuptake Inhibitors (SARIs)

Trazodone is classified as a SARI. At lower doses, it antagonizes serotonin, histamine and α-1 adrenergic postsynaptic receptors.[17] At higher doses it blocks SERT (serotonin transporter) and antagonizes additional postsynaptic serotonin receptors.[17] Recent research indicates that it may also modulate GABA, revealing a mechanism of action separate from that of SSRIs and SNRIs.[9] Trazodone is rapidly absorbed, reaching peak plasma levels 1 hour after administration and is therefore appropriate for both PRN and maintenance use.[4] There is some evidence that trazodone works synergistically with SSRIs and SNRIs, and ongoing research in dogs for treatment of anxiety indicates that it is well tolerated.[4] As with SSRIs and SNRIs, SARIs should be used with caution in animals already receiving other medications that affect serotonin levels. Trazodone is used to treat insomnia in people and has been suggested for use in addressing the sleep cycle changes seen in cognitive decline.

In dogs, a common starting dose for trazodone is about 2–3 mg/kg as needed. The dose can be slowly increased up to a total of 7 mg/kg every 12 hours, depending on the problem and what other medications the animal is taking. Trazodone has been used in cats at doses ranging from 12.5–50 mg per cat as needed.

Azapirones

Buspirone is the main drug from this category used in veterinary medicine. It is often used as an augmentation drug in conjunction with a primary maintenance medication such as an SSRI. It is a serotonin 1A partial agonist and an antagonist of dopamine receptors. It has an anxiolytic effect. It takes 6 weeks or more before reaching maximum effect and is short acting, requiring twice or three times daily dosing. One interesting side effect noted is increased social behavior in cats, and this effect deserves more study in other species.[3]

Buspirone side effects are very uncommon, but in some cases may include dizziness, insomnia, nervousness, nausea, headache fatigue and mania. Buspirone may take several weeks to take effect but is safe for use in geriatric and pregnant patients. It should not be given with MAOIs, and caution should be used if giving with erythromycin or itraconazole.

The dose for treating cats with buspirone is 2.5–7.5 mg/cat every 12 hours or 0.5–1.0 mg/kg every 12 hours. Treat dogs with buspirone at 0.5–2.0 mg/kg every 8–24 hours.

Monoamine Oxidase Inhibitors (MAOIs)

MAOIs interfere with the action of monoamine oxidase A and B which are the primary enzymes responsible for the breakdown of multiple catecholamines including serotonin, dopamine, adrenaline and noradrenaline. Increasing these substances should lead to an elevation of mood. Selegiline is the MAOI most often used in the United States. The effects of MAOIs are more extensive than just neurotransmitters. They affect many systems in the body and as such should be used with caution in combination with other drugs. Selegiline is licensed for use in cognitive decline in dogs in the United States and for other behavior disorders in Europe.[2,8] It has some effect on anxiety, but because of its delayed action and restricted use in combination with other medications, it is used less in the U.S. for behavioral problems not associated with cognitive decline.

Alpha-2 Adrenergic Agonists

Clonidine is an α-2 agonist used in humans for the treatment of hypertension, attention deficit hyperactivity disorder (ADHD), post-traumatic stress disorder (PTSD) and impulsivity. It works by blocking norepinephrine release from α-2 receptors on presynaptic neurons. A single study showed that clonidine is efficacious in the treatment of canine anxiety.[12] Clonidine takes 1–2 hours to take effect and lasts for approximately 6 hours. Side effects are rare, but the drug should be used with caution in animals with cardiac conditions, as it can cause hypotension.

Antipsychotics

Antipsychotic agents include the phenothiazine tranquilizers, acepromazine and chlorpromazine and the butyrophenones, haloperidol and azaperone. These agents block the action of dopamine. Dopamine depletion results in behavioral quieting, depression and extrapyramidal signs (EPS). EPS are Parkinsonian-like symptoms such as difficulty initiating movements, muscle spasms, motor restlessness, and increased muscle tone resulting in tremors and stiffness.[3] In addition, the blockade of dopamine receptors affects brain regions responsible for controlling thermoregulation, basal metabolic rate, emesis, vasomotor tone and hormonal balance. Antipsychotics also produce a state of decreased emotional arousal and a relative indifference to stressful situations. With chronic use, tardive dyskinesia may develop as a result of upregulation of dopamine receptors. This is an inability to control movements and hyperkinesis. Chronic side effects can occur after as little as three months of treatment and are potentially irreversible even after discontinuation of the medication.

Although their effects can be quite rapid, the use of these drugs can produce very inconsistent results, especially when used to treat aggression. They have actually been known to increase aggressiveness in animals with no known history of aggression.[13] Due to their wide-ranging dangerous side effects and the availability of several safer and likely more efficacious choices, these drugs should not be the first choice of behavioral drugs in any animal species.

Conclusion

While much remains to be learned about the role of the different neurotransmitters on behavior and the effects of the psychotropic drugs, for more than 20 years these drugs have been used successfully to decrease suffering in many animals. With careful extrapolation, the newer, safer drugs such as the SSRIs, the SNRIs and the SARIs should be used more frequently and older classes of drugs such as the antipsychotics only used as a last resort when treating problem behavior in captive wild animals.

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Rehabilitation of a Bobcat (*Felis rufus*) Incapacitated by a Taser Gun
American Association of Zoo Veterinarians Conference 2008

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ABSTRACT

Electromuscular incapacitating devices (EMDs) are electronic immobilization weapons that have been available for over 30 years. The purpose of these non-lethal weapons is to incapacitate humans or animals using high-voltage electricity. Research on the effects of EMDs concluded that while EMDs may increase heart rate, they have no effect on cardiac rhythm or morphology in normal subjects.[3,6,11] Other studies investigated the changes in blood factors following single or repeated taser exposure and reported transient increases in acidosis, lactate, hematocrit, and other factors.[2,4,10] Potential injuries may include thoracic spine compression fractures.[9,12] However, no studies were found to suggest that EMDs cause paralysis or paresis of limbs in humans or animals. This is a case report of a 9-month-old bobcat that was tasered at the T10 spinal level resulting in temporary hind limb paralysis and residual paresis. Routine rehabilitation of muscle weakness includes exercise and electrical stimulation. Research demonstrated mixed results on the effectiveness of these methods.[1,5,7,8,13] The bobcat received daily treatments consisting of range-of-motion exercises and sensory stimulation. One year post-incident, electro-acupuncture and rehabilitation techniques (spinal and soft tissue mobilization) were implemented. Environmental modifications were designed and changed periodically to encourage pelvic limb muscle strengthening and to facilitate muscle re-education. After four months of treatment, the bobcat could ascend/descend stairs and initiate walking. Although the movement patterns were not consistent, the bobcat continues to demonstrate progressive improvement.

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Semiochemicals and Their Potential Applications in Zoo Animal Housing and Welfare
2016 Joint AAZV, EAZWV, IZW Conference
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ABSTRACT

Chemical communication is the oldest and most widely used form of communication among animals. The term semiochemical refers to any chemical involved in a chemical interaction between animals. Pheromones are a subclass of semiochemicals and are defined as "substances secreted outside of the body by one individual and received by a second individual of the same species, in which they release a specific reaction."[7] The response to pheromones is innate and in many instances behavior or endocrine changes occur in the receiver as a result of exposure.

Man has exploited this knowledge of chemical communication in animals for years and recent research into the use of pheromones has found them to be useful in parasite control in a variety of species,[2,3] to decrease aggression in group housed swine,[5] to reduce stress in commercially housed broiler chickens[4] and to decrease aggression between cats in the multi-cat household.[1]

Research into the use of pheromones in captive wild animals remains limited but shows similar promise. Pheromones have been used in different species to aid in introductions and to aid in reducing stress associated with travel. The author is aware of a great deal of other anecdotal use that continues to be unreported and undocumented.

Appeasing pheromones (also referred to as appeasines) show particular promise. The appeasines are semiochemicals produced by nursing females from sebaceous glands located in the intramammary sulcus.[6] They have a calming or soothing effect on the young, and animals have been shown to be capable of responding the same way to this pheromone into adulthood. The first appeasine was identified in sows and they have since been identified in bitches, mares, cows, queens, ewes and does.

Appeasing pheromones have the potential to aid in reducing stress in captive wild animals. They may prove useful in aiding introductions of unrelated animals, decreasing stress during movement between zoological parks or between enclosures. They may be useful in managing events that have been shown to be stressful for certain animals such as busier or nosier times of year in zoological parks. The presence of pheromones in enclosures may even serve as a form of environmental enrichment for some individuals.

Further study is needed in all of these areas to demonstrate if this particular form of therapy is as effective as it is safe. Pheromone therapy is currently an underutilized form of therapy, most likely due to the fact that the majority of veterinarians have been taught very little about chemical communication or behavior problems and behavior therapy in animals. This form of therapy is deserving of further investigation. It could potentially avoid the need for anxiolytics in many situations and yet due to the fact that it acts uniquely from pharmaceuticals it can also safely be used as an adjunct with any medication. In companion animal behavior therapy it is often used as a component of multi-modal therapy. Pheromones take effect more rapidly than drugs, are not taken up into the bloodstream, so require no metabolism or elimination from the body. Thus they are safe to use in any animal regardless of their age or state of health.

In order to collect useful information about their effects, it will be important that good behavioral data, using consistent, published ethograms (when possible) be collected prior to and after the use of the pheromones. Sharing this data amongst the zoological community can then aid in better use of this potentially valuable tool.

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Serum Concentrations and Behavioral Effects of Oral Haloperidol in Bongo Antelope (*Tragelaphus eurycerus*)
American Association of Zoo Veterinarians Conference 1999

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Abstract

Neuroleptic drugs have been used to reduce anxiety, excitement, and motor activity in ungulates. These drugs facilitate the handling and transportation of both captive and free-ranging animals. Haloperidol, an antipsychotic, tranquilizing agent, is used in humans to reduce psychomotor agitation and aggression. Parentally administered haloperidol has also been shown to produce desirable psychomotor effects and tractability in a number of ungulate species.[2,4] The pharmacologic effects of haloperidol in bongo antelope have not been reported, and further, such effects have not been correlated with plasma concentrations. There is little information on the oral effectiveness of haloperidol in any nondomestic species. The ability to administer an oral tranquilizing agent could obviate the need for repeated administration by remote injection to maintain a desired level of tranquilization.

A dose of 1 mg/kg has been suggested as an oral haloperidol dose.[1] Recent clinical observations (S. Mikota, unpublished data) have shown that a 1 mg/kg dose of haloperidol, administered once daily in the food for 5 days, produced a level of tranquilization which permitted restraint and blood sampling without incident in captive bongo conditioned to enter a custom-designed chute. These observations suggested that haloperidol is palatable orally and is absorbed and distributed to the central nervous system. The purpose of this study was to systematically evaluate the behavioral effects of orally administered haloperidol in bongo antelope and to correlate these effects with plasma concentrations.

As part of an ongoing project to evaluate steroid hormones and anti-tuberculosis drug levels, each of four adult female bongo received haloperidol at 4:00 p.m. for 28 days at an approximate dose of 1 mg/kg/day (1.04–1.62 mg/kg). Haloperidol is supplied as 20-mg tablets, and oral dosing was accomplished by inserting 10 tablets into bananas which were hand fed to individual animals by a keeper who had established the animals' trust.

A push wall directed bongo to enter a chute and squeeze box. Bongo were blindfolded upon entering the chute and two straps placed dorsally across the back to discourage jumping. Venipuncture sites were shaved with a disposable razor and a 4% tetracaine ointment applied. (Application of tetracaine alone did not result in analgesia sufficient for blood sampling.; S. Mikota, unpublished data). Blood samples to measure plasma progesterone and estradiol were collected daily for 29 days.

On day 20, blood was drawn at 6:30 a.m. (time 0); haloperidol was administered orally as described; and anti-tuberculosis drugs were administered orally and/or parentally. Bongo were bled at 1, 2, 3, 5, 8, 10 and 12 hours post-administration to measure serum concentrations of anti-tuberculosis drugs and haloperidol over time.

Bongo were observed under four sets of conditions as follows:

- Condition 1: Confined to pen; on haloperidol
- Condition 2: Manipulation through chute; venipuncture; on haloperidol
- Condition 3: Manipulation through chute; venipuncture; not on haloperidol
- Condition 4: Manipulation through chute; venipuncture; on haloperidol (4-day study)

Score cards, devised to subjectively grade the degree of tranquilization observed under conditions 1–4, were completed by all personnel involved in the procedure. Parameters included behavior in pen, behavior in chute, appetite, and response to treats. Pen and chute behaviors were scored using a 7-point subjective scale that described the animal's behavior in each setting. The behavioral scores ranged from unresponsive to violent. Overall behavior was scored using a 4-point scale that described general impressions of the performance of the tranquilizer. These scores ranged from unacceptable to excellent. Temperature, pulse, and respiration were measured at each time point and animals were observed for possible side effects (repetitive muscle jerks [dystonia], drooling, worm-like movements of the tongue [lingular vermiculation], spontaneous rolling back of the eyes [oculogyric crisis] or slow, repetitive, purposeless movements [tardive dyskinesia]). Behavioral data from all observers was averaged and a single score generated for each animal and variable.

Condition 4 behavioral data was collected for 4 consecutive days following 13 days during which bongo did not receive haloperidol.

Serum haloperidol was measured using a commercially available enzyme-linked immunosorbent assay (ELISA) in a 96-well microtiter plate format. The assay was validated for bongo serum using samples from untreated animals and fortification of the samples with haloperidol reference standard. Samples were assayed in singlicate against blanks and blank fortified reference standard controls.

At time 0, 14.5 hours since the last haloperidol dosing, mean serum concentration of haloperidol was 12.6 ng/ml and overall behavior was scored as fair to good (1.7). Over the next 1–3 hours, the steepest increases in haloperidol concentration and overall behavior score were observed. At 2 hours post-dose, overall behavior was scored as good to excellent (2.7), and serum haloperidol concentrations had risen to 16.2 ng/ml. While serum concentrations continued to rise for 10 hours post dose, increases became more gradual from 3–10 hours, reaching a peak at 10 hours (19.5 ng/ml). Overall behavioral scores remained fairly constant (from good to excellent) from 3–10 hours post. During this time, the animals could be easily approached and did not attempt to escape the chute. They readily tolerated venipuncture, blindfolding, restraint with dorsally placed straps, stethoscopic auscultation, and the insertion of a digital thermometer. The bongo also complied with physical coaxing towards the chute and ambulated normally upon leaving the chute. Little or no change in chute or overall behavior was reported during that time. Although behavior was not scored, serum haloperidol concentration began to decline (17.3 ng/ml) by 12 hours post dose.

General appetite, as measured by treat consumption, increased from partial consumption at time 0 to complete consumption by 3 hours post dose. Consumption remained complete for the remaining observation period. Respiratory rate, body temperature, and ambient temperature rose gradually during the 10-hour observation period. Pulse rate was variable.

The data obtained from conditions 1–3 indicated that adequate plasma concentrations of haloperidol could be achieved in bongos via the oral route of administration. Furthermore, the data indicated that serum concentrations could be correlated with changes in behavior. The most dramatic improvements in tranquilization were seen during the most rapid increases in serum concentrations (i.e., 1–3 hours post dose). The data also demonstrated that plasma haloperidol concentrations appear to peak at 10 hours post dose and that good to excellent tranquilization could be achieved at 15–19 ng/ml.

Residual haloperidol concentrations of 8.38–8.5 ng/ml were measured at 24 hours post dose, suggesting that haloperidol is absorbed gradually and reliably from the gastrointestinal tract, even in the presence of food. Plasma concentrations of 5–15 ng/ml have been associated with positive therapeutic responses in humans.[3] Similar plasma concentrations were achieved in our study, suggesting that the therapeutic range for humans and bongos is similar. In conclusion, a once-daily oral dose (200 mg) of haloperidol produced a desirable level of tranquilization in bongos that permitted manipulation and blood sampling.

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Standing Castration in a Two-Year-Old Reticulated Giraffe (*Giraffa camelopardalis reticulata*)
American Association of Zoo Veterinarians Conference 2002

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Abstract

A chute conditioned 2-year-old reticulated giraffe (*Giraffa camelopardalis reticulata*) was castrated using standing sedation and an EZE bloodless castrator.[1] The decision to castrate this young male giraffe was based on the inability of the Cheyenne Mountain Zoo to accommodate two adult male giraffes in their current enclosure. This 2-year-old bull was beginning to spar and exhibit aggression with the adult bull in the giraffe herd (his sire). Shipping this young male was not an option at the time.

Among the anesthetic challenges facing zoo veterinarians, giraffe anesthesia is considered to have a historically high mortality rate associated with it.[2] For this reason, we decided to perform the castration using a standing sedation protocol with the alpha-adrenergic agonist xylazine. Before attempting this procedure, the keeper staff intensely chute conditioned this giraffe over a period of several weeks. The conditioning was gradual, and by the end of the conditioning the giraffe was allowing the placement of bellybands and a quick release head halter. The decision to use a banding castrator rather than performing an open castration was based on the temperament of the giraffe and the limited access to the scrotum and testes in the standing position.

Methods

A 2-year-old male reticulated giraffe weighing 632.0 kg was placed in a box-type chute with removable side panels. Two 6-inch-wide nylon mesh straps were placed in a ventral abdominal position, one just caudal to the axilla, and one just proximal to the scrotum. The giraffe was given 100 mg of xylazine IM (Rompun, Miles Laboratories) and within 15 minutes the giraffe was so sedate that he began to buckle on all four limbs, using the bellybands to support most of his weight. The scrotum was then prepared aseptically for the castration. Fifteen milliliters of buffered lidocaine (1:1 dilution of 2% lidocaine and 8.4% sodium bicarb) was infused by injection in and around the proximal portion of the scrotum and spermatic cord. Sedation was profound enough at that time to cause laxity of the giraffe's head and neck. At this time, a quick release halter was placed on the giraffe to support his head and neck, and a nasal cannula was placed providing 100% oxygen supplementation, heart rate and oxygen saturation were monitored via pulse oximetry. The scrotum and testes were manually isolated from the body wall and two rubber-castrating bands were placed as tightly as possible between the testes and the body wall. Blood was drawn for a CBC and serum chemistry panel; and the following medications were given: 600 mg of flunixin meglumine IM (Banamine, Schering-Plough Animal Health) 10 ml of penicillin G procaine IM (Dura-Pen, Vedco, Inc.), 2 ml of tetanus toxoid IM (Fort Dodge Laboratories), 12 ml of vitamin E/Se IM (Bo-Se, Schering-Plough Animal Health). Reversal was achieved with 50 mg of yohimbine, 50% IV and 50% IM (Yobine, Lloyd Laboratories) The giraffe was able to walk out of the chute within 20 minutes of reversal and was eating and drinking with no signs of pain or discomfort 6 hours later. We continued him on oral Banamine and trimethoprim/sulfadiazine powder (Tucoprim, Pharmacia & Upjohn) for the next 7 days. For follow up, the giraffe was placed in the chute weekly to exam the bands and the scrotum, the scrotum and testes steadily became atrophic and desiccated. In bulls banded by the EZE bloodless castrator the scrotum becomes completely desiccated and drops off within 3 weeks. Three months later our giraffe still had the remnants of his scrotum and testes and although there were no apparent complications, we decided to amputate the scrotum in case the bands would act as a nidus for infection and inflammation. The giraffe was again placed in the chute with bellybands and given 25 mg of xylazine IM, this dose was just enough to perform the amputation without additional anesthesia. The rubber bands were removed with a pair of tin snips and the scrotum was amputated in the crush created by the bands. There was a small area of granulation tissue at the surgical site but no active bleeding. Twenty-five milligrams of yohimbine were given IM for reversal, and the giraffe was bright and alert in 15 minutes. The keepers were instructed to place betadine ointment on the granulation tissue once daily for the next 10 days.

Discussion

We feel we were able to perform this castration in a standing position because of the extensive chute training and conditioning the giraffe received from the keepers. Without having a calm animal in the chute, we would not have been able to castrate him with xylazine alone. The EZE bloodless castrator has been used in the field with cattle for several years, complications noted by the manufacturers are mostly related with poor placement of the bands. If the bands are not placed correctly or tight enough there can be partial vascular and spermatic cord occlusion resulting partial necrosis and the production of toxins leading to endotoxemia and possibly septicemia. We feel the reason that the scrotum did not fall off on its own as it should, was that the tissue on the neck of the scrotum was too thick, if we had performed the procedure on a younger animal the results may have been more or less what was expected. In the future, when planning another castration, we will hope to have the animal chute trained before it is 1 year old, hopefully avoiding having to amputate the scrotum months later.

Acknowledgments

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The Big Picture: Evaluation and Management of Aggressive Behavior in Captive Animals
American Association of Zoo Veterinarians Conference 2013

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ABSTRACT

Aggressive behaviors are one major reason that zoo staff seeks assistance from veterinarians. A wide range of behaviors may be considered aggressive and assistance is often sought only after the frequency, duration, or intensity of the relevant behaviors have become intolerable to husbandry staff or are considered significantly atypical for the species. In many cases, the behavior has escalated to the point where the animal is consistently injuring itself or other animals, or threatening human safety.

Behavior, and why behavior develops or changes, can be examined and understood with a variety of sciences or models (e.g., neuroendocrine, genetic, physiology, etc.). These different approaches lead to different hypotheses about why the behavior is happening and different treatment or management strategies. Three major models directly relevant to clinical veterinarians include medical, ethological (natural history), and applied behavior analysis. These approaches are not mutually exclusive and when utilized together enhance the development and success of humane behavior change strategies.

Veterinarians are trained to consider medical causes for behavior. For example, increased aggression (e.g., biting when approached) can be a sign of disease such as pain, a brain tumor, or abnormal neurochemistry. Neurophysiologic research has demonstrated that some problem behaviors may be due to differences in brain activity at a molecular level.[1,5] The development of some problem behaviors is likely a combination of both biological predisposition and development events. For instance, animals raised in barren environments or under a great deal of stress during the early weeks, months or years of development have fewer neurons in the brain, decreased dendritic branching and spine density, and reduced synaptic connectivity compared to animals raised in enriched environments.[1,5] Many captive animals are reared in environments dissimilar to natural environments and this may contribute to neurophysiologic abnormalities, though this is currently speculative.

Whatever the cause, it is likely that some portion of a given population has neurophysiologic dysfunction that limits the individual's ability to learn and behave normally in common environmental situations. In addition, some animals may be normal but less able to cope with the physical, mental, and behavioral limitations of a given captive environment, either temporarily or long term. In these cases, using appropriate psycho-pharmaceutical medications such as serotonin reuptake inhibitors (e.g., fluoxetine) or benzodiazepines (e.g., alprazolam, diazepam) may be effective in reducing aggression.[2] Antipsychotics, such as haloperidol, produce inconsistent results for the treatment of aggression and may increase aggression in some cases. Antipsychotics lead to overall suppression of behavior and their high incidence of side effects make them inappropriate for long-term therapy.[2] The effectiveness of any psychotropic medication can be challenging to predict. In addition, many of these medications take a long time to show efficacy. This needs to be taken into account when effectively planning interventions. It is inappropriate to expect medication to compensate for a poor environment. In addition to medications, increasing the animal's behavioral control and choice through appropriate enrichment and effective positive reinforcement training is generally critical to successful management plans, including those in which medication is called for and effective.

In the zoological field, we often consider ethological correlates for behavior and behavior change, i.e., the behavioral adaptations that have evolved to fit the animals' ecological niche. For example, increased aggression can be understood as an inherited modal action pattern such as a territorial defense chain elicited by breeding season cues, or secondary to social, hierarchical influences within a group. To complicate matters, many captive animals have not been reared in normal social groups and may not have learned to respond to other animals' cues typically, leading to increased or inappropriate levels of aggression.

Animals may display aggressive behaviors which are typical for the species, but which are disruptive to captive management goals or displayed at a greater intensity than desired for success in captivity.[7] These behaviors are often relevant to the reproductive cycle. In these cases, medications that specifically reduce reproductive hormones may reduce aggressive behaviors; examples include GnRH agonists (e.g., deslorelin or leuprolide), or progestins to suppress ovarian cycling (e.g., melengestrol acetate, megestrol acetate, medroxyprogesterone acetate). In addition, a thorough review of the individual (and where applicable, the group) behavior pattern is appropriate to better understand and document social interactions and other environmental stimuli that are associated with aggressive behaviors. For example, a subordinate (versus the more easily identified aggressor) may be precipitating aggressive events through inappropriate responses to social cues. Understanding the natural history of a species is important when conducting a thorough evaluation of the animal's environment, as well as ensuring that staff expectations for behavior are appropriate.

In addition to these more familiar models, behavior analysis is critical for understanding how a specific behavior emitted by an individual animal is learned and maintained, due to interaction with the environment in which it occurs.[4] Behavior analysis is a trans-species science that investigates the universal laws of behavior change due to experience, i.e., learning. Applied behavior analysis (ABA), the behavior change technology derived from behavior analysis, takes the individual animal's learning history and current environmental conditions into account and investigates the purpose (i.e., function) the behavior serves for the animal. In the above example, we can hypothesize that the increased aggressive behavior is the result of learning, i.e., the behavior was reinforced in the past. Even complex, severe aggressive behaviors are responsive to this approach.[7]

From the ABA perspective, understanding and changing behavior results from identifying the discriminative stimuli that set the occasion for the behavior (i.e., setting events, motivating operations, and discriminative stimuli), and the consequences that give the behavior strength (frequency, duration, intensity, etc.). The focus of the behavior change plan is to modify the environment to set the occasion for appropriate alternative behaviors and reinforce them when they occur. With ABA, we change the environment to change the animal's behavior.

Reviews of behavior analysis science for veterinarians exist and a functional assessment and intervention design (FAID) worksheet for evaluating problem behavior and developing appropriate behavior support plans is also available.[3,4,6,7] The FAID worksheet provides a standardized approach to cases (similar to a SOAP format) and prompts a complete, individualized evaluation of the problem behavior situation and development of a plan specific to that individual in that environment. A summary of five major questions related to behavior is provided (Table 1). This model provides a powerful, systematic method of behavior evaluation and intervention. The ABA approach is under-utilized by most veterinarians and husbandry staff due to lack of training and general under-estimation of the importance of prior learning and current conditions as a major factor governing actual behavior in individual animals.

Veterinarians should utilize all three models when diagnosing and managing aggressive behavior displayed by animals so that relevant medical conditions, ethological, and learning variables are all evaluated.

Table 1. Summary questions to prompt investigation of the environmental factors related to problem behavior

Question	Purpose of Question	Example
What does the behavior look like?	Reduce use of labels and focus on actual, observable behaviors in preparation for identifying relevant environmental stimuli that predict and maintain the behaviors. If multiple disruptive behaviors are present, each should be evaluated individually.	Labeling the animal: The animal is aggressive. Operationalized behavior: Behavior A: The animal lunges at the door and bites the air. Behavior B: The animal pushes into the other male and bites his neck.
What conditions predict when the behavior will occur (when is the behavior most likely)?	Identify the relevant environmental stimuli that cue or set the stage for the behavior.	Behavior A happens when keepers approach the door with food. Behavior B happens when browse has been added to the enclosure.

What does the animal get from or get away from by doing the behavior?	Identify the relevant environmental stimuli that are reinforcing (maintaining) the behavior.	After behavior A happens, food is left in the enclosure and the keeper leaves the area. After behavior B happens, the other animal leaves the area and the first animal has access to the browse.
Under what conditions does the animal not exhibit the behavior (when is the behavior least likely)?	Identify the environment when the animal is most successful. This step helps staff realize there are environments in which the animal is successful and the problem behavior is not occurring.	Behavior A is least likely to happen if a keeper approaches without food. Behavior B is least likely to happen when the females, as well as other males, are present or the two males are fed hay.
What can the animal do instead?	Identify another behavior the animal can do in place of the problem behavior. These are behaviors that can be trained (reinforced). In some cases, reinforcing another behavior is not possible and management of environmental stimuli to not cue the problem behavior is appropriate.	Instead of doing behavior A, the animal can stand with his head near the water bowl when food is added to the enclosure. Instead of doing behavior B, the animal can eat browse in a separate part of the exhibit, or the two males are not fed browse when they are being housed without the females.

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The Search for a Reversible Male Birth Control in the Lion-Tailed Macaque as a Model for Other Primate Species
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Introduction

The carrying capacity determined by the Species Survival Plan (SSP) for lion-tailed macaques (*Macaca silenus*) (LTM) in North American zoological institutions is 250 individuals. It is the goal of the LTM SSP to conserve the greatest possible genetic diversity within this small population over a long period of time. Detailed pedigrees are maintained for each individual, and each is assigned a calculated breeding coefficient that correlates with that individual's genetic representation in the captive population. It is desirable to breed under-represented animals by natural and/or artificial means.

Because an individual LTM's genetic representation may change with time, reversible forms of contraception are utilized. Subcutaneous implants containing progesterone or melengestrol acetate, intramuscular injections of medroxyprogesterone acetate or leuprolide acetate, and oral human contraceptives have been utilized successfully in female macaques.

To date, reversible male contraceptive techniques have not been utilized in macaques. Reversible male contraception is desirable as males quickly become over-represented when housed within normal multi-female troops. While removal of an over-represented male and introduction of a less well-represented LTM might be one way of controlling genetic representation of males, it is disruptive and dangerous to change troop males, which are very aggressive and often practice infanticide when first introduced to LTM females with infants. Reversible male contraception would be beneficial in that a) troop behavior and dynamics would not need to be altered frequently, b) the need for the use of contraceptives in females, with their associated potential long-term complications, would be eliminated, and c) genetic management of an entire troop could be controlled through a single animal. Under-represented cycling females could be removed from the group, impregnated by underrepresented males, and reintroduced. Since the troop male would be present during gestation and parturition, the probability of infanticide would be markedly reduced. In addition, as LTM behavior and troop dynamics allow for only one adult male per troop, and as males comprise half the captive LTM population, many must be housed singly, often in sub-optimal conditions. A potential benefit might be the ability to take advantage of contraceptive-induced reductions in serum testosterone levels to create multi-male bachelor groups.

The testis is an organ of dual function: spermatogenesis and androgenous steroid hormone secretion. These testicular functions are intimately related, as testosterone synthesis is required for sperm production, as well as for the development of secondary sexual characteristics and normal sexual behavior. The anterior pituitary controls both spermatogenesis and testosterone secretion through its secretion of the gonadotropins, LH and FSH. In turn, the anterior pituitary is regulated by hypothalamic secretion of GnRH, also known as luteinizing hormone-releasing hormone, which is transported to the anterior pituitary via the hypophyseal portal circulation.[1] To date, there has been no convincing evidence of a separate FSH-releasing factor.

LH and probably FSH are released in episodic bursts, with pulses occurring approximately every two hours, although there is a diurnal pattern in which gonadotropin levels peak in the morning and reach a nadir in the evening.[5] For LH, this episodic release has been clearly demonstrated; the half-life of circulating LH is one hour. LH pulses result from the episodic release of GnRH by the hypothalamus. Recent studies indicate that the rate and amplitude of GnRH pulsatile stimulation alters the plasma levels of both LH and FSH. This, in turn, influences testicular function. LH binds to surface receptors on Leydig cells leading to increased testosterone synthesis. Testosterone is released into the blood following LH stimulation of Leydig cells. In humans, testosterone levels are pulsatile in response to the episodic release of LH; peak levels occur approximately 30 minutes after the episodic LH burst. Normal human peripheral plasma testosterone levels are 2.5–12 ng/ml.[5,9]

Luteinizing hormone affects spermatogenesis only indirectly, in that it stimulates endogenous testosterone production. The Sertoli cells possess specific high-affinity FSH receptors. Thus, it is testosterone and FSH that are directed at the seminiferous tubule epithelium.

The hormonal requirements for initiation of spermatogenesis appear to be independent of the underlying maintenance of this process. For spermatogenesis to be maintained immediately after hypophysectomy (pituitary obliteration), testosterone alone is required; to reinitiate spermatogenesis after the germinal epithelium has been allowed to regress completely, both FSH and testosterone are required.[5]

Methods and Materials

This study examines the efficacy of a GnRH agonist and a GnRH antagonist as reversible male contraceptives in LTMs. The five objectives of this study were 1) to assess seven sexually mature LTM males for normal serum gonadotropin and testosterone levels and to relate these to semen quality as well as to age in individual macaques; 2) to assess the efficacy of a depot GnRH agonist in decreasing testosterone levels and sperm production (endpoint: azoospermia) in six LTM male; 3) to observe behavior in GnRH agonist-treated males following four months of treatment to assess male/male aggressive interaction and the potential for the formation of artificial LTM bachelor groups; 4) to determine whether, after six months of GnRH agonist treatment, three males supplemented with depot testosterone to mimic physiologic serum testosterone levels will remain azoospermic; and 5) to monitor whether or not serum testosterone levels and sperm production in three GnRH agonist-treated males rebound after discontinuation of agonist administration. In the event of failure of GnRH agonist treatment, the study would be repeated using a GnRH antagonist.

Objective 1, Assessment 1

Each LTM male was anesthetized with ketamine hydrochloride (Ketaset, Fort Dodge Laboratories, Inc., Fort Dodge, IA) at a dosage of 10 mg/kg injected intramuscularly. Right testicular volume was measured using calipers (length, width, depth). The urinary bladder was catheterized, flushed with 20 cc of 0.9% NaCl solution, and filled with 20 cc of TALP-HEPES medium;[7] the catheter was then removed. Semen was collected using rectal probe electroejaculation (Lane Pulsator III, Lane Manufacturing, Inc., Denver, CO) (three series of 15 stimulations each). The bladder was then recatheterized and bladder contents aspirated into a 20-cc syringe. The ejaculate and bladder samples were assessed for total volume, concentration, and total numbers of motile sperm. Evaluations were made utilizing a Makler chamber (T.S. Scientific, Perkasie, PA), and all samples were recorded on videotape. The animal was then intubated and maintained on 2% halothane for 120 minutes. During this time, blood was collected from the saphenous vein at 15-minute intervals for serum FSH, LH, and testosterone level determination. Serum FSH and LH were assayed using specific double-antibody radioimmunoassay (RIA); serum testosterone was assayed using a solid-phase 125 I RIA (Coat-a-count®, Diagnostic Products Corp., Los Angeles, CA).

Objective 1, Assessment 2

Each male was again anesthetized with ketamine hydrochloride two weeks after immobilization for completion of Assessment 1. Right testicular measurements were recorded, the bladder was flushed and filled with TALP-HEPES medium, the animal electroejaculated, and ejaculate and bladder samples evaluated as described for Assessment 1. Blood was collected from the saphenous or femoral vein for serum testosterone level evaluation. Values determined from evaluation of ejaculate and bladder samples and from serum testosterone determinations from Assessments 1 and 2 were considered pre-gonadotropin releasing hormone (GnRH) baseline data.

Objective 2

One LTM male served as a control animal, receiving monthly intramuscular saline injections. Intramuscular injections of the GnRH agonist, Lupron Depot® (leuprolide acetate for depot suspension, TAP Pharmaceuticals, Deerfield, IL), were administered to the six remaining males at a dosage of 2 mg monthly for six months. Blood was collected for serum testosterone level determination every third day for 15 days following initial injection. Individuals were anesthetized, catheterized, and electroejaculated, and samples collected were

assessed as described on days 15 and 29, and then every three weeks until 180 days post-initial GnRH treatment. Serum testosterone levels were evaluated on day 22 and at the time of each subsequent electroejaculation.

Objective 3

Following four months' treatment with Lupron Depot®, individuals were subjectively assessed for behavior, particularly in regard to aggressive behaviors, and for changes in secondary sex characteristics. Animals were placed in adjoining enclosures separated by an introduction (steel mesh) door. It was felt that if aggressive interactions were consistently reduced, multiple male introductions would be attempted. If introductions were successful, males would be group-housed until day 180, at which time subjective behavioral assessment would be repeated.

Due to inconsistent responses in Objectives 2 and 3, Objectives 4 and 5 were not pursued. Proposed methods and materials of these objectives follow. After 180 days of GnRH agonist administration, the six treatment monkeys were to have been divided into two groups of three each.

Objective 4

Group one was to have continued to receive monthly intramuscular Lupron Depot® injections; a single intramuscular injection of 40 mg of testosterone ester testosterone-trans-4-n-butylcylohexyl carboxylate (20-Aet-1) was to have been administered at the beginning of this period. Each animal was to have been immobilized and electroejaculated every three weeks for 160 days; serum testosterone levels were to have been determined during each manipulation. Changes in aggressive behaviors and secondary sex characteristics were to have been subjectively assessed. After the 160 days, all treatments were to be discontinued.

Objective 5

Lupron Depot® administration was to have been discontinued in the three group 2 treatment males at day 180. Animals were to have been immobilized every three days for 15 days and weekly until day 29 for venipuncture for serum testosterone determination. The animals were then to have been immobilized and electroejaculated every three weeks for the next 180 days; sperm production was to have been evaluated and compared quantitatively and qualitatively with pre-treatment samples. Serum testosterone levels were to have been determined each time the animal was immobilized for electroejaculation. Behavior and secondary sex characteristics were to have been assessed, as was testicular volume.

As GnRH agonist treatment did not produce the desired results, the above protocols are being repeated using a GnRH antagonist, Antide®, ([Acetyl-B-(2-Naphthyl)-D-Ala-D-p Chloro-Phe-B-[3-Pyridyl]-D-Ala-Ser-Ne-[Nicotinoyl]-Lys-Lew-Ne-[Isopropyl]-Lys-Pro-D-AlaNA2), Sigma Chemical Co., St. Louis, MO]. Two baseline assessments were made at a two-week interval beginning eight months after Lupron Depot® treatment had been discontinued. As ceramic implants have never been utilized with Antide® and no other implant has ever been able to deliver Antide® consistently to attain effective serum levels, ceramic implants were first tested in castrated sheep. The sheep were chosen as a model because of availability and ease of venipuncture. Five subcutaneous ceramic implants, each containing 100 mg of Antide®, were placed in one castrated sheep, while a second received five sham ceramic implants. Upon completion of the preliminary sheep study, one control LTM was implanted subcutaneously in the dorsal thoracic area with a sham ceramic implant; five LTM's were each implanted with a single ceramic implant containing 100 mg of Antide®. Serum Antide®, FSH, and LH levels are being measured at three-week intervals, in conjunction with immobilization for electroejaculation, with semen evaluation and serum testosterone determination as described for the Lupron Depot® study.

RESULTS

Baseline Study

Baseline serum testosterone levels for LTM are shown in Table I. As can be seen, there can be as much as a 3.5-fold difference in testosterone levels within individuals over a short period of time. There was great variation in the values between individuals, but the individual ranges of testosterone levels tended toward either high, low, or mid-range. The overall mean serum testosterone was 8.2 ng/ml+0.86; the overall range, 1.6–19.5 ng/ml.

Baseline serum FSH levels are presented in Table 2. The overall FSH mean was 73.2 ng/ml + 4.39, and the overall range was 40.5–136 ng/ml. Serum LH values (Table 3) had an overall range of <19.2–77.2 ng/ml; the overall mean could not be determined from the raw data since many values were below the sensitivity range of the test (<19.2 ng/ml). Table 4 shows individual mean pre-GnRH serum testosterone, FSH, and LH levels. Total motile sperm concentrations and the ages of individual animals are also presented.

Table 1. Serum testosterone levels (ng/ml) over a two-hour period in normal lion-tailed macaques

Individual animals							
Time in minutes	**Control (Lenny)**	**Travis**	**Beeper**	**Saluto**	**Tonto**	**King WM**	**Doobie**
T0	4.6	15.0	1.6	10.5	4.2	13.0	9.8
T15	7.7	12.5	2.5	11.0	4.0	13.0	9.7
T30	7.6	10.5	5.7	19.5	4.2	12.9	8.0
T45	8.2	10.5	4.1	14.0	3.9	12.9	7.1
T60	6.5	8.0	5.7	12.0	4.1	12.5	7.1
T75	9.8	7.9	4.0	12.0	4.2	11.5	5.4
T90	11.5	7.4	3.1	9.3	3.9	10.0	7.0
T105	13.0	7.4	2.5	9.3	3.6	13.0	7.0
T120	—	6.5	2.6	8.5	3.9	11.5	7.2
Mean	8.6	9.5	3.5	11.8	4.0	12.3	7.6
Range	4.6-13.0	6.5-15.0	1.6-5.7	8.5-19.5	3.6–4.2	10.0–13.0	5.4–9.8

Mean of the means = 8.2 ng/ml + 0.9
Range of the means = 3.5–12.3 ng/ml
Extremes of range in normal macaques in this study = 1.6–19.5 ng/ml

Table 2. Serum FSH levels (ng/ml) over a two-hour period in normal lion-tailed macaques

Individual animals							
Time in minutes	**Control (Lenny)**	**Travis**	**Beeper**	**Saluto**	**Tonto**	**King WM**	**Doobie**
T0	91.8	40.5	56.2	67.5	55.8	74.6	60.7
T15	135	43.8	61.7	71.0	53.1	88.4	53.7
T30	136	43.6	52.7	59.6	53.0	88.5	54.5
T45	129	42.1	66.8	69.6	58.7	79.1	58.2
T60	128	50.1	77.4	68.9	54.8	86.2	57.6
T75	134	44.9	81.5	74.0	58.6	907	5.3

T90	117	40.5	70.0	-	65.4	85.6	67.7
T105	115	41.7	79.9	80.8	61.2	98.0	62.6
T120	104	45.9	88	81.2	64.0	90.5	61.1
Mean	121.6	43.7	70.0	71.6	58.3	86.8	60.2
Range	96.8–136	40.5–50.1	52.7–83.8	59.6–80.8	53.0–65.4	79.1–98.0	53.7–65.3

Mean of the means = 73.2 ng/ml + 4.4
Range of the means = 43.7–121.6 ng/ml
Extremes of range in normal macaques in this study = 40.5-136 ng/ml

Table 3. Serum LH Levels (ng/ml) over a two-hour period in normal lion-tailed macaques

Individual animals							
Time in minutes	**Control (Lenny)**	**Travis**	**Beeper**	**Saluto**	**Tonto**	**King WM**	**Doobie**
T0	27.0	<19.2	36.6	43.3	<19.2	31.7	26.9
T15	77.2	<19.2	28.3	39.6	<19.2	31.7	26.9
T30	68.4	<19.2	24.4	36.0	<19.2	27.5	<19.2
T45	56.9	<19.2	21.3	29.7	<19.2	26.4	20.0
T60	51.2	<19.2	19.5	25.1	<19.2	19.8	<19.2
T75	45.5	<19.2	20.2	24.1	<19.2	<19.2	29.2
T90	39.8	<19.2	<19.2	20.1	<19.2	<19.2	28.9
T105	36.0	<19.2	19.2	<19.2	<19.2	<19.2	22.6
T120	29.9	<19.2	21.7	<19.2	<19.2	<19.2	20.0
Mean	48.0	<19.2	23.4*	28.58*	<19.2	23.7*	23.2*
Range	27.0–77.2	<19.2	<19.2–36.6	<19.2	<19.2	<19.2–31.7	<19.2–29.2

Mean of the means = 26.5 ng/ml
Range of the means = <19.2–48.0 ng/ml
Extremes of range in normal macaques in this study = <19.2–77.2 ng/ml
Calculated means are falsely elevated; calculation utilized a value of 19.2 ng/ml for values listed as <19.2 ng/ml.

Table 4. Mean pre-GnRH agonist serum values, motile sperm concentrations and ages of individual male LTMs

	Mean testosterone (ng/ml)	**Mean FSH (ng/ml)**	**Mean LH**	**Motile sperm ($x10^6$/ml)**	**Age (years)**
Tonto	4.0+0.2	58.3+4.5	<19.2	28	5
Beeper	3.5+1.5	70.0+11.4	23.4*	76.2	9
Travis	9.5+2.8	43.7+3.1	<19.2	21	11
Doobie	7.6+1.4	60.2+4.7	23.2*	263.5	13
Saluto	11.8+3.4	71.6+7.1	28.5*	39.4	20
King Wm	12.3+1.1	86.8+6.8	23.7*	49.5	23
Lenny (control)	8.6+2.7	121.6+15.4	48.0	21	24

*Means are averages of LH values which, due to test sensitivity, may be falsely elevated

GnRH Agonist (Lupron Depot®)

All six treatment animals displayed the expected rise in mean serum testosterone levels above baseline. Testosterone levels peaked an average of nine days following initial Lupron Depot® injection, and slowly declined thereafter. Table 5 shows motile sperm concentrations and mean serum testosterone levels pre-GnRH, the same values after four months of Lupron Depot® administration and eight months after the final Lupron Depot® injection.

The reduction in testicular volume in treatment animals from pre-Lupron Depot® volume to 60 days post-initial treatment is presented in Table 6. Table 7 illustrates the percent reduction in individual testicular volumes during the study period. No explanation can be offered for the 18% reduction of the control monkey's testicular volume.

No changes in behavior or secondary sex characteristics were appreciated; therefore, male/male introductions were not attempted. Lupron Depot® was discontinued due to the inconsistency of the results.

Table 5. Sperm counts and serum testosterone levels before and after GnRH agonist (Lupron Depot®) treatment and eight months after cessation of treatment

	Ejac. volume (ml)	**Motile sperm conc. ($x10^6$/ml)**	**Vol bladder sample (ml)**	**Motile sperm conc. ($x10^6$/ml)**	**Total # motile Sperm (years)**	**Mean testost. (ng/ml)**
Pre-GnRH agonist						
Lenny (control)	0.75	28	21	0	21	8.6±27
Travis	0.85	24.5	26	0	21	95±28
Beeper	0.25	17.5	20.5	3.5	76.4	35±15
Saluto	0.75	52.5	20	0	39.4	118±14
Tonto	0.8	35	23	0	28	4.0±02
Doobie	0.65	42	22.5	10.5	263.5	7.6 ± 1.4

King Wm	0.55	49	22.5	1	49.5	123± 1.1
Four months GnRH agonist						
Lenny (control)	0.9	158	22	3.5	219	4.5
Travis	0.6	35	23	0	21	3.3
Beeper	0.75	10.5	25	0	7.8	6.2
Saluto	0.6	7	21	0	4.2	0.32
Tonto	2.5	3.5	21	0	8.8	4.5
Doobie	0.6	42	19	10.5	22.7	2.2
King Wm	0.3	10.5	19	0	3.2	0.9
Eight months post GnRH agonist						
Lenny (control)	2.5	12	29	1.5	73.5	*
Travis	0.75	18.8	22	3	80.1	*
Beeper	2.4	95	19	3.8	300	*
Saluto	2.5	1.8	22	2.8	65.5	*
Tonto	4.0	25	22	0.25	105.5	*
Doobie	2.2	70	19	5	249	*
King Wm	0.25	5.3	24	2.5	61.3	*

*Results pending

Table 6. Testicular volume reduction

	Range	Average
Testicular volume at the beginning of the study	13–44 mm^3	28 mm^3
Testicular volume after 60 days of Lupron injections	12–27 mm^3	19 mm^3

Table 7. Percentage of reduction of testicular size over the treatment period

	Monkey	% Reduction
Treatment group	Saluto	45%
	Doobie	40%
	Beeper	33%
	Travis	26%
	King Wm	17%
	Tonto	8%
Control	Lenny	18%

GnRH Antagonist (Antide®)

Within 24 hours of placement of Antide® implants into a castrated ram, serum LH levels dropped from 38 to 1.2 ng/ml. At 48 hours, the serum LH level was 0.3 ng/ml where it remained for the 14-day duration of the preliminary study. Serum FSH decreased more slowly, dropping from 200 to 159 ng/ml in 24 hours and gradually decreasing to 70 ng/ml by the end of the study. Serum LH levels in the sheep in which a sham implant had been placed approximately 24 ng/ml throughout the study; FSH levels consistently remained around 190 ng/ml.

Antide® implants (100mg) were placed in five LTMs; a sham implant was placed in one LTM. No appreciable side effects from either the Antide® or the implants have been recorded to date. Semen evaluation and hormonal data collection are being performed as this manuscript goes to press.

Discussion

If in the present study, reduction in serum testosterone levels following GnRH agonist or antagonist stimulation affects social standing among troop males, testosterone replacement may be accomplished with testosterone-trans-4-n-butylcyclohe xyl-carboxylate.[6] However, it has not been determined whether spermatogenesis would be reinitiated after testosterone supplementation following GnRH antagonist or agonist-induced FSH reduction.

Baseline Data

All serum parameters measured in this study are variable over time. Sperm collection by electroejaculation is a highly variable process as semen volume and sperm quality may be affected by slight differences in technique, as well as by prior masturbation. Electroejaculation on a periodic basis, therefore, may or may not accurately reflect testicular sperm production. There is also a degree of variability in counting motile sperm, even within the same sample.

With these factors in mind, static serum values or those gathered over short periods of time may not accurately reflect the physiologic hormonal situation. When compared with electroejaculated sperm samples, the true dynamic situation may be further confused. The pulsatile pattern of LH release, which has a 60–90 minute cycle in the Rhesus monkey, was not seen in this study. Serum testosterone levels were variable over time but did not seem to be associated with serum LH. Normal ranges for serum FSH, LH, and testosterone were established for mature fertile male lion-tailed macaques. Although there appears to be a loose direct correlation between age and mean testosterone levels, sperm counts did not correlate with age or serum testosterone levels. Low numbers of animals and samples collected during this study may decrease the validity of these statements.

Lupron Depot®

The GnRH agonist, Lupron Depot®, was chosen because of its availability and ease of administration. At a dosage of 2 mg every 30 days, it consistently produced the expected transient rise in serum testosterone levels.[2,4] However, even though serum testosterone peaked and dropped in all animals, after four months of Lupron Depot® administration, testosterone levels remained higher than baseline in two males, were <30% of baseline in two males, and dropped to castrated-male levels in two animals. Reduction in motile sperm counts occurred in five of six treatment animals; oligospermia was noted in four of six treatment animals. Azoospermia was not produced in any male. Studies in other

macaque species and in man show that there is variability in sensitivity to GnRH agonists; in general, using other GnRH agonists, results similar to those obtained in this study have been noted.[2,4] In this study, the reduction in motile sperm collected from treatment animals ranged from 0 to 94%, with an average reduction of 62.4%. In a study exploring the effect of another GnRH agonist in seven human subjects, although azoospermia was not achieved, an 83% decrease in sperm counts was noted.[2] Results from a study using still another GnRH agonist in rhesus macaques suggests there may be dosage dependency; at a low dosage of agonist (5–10 µl/day), none of five monkeys became azoospermic, at a higher dosage (25 µg/day) four of five males became azoospermic; and at the higher dosage of GnRH agonist (25 µg/ml), administered in combination with testosterone, azoospermia was attained in five of five males.[4] The failure of the current study to produce azoospermia may be dose-related. This would also be supported by the fact that in this study, administration of Lupron Depot® resulted in a 32% reduction in testicular volume, whereas in the rhesus study,[4] low levels of GnRH agonist produced a 44% reduction in testicular size; in the high-dose-level group, a 72% reduction was obtained. No significant behavioral changes were appreciated in any of the Lupron Depot® males, even though serum testosterone in two of the six treatment animals reached castrate levels. Most behavioral studies with castrated male primates have focused on male/female interactions, copulation attempts, and ejaculations.[6,8,10] One GnRH-agonist study concluded that chemically castrated rhesus macaques reacted to females as would surgically castrated males.[10] A study using the brown-headed tamarin, *Saginas fusicollis*, suggests that non-sexual aggression may not vary directly with serum testosterone levels.[3] It is difficult to draw conclusions regarding the current study as castrate serum testosterone levels were attained in only two animals and were maintained at this level for only 30 days due to cancellation of the agonist portion of the study. More data will be gathered on male/male aggressive interaction as the GnRH antagonist study progresses.

Antide® Study

GnRH antagonists immediately block GnRH activity and reduce serum FSH, LH, and testosterone levels.[12] Antide® was selected for this study because of its low histamine-release activity; histamine release is a serious side effect of other GnRH antagonists. No histaminic side effects have been appreciated in either the sheep or macaques implanted with ceramic Antide® implants. The dramatic results noted in the sheep would suggest that both the drug and the ceramic delivery system are effective. We are unable to comment on the efficacy of either the Antide® or the ceramic implants in LTM males, as data collection is ongoing as this paper is being written.

GnRH agonists and antagonists may be powerful tools in the genetic management of primate species. Further research is required before they can become practical for use as reversible male contraceptives.

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The Use of a Long-Acting Neuroleptic in the Mongolian Wild Horse (*Equus przewalskii przewalskii*) to Facilitate the Establishment of a Bachelor Herd
American Association of Zoo Veterinarians Conference 1997
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ABSTRACT

Many animal species have developed social structures which favor the formation of harem-type social groupings. For these species, there is typically a single dominant male in the group along with multiple mature females and their respective offspring. Species with this type of social structure have presented some difficult problems for captive breeding programs in traditional zoos: although the ultimate structure of these groups is typically composed of more females than males, a similar number of both sexes are born. This gender ratio is further complicated by the fact that the majority of traditional zoo facilities cannot provide adequate space for the subordinate males to break away from the main group (as they would do in the wild) to escape physical harm from conflicts with the dominant male. The result is that captive populations often have numerous males that are difficult to maintain in a social group. The aim of this study was to assess the effectiveness of long-acting neuroleptics as an aid in the establishment of a bachelor herd comprised of mature male Mongolian wild horses.

The Mongolian wild horse (also known as Przewalski's horse), which generally exhibits a single male, multi-female social structure, is extinct in the wild and has been one of the true success stories of organized captive breeding efforts around the world.[2] Previous attempts to have more than one mature (older than 5 yr) stallion in a social grouping have resulted in extreme aggression between the males, often resulting in significant injury and on occasion, even death.[5] As a result, the large number of males that is necessary for the genetic and demographic aspects of the captive population are maintained individually in zoos, thereby utilizing significant amounts of the limited space which is available for captive breeding programs. Working with the Mongolian wild horse Species Survival Plan (SSP), the Wilds identified eight mature (mean age 6.6 yr) males and established a fenced, 200-acre enclosure in which these animals could be maintained together as a bachelor group.

To facilitate the formation of this group, each animal was administered a long-acting neuroleptic (LAN), perphenazine enanthate (Trilafon® enanthate 100 mg/ml, Schering-Plough, 2000 Galloping Road, Kenilworth, NJ 07033 USA) in combination with a mid-duration neuroleptic, haloperidol (haloperidol tablets, USP, 10 mg, Par Pharmaceutical, Inc., Spring Valley, NY 10977 USA) prior to release into the pasture. Long-acting preparations of neuroleptic agents have been used in the medical field for many years to aid in the treatment of human psychoses, but have recently been used extensively in wildlife species in southern Africa to aid in the translocation and the adaptation of wild animals to new environments.[3]

Perphenazine is a member of the phenothiazine group of neuroleptic drugs. The effects of the long-acting formulation are generally not seen for 10–12 h after deep, intramuscular injection but tranquilization remains effective for approximately 7 days.[4] The peak effect is usually reached after a period of 72 h, and for this reason, perphenazine enanthate is often combined with another, more rapidly acting neuroleptic such as haloperidol. Haloperidol is a neuroleptic drug that is a member of the butyrophenone group of compounds and may be injected or administered orally. The effects of this drug are seen within several hours of oral administration and last for approximately 10–12 h.[1]

In this study, weights of individual animals were estimated (325–375 kg) and perphenazine was given by intramuscular injection at a dose rate of 0.5 mg/kg and was administered 48 h prior to release of the animals into the pasture. The drug was delivered by projectile syringe (Pneu-Dart Inc., Williamsport, PA 17703 USA) and was injected into the muscles of the neck or shoulder. In addition, each animal was administered oral haloperidol at a dose rate of 0.3 mg/kg 2 h prior to release. All animals were individually identified and marked and all entered the new pasture area within a 1-h period. Observations of the release were performed and all animal interactions were recorded daily for a period of 10 days. Several phases of the introductory period were recorded on video tape.

Close observation revealed minimal interaction between animals upon release and there was significantly less aggression exhibited than expected. The animals formed a loosely structured group shortly after being placed together and the 7–8 day period of tranquilization was characterized by minimal aggression, excitement and anxiety without significant sedation. During this time, the animals became familiar with their surroundings, the boundaries of the pasture and with each other. The effect of tranquillization on herd formation was remarkable: by the end of the observation period, when the neuroleptic drugs were assumed to be no longer effective, it was evident that a level of dominance and social order had been effectively established within the group, with no significant injuries incurred as a result of fighting. The eight Mongolian wild horses involved in this study continue to thrive in this bachelor group and after 4 mo of daily observation, the initial social order appears to have remained intact and there has been no significant aggression observed between the animals.

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The Use of Diazepam for Increasing Infant Survivability in the Cotton-Top Tamarin (*Saguinus o. oedipus*)
American Association of Zoo Veterinarians Conference 1987

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Introduction

Low survivorship of neonates in the first week of life is a problem common to many endangered species kept in captivity (Benirschke *et al.* 1980). Factors influencing neonatal survivorship are multiple and include nutrition, housing, management and behaviour. Maternal abandonment with subsequent starvation, parental attacks of newborn infants and attacks by conspecifics have been reported in a variety of species (Langenberg, Montali 1983; Kirkwood *et al*. 1987; Mallinson *et al*. 1973; Hopf 1981) and similar problems are encountered in laboratory colonies of callitrichids (Kirkwood *et al*. 1983; Kilborn *et al*. 1983).

It has been well established that in callitrichids, experience gained from the social influence of family groupings is important in the development of parental behaviour and the subsequent infant survival (Tardif *et al*. 1984). Improved breeding results have been recorded relative to parity and have been assumed to be related to increasing experience with each parturition (Kirkwood *et al*. 1985; Snowdon *et al*. 1985).

However, it is still not unusual for some “experienced” animals to neglect or attack their offspring, and the breeding performance of captive-bred parent animals is frequently reported to be inferior to that of wild-caught animals (Kilborn *et al*. 1983; Scullion in prep).

An improvement in the infant survival rate of captive-bred animals treated with diazepam (Valium, Roche) for one week post-partum is reported in this paper.

Materials and Methods

The husbandry and management of the unit have been outlined previously (Kirkwood *et al.* 1983). A standard dose of 0.25 mg (i.e., 0.5–0.8 mg/kg in 300–500 g animals) of diazepam was given in bananas daily for one week post-partum to each of the adult members in all family groups where both the parents were captive bred. Data were collected over a one-year period from 25 families. The percentage survivability of youngsters on the treatment regimen was compared with results from five years of accumulated data from captive-bred parents as a control.

Cleaning and changing of any cages were postponed on the day of parturition in a room where a birth had occurred, and only feeding and watering was carried out. Other than this, the routine maintenance and management were similar to that of the animals used as the control group.

Statistical analysis of data using a chi-square test was carried out.

Results

Overall survivability (Table 1) of youngsters born to captive-bred parents was 42% in families which were given diazepam. This compared with an overall infant survivability of 29% calculated from data collected from captive-bred parents over a five-year period of second-generation breeding in the unit. The improvement in overall survivability was statistically significant ($p<0.05$).

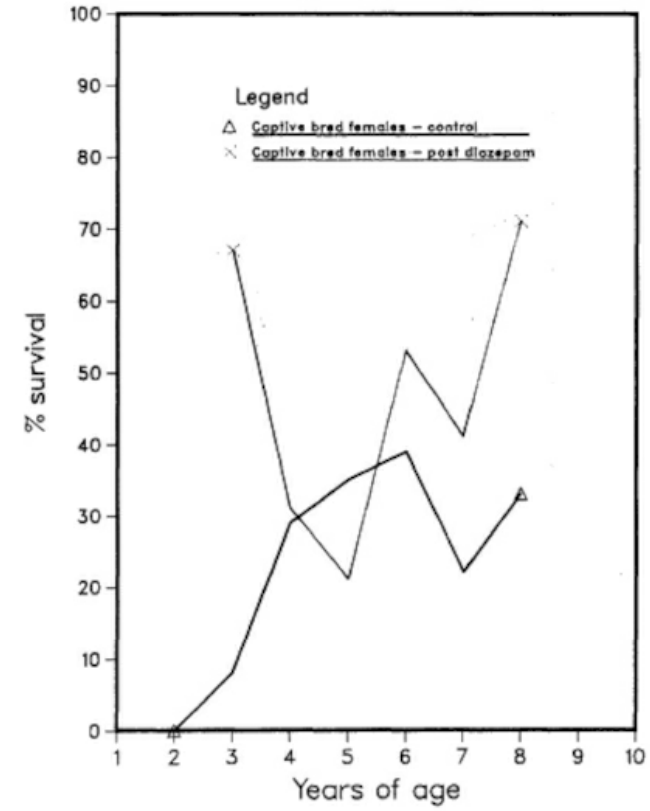
Table 1. Effects of one-week course of diazepam to adult tamarins post-partum on infant survivability

	No. offspring surviving (%)	No. offspring dead (%)	Tot. no. born
Diazepam-treated group*	37 (42)	52 (58)	89
Control group	75 (29)	185 (71)	260

*$p<0.05$

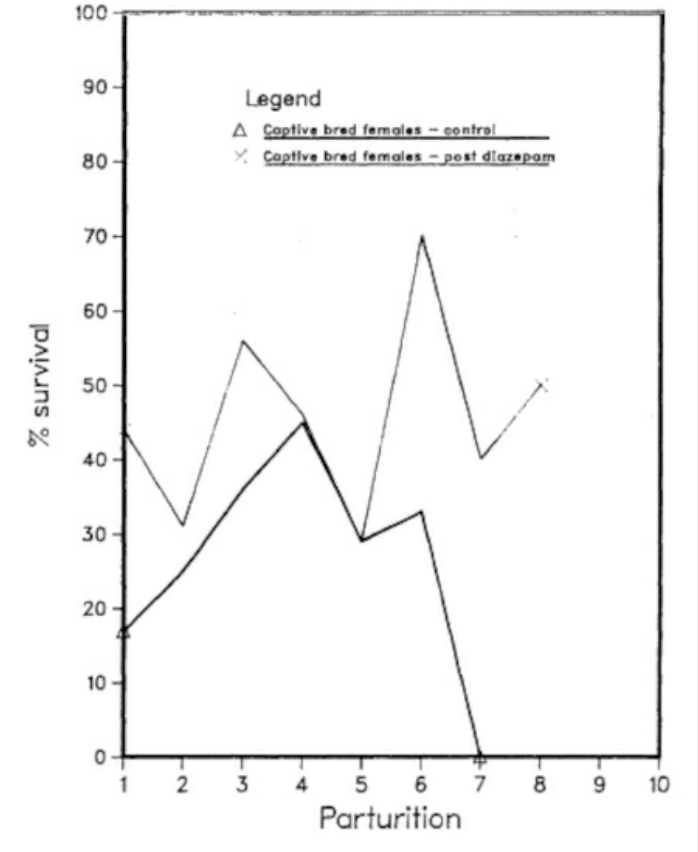
Figure 1 illustrates the trend of improvement in relation to maternal age at parturition. There was a significant improvement in percent survival of offspring born to three-year-old parents ($p<0.05$). Figure 2 illustrates the trend of improvement in relation to parity. There was a significant improvement in percent survival of offspring born to females at first parity ($p<0.05$).

Figure 1. Effects of diazepam treatment on the percentage survival of offspring in captive-born parents in relation to maternal age



p<0.5 for three-year-old females.

Figure 2. Effects of diazepam treatment on the percentage survival of offspring in captive-born parents in relation to parity



p<0.5 for females at first parity.

DISCUSSION

Diazepam is a benzodiazepine derivative which is used in animals as a tranquillizer. In humans, diazepam is used to modify the effects of stress and the associated feelings of

discomfort, tension and anxiety.

In a somewhat analogous situation, azaperone, a tranquillizer, is recommended for use in the domestic pig to prevent the savaging of piglets by sows at parturition (Smith *et al*. 1986), and the condition is generally believed to be related to stress (Hansen, Curtis 1980). The suggestion that stress at parturition may influence parental behaviour in callitrichids is not new (Hampton *et al*. 1966; Epple 1970; Scullion 1987).

The factors which may cause stress at parturition in *S. oedipus* have yet to be defined. Snowdon *et al*. (1985) have suggested that the total survival rate of infants is greatest in those colonies with the largest and most complex cages. Other workers have suggested that the proximity of a viewing public in a zoo environment may be affecting survival rate in zoo-bred tamarins where, despite larger and more complex housing than the laboratory breeding units, the survival rate of infants is low (Glaston *et al*. 1984).

While the small sample size makes interpretation of results in terms of the effect of diazepam on aged animals and multiparous females difficult, the trend is generally one of improvement. This was despite the fact that, in some cases, youngsters that were found on the cage floor (rejected or attacked) on the day of parturition were still included in the results. Diazepam had the effect of causing the parents to reaccept the youngsters, but, in most of these cases, the youngsters died because they were unable to maintain their grip on the parent and would fall off again. If it were possible to accurately predict the day of parturition, then diazepam could be given prepartum, and this may increase the survivorship further. The problem of genetic bottlenecks in small populations is a threat to a number of endangered species (Conway 1980). The technique described herein was also valuable in introducing new blood into the breeding colony. One female was nine years old and was at her fifth parturition before she successfully reared a youngster after a course of diazepam at parturition.

It is not suggested that this technique should be used in preference to a systematic search for stressors, but until such factors are identified, the administration of diazepam at parturition to cotton-top tamarins may be valid. The development of similar techniques in other endangered species, where parental aggression and neglect are paramount in neonatal mortality, should be investigated.

ACKNOWLEDGEMENTS

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 # The Use of Leuprolide Acetate for Male Contraception in a Northern Fur Seal (*Callorhinus ursinus*) Colony

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The Use of Leuprolide Acetate for Male Contraception in a Northern Fur Seal (*Callorhinus ursinus*) Colony
American Association of Zoo Veterinarians Conference 2005

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ABSTRACT

Due to the relatively smaller populations of pinnipeds maintained in zoos and aquaria compared to other non-domestic species, a greater emphasis has been placed upon the development of successful captive reproduction programs, rather than contraceptive techniques, for these species. However, effective population management often requires selective breeding, and the development of reversible contraceptive techniques provides a management tool to achieve these objectives. To date, there have been limited contraceptive attempts in pinnipeds.[1,3,6,7]

Most pinnipeds, including the Northern fur seal (*Callorhinus ursinus*), have a highly seasonal reproductive pattern. Contraception can therefore be achieved through limited intervention during the breeding season. Strategic intermittent administration also minimizes the potential for adverse effects from contraceptive use.[3,7]

The New York Aquarium maintains a colony of Northern fur seals that included six animals (one 11-year-old breeding male, two immature males, and three 13- or 14-year-old females) at the initiation of the study. Two females had conceived eight times in the preceding 6 years. Contraception was achieved by the IM administration of leuprolide acetate for depot suspension (Lupron Depot 3.75 mg, TAP Pharmaceuticals, Inc., Lake Forest, IL, USA). Utilizing a trained presentation behavior, 18.75 mg (five vials reconstituted with 3 ml diluent) was administered monthly for 6 months through the breeding season (28 April to 29 September 2003 and 7 May through 1 October 2004). Male Northern fur seals undergo marked weight changes during the breeding cycle, and throughout the treatment interval his weight ranged from an early high of 260 kg to a terminal low of 130 kg. There were no births in 2004, and no evidence of pregnancy to date in 2005.

Leuprolide acetate has been used successfully for male contraception in Atlantic bottlenose dolphins (*Tursiosp truncatus*),[2,3,7] California sea lions (*Zalophus californianus*),[3,7] and harbor seals (*Phoca vitulina*),[3,7] and to control aggression or other male-associated behaviors among all male groups of California sea otters (*Enhydra lutris*)[4] or California sea lions.[5] Adverse injection site reactions observed in California sea lions in another study[5] did not occur in this Northern fur seal. The seasonal use of leuprolide acetate for male contraception in this Northern fur seal colony proved to be an effective and practical contraceptive technique and may have application to other colonial, seasonally reproductive, pinniped species.

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The Use of Medetomidine as an Oral Sedative in Galliformes
American Association of Zoo Veterinarians Conference 1999

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ABSTRACT

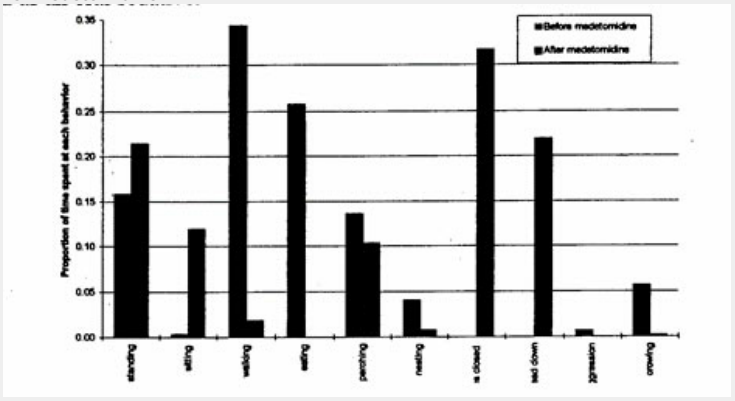
The purposes of this study were to investigate medetomidine as an oral sedative in Galliformes, to determine an effective dose range, and to determine if the effects of this alpha-2 agonist were reversible.

Six male and six female 9-mo-old domestic chickens (*Gallus gallus*) were used in this study with the males housed separately from the females. An ethogram, to document the effects of sedation, was developed prior to the onset of the study. Behaviors that were common to both sexes included standing, sitting, walking, perching, eating, eyes closed, and head down. Male behaviors also included aggression and crowing, while female behaviors included nesting.

The males and females were observed at 2-min intervals for 30 min at the end of which each animal was hand caught and the males were given 0.6 mg medetomidine (0.19–0.2 mg/kg) (Domitor, 1.0 mg/ml, Pfizer Animal Health, Exton, PA, USA) and the females were given 0.4 mg medetomidine (0.21–0.31 mg/kg) PO via a 1-ml syringe (Becton-Dickinson & Co., Franklin Lakes, NJ, USA). After administration of the medetomidine the birds were returned to their enclosures and behaviors recorded for an additional 45 min. The animals were then divided into two groups. Group A (three males and three females) received IV atipamezole (Antisedan, 5.0 mg/ml, Pfizer Animal Health) (3 mg and 2 mg, respectively), in a wing vein. Group B (three males and three females) were not reversed and were bled for plasma biochemical analysis. Behaviors were recorded for an additional 2.5 h. Data for the two groups were compared.

The results of time spent at each behavior before and after medetomidine are presented in Figure 1. The initial effects of the medetomidine were seen within 4 min, the average time for sedation was 6.2 min, and all animals were fully sedated by 10 min. Subjectively, after treatment, all animals had decreased activity, were minimally rousable, and were easy to catch and manually restrain. As evident in Figure 1, walking and eating decreased substantially after the medetomidine was given, whereas eyes closed and head down behaviors increased. Before the medetomidine was administered, the males vocalized an average of 5.6 times in 2 min and the females vocalized constantly. Ten minutes after the medetomidine, there were no vocalizations by either sex.

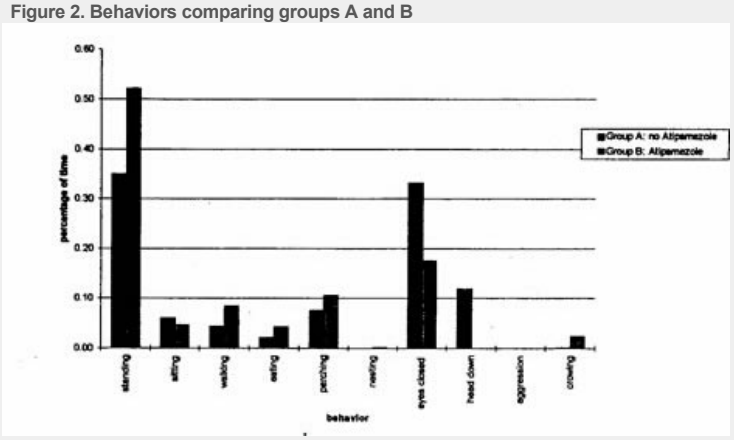
Figure 1. Behaviors of chickens (*Gallus gallus*) before and after the administration of medetomidine



Adverse effects of the medetomidine included one male and one female which were tachypneic at 12 min (respiratory rates approximately 60 bpm). The tachypnea resolved without intervention between 24 and 26 min. The plasma biochemistry results were within normal limits for the species.

After atipamezole was given, initial reversal effects were observed within 30 sec. Figure 2 depicts the behaviors of both groups. This figure demonstrates that group A (animals that received atipamezole IV) spent less time with their eyes closed and heads down. Subjectively, they were also more alert, moved more, and were more easily rousable than group B. Animals in group B remained stationary and were minimally rousable. Approximately 50 min after the administration of the atipamezole, the animals in group A appeared to resedate even though they remained more easily rousable than those animals in group B. There were no adverse effects noted of IV atipamezole treatment and both reversed and non-reversed birds were normal approximately 2.5 h after the administration of the medetomidine.

Figure 2. Behaviors comparing groups A and B



In conclusion, medetomidine (0.25–0.34 mg/kg PO) appears to be a good sedative for chickens when administered orally into the crop in fasted animals. The induced sedation was reversible with atipamezole (1.3–1.6 mg/kg IV). More research is needed in order to determine if medetomidine can be used effectively in food as an oral sedative.

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The Use of Positive Reinforcement Techniques in the Medical Management of Captive Animals
American Association of Zoo Veterinarians Conference 1998

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Abstract

Positive reinforcement training is gaining acceptance as a valuable animal care and management tool to aid in husbandry activities, veterinary procedures, and research protocols. The benefits of such work include less stress on the animal, greater flexibility and reliability in data collection, and a reduced use of anesthesia. This paper presents examples of the use of training techniques to address various medical situations in a number of species in the zoological setting.

Introduction

The comprehensive use of positive reinforcement training has revolutionized the way we care for captive animals.[4,6] By using recognized techniques, many tangible results and benefits can be achieved. Animals are desensitized to frightening or painful events, like getting an injection, so the stress associated with these events is significantly reduced.[5,7] Animals gain the opportunity to voluntarily cooperate in these procedures, rather than being forced to comply. With a greater accessibility to more cooperative animals comes the opportunity to initiate preventative medicine practices and to explore techniques previously seen as less practical on a routine basis such as ultrasound or tube insertions for artificial insemination.[3] With this cooperation comes a reduction in the use of restraint and anesthesia.[1] Many husbandry and veterinary procedures can be implemented with less disruption to all animals, by reducing the need to separate animals from their social groups for many procedures. Finally, experience has shown that trained animals maintain a high degree of reliability in participating in these procedures and are less stressed while doing so.[8]

Methods

The training referred to throughout this paper, and recommended as the approach of choice, is positive reinforcement training. Animals are reinforced with pleasurable rewards for the desired behavioral response. Operationally, it means that the positive alternatives are exhausted before any kind of negative reinforcement is used. On the rare occasions when an escape-avoidance technique is necessary, it is kept to a minimum and balanced by positive reinforcement the vast majority of the time. Punishment, which by definition is used to eliminate a behavior, is only appropriate in a life-threatening situation for person or animal. To dispel a common misperception, positive reinforcement training does not require any food deprivation. Animals are fed their daily allotment of food, and rewards for training use that diet, or consist of extra treats. Finally, this training relies on voluntary cooperation by the animal to be successful.

Through a process termed desensitization, animals learn to tolerate presumably scary or uncomfortable stimuli. In basic terms, desensitization is a process designed to “train out,” or overcome, fear. By pairing positive rewards with any action or object that elicits fear, that fearful entity slowly becomes less negative, less scary, and presumably less stressful. Using this technique, animals have been desensitized to husbandry and veterinary procedures, new enclosures, unfamiliar people, negatively perceived people like the veterinarian, novel objects, strange noises, and other possible aversive stimuli. In fact, the authors have previously reported that animals being desensitized to specific stimuli can, over time, become generally desensitized to anything novel or unexpected.[2]

Voluntary Acceptance of Injections

One of the most useful applications of husbandry training is the conditioning of animals to voluntarily accept injections. When training an animal to accept an injection, the feeling of a needle piercing the skin is a potentially frightening and painful experience. Effective desensitization requires pairing many positive rewards directly with that experience, or with a similar experience. Training may include pairing positive rewards with the experience of being touched with a progression of items, starting with the trainer’s finger, then a capped syringe, and then to a needle with the end cut off so it is blunted, and finally the real needle. The animal must experience this over and over again, with the touch slowly moving from very light to the final experience of actually piercing the skin. If desensitization is done well, the animal will voluntarily accept the injection and recognizable signs of stress and fear will be diminished or absent. To date, injection training has been successfully implemented with many different species and it continues to be a priority behavior for many zoos.

Husbandry Training of Elephants in Protected Contact

Protected contact, as a system for managing elephants, is based on the use of positive reinforcement techniques. All elephants in protected contact should be trained on a wide range of husbandry behaviors, including skin care, body exam, foot care, tusk trimming, blood sampling, vaginal exam, and rectal palpation. Until very recently, many in the zoo community were skeptical of the ability to provide comprehensive medical care for animals functioning in a positive reinforcement-based system where compliance in behaviors is voluntary. That skepticism is eroding away as more examples of successful medical treatment under these conditions are being produced. The following examples illustrate the advances being made in the management of elephants in protected contact.

The Houston Zoo manages two male and four female Asian elephants in a protected contact system. Thailand, the 33-year-old bull, has had chronic nail cracks and abscesses in its front feet for over 10 years. Prior to protected contact, this elephant was maintained in a no contact system, which meant no routine foot care was being performed. Even as nail condition worsened, only minimal foot work was possible. With the introduction of protected contact and positive reinforcement techniques, the animal was easily trained to present its feet through an opening in the training wall or the barn door for foot work.

Over the past 5 years, the elephant has tolerated routine trimming as well as deep trimming into the abscessed areas. The animal has also complied in daily treatment of the abscesses and regular foot soaks in Epsom salts or Nolvasan (Chlorhexidine diacetate, Fort Dodge Animal Health, Overland Park, KS, USA) and warm water once or twice daily for 10 minutes. With the expanded access to the elephant, cooperation with diagnostic techniques was now possible. Radiographs were taken to determine the depth of the infected tissues and to see if there was any bony involvement. Radio-opaque dye was injected into the hole in the foot so that the tract could be identified. The elephant was trained for the procedure by first teaching the animal to extend a front leg through the foot hole and place its foot on a custom-built footrest. Next an old radiograph cassette was used to train the animal to hold steady with the plate in a variety of positions under and around its foot. The final step was to move the large machine in position for the procedure while the animal placed and held its foot in the proper positions.

Currently, the animal’s feet are greatly improved. Granulation beds have formed where the abscesses were, and only small holes are visible on each foot. Routine foot care continues. The feet of this elephant will always be a concern, but through training, the keepers and veterinarians maintain the ability to monitor and treat the animal’s condition, as necessary.

In another case, Kiba, a young bull, was born at the zoo in 1987 with an umbilical stump that was excessively long and soon became infected. Although it was treated daily with Betadine (Purdue Frederick, Norwalk, CT, USA) the infection persisted, and a cantaloupe sized bulge remained present on its abdomen. In February 1992, the elephant was sedated and an ultrasound exam on the herniated area was done, specifically, to check the integrity of the abdominal wall and the potential for entrapment of intestinal loops. The ultrasound showed the area to have healed well. In November 1995, the animal’s umbilical area appeared very swollen. The immediate concern was that a loop of bowel had become trapped in a previously undetected defect. An ultrasound was again needed, but this time, the elephant staff had the opportunity to train the elephant for this procedure. The animal was taught to present its body parallel to the training wall. The animal was then desensitized to the ultrasound exam including palpation of the area, the close proximity of the equipment, the feeling of the contact gel, and pressure of the transducer.

This elephant is an extremely responsive animal and was ready for the ultrasound within days. Fortunately, the ultrasound showed no loops of bowel or defects; the swelling was likely due to mild trauma. The swelling decreased within 2 weeks and has not reoccurred.

Medical Training and the Human/Animal Bond

In November 1994, trainers noticed that lower teeth appeared loose, and ulcerations were present on the mandibular tissue in a California sea lion, Gertie. In December, the animal was immobilized for a biopsy of the ulcerations and to radiograph the mandible. The lower left incisors had severe bone resorption around the roots; the adjacent teeth (right central incisor and left canine) were loose and easily removed. The animal's condition significantly worsened when a pronounced swelling at the medial aspect of the lower left premolar appeared. Due to the severe deterioration of the mandible, a mandibulectomy was scheduled. The oral lesions appeared aggressive and necrotic, predominantly involving the proximal left mandible, part of the right, and the surrounding tissue. Diagnosis showed widespread squamous cell carcinoma throughout the lower mandible.

The prognosis for such a radical surgical procedure was not favorable, but the sea lion came through the procedure better than expected. Several days following the surgery, the animal was completely lethargic, not eating, and in an overall depressed condition. The animal was injected with analgesic antibiotics but little to no response was the result. The decision to euthanatize the animal was made as her condition worsened and recovery seemed unlikely. A trainer with a 7-year history training this animal in a variety of husbandry and show behaviors was brought in as a last resort. Immediately, the sea lion responded to the trainer and was eating fish within days. A diverse behavioral repertoire offered many options to monitor the healing progress as well as help the animal relearn to eat. The animal was trained for a full mouth exam, allowing all teeth and areas of the mouth to be touched and manipulated. This behavior proved instrumental in the recovery. As the area began to heal, suture material had to be trimmed as it worked out of the tissue. This involved the animal holding its mouth open and allowing scissors in and around the surgery site. Topical treatment and cleaning of the site was required, and the animal tolerated this remarkably well.

The sea lion's recovery took over 3 months but was fully successful. The animal was reintroduced to the group and the exhibit pool. Full recovery was largely due to the training that had occurred in the years before the surgery and the trust between animal and trainer that is an inherent and powerful part of positive reinforcement training.

The Versatility of Husbandry Training

As husbandry training grows in the zoological community, many applications and benefits not initially perceived continue to emerge. Some examples of novel application of husbandry training include:

- Getting saliva samples on cotton balls from gorillas
- Training free-ranging hoofstock to accept yearly vaccinations
- Milking a female rhinoceros for supplementation of hand raised offspring
- Performing a vaginal swab on a female warthog
- Training female drill baboons on tube insertion for artificial insemination
- Blood collection on rhinos, tapirs, and adult chimpanzees
- Getting weights on rhino, pygmy hippos, giant anteater, and tapirs
- Holding giant anteaters on target while body measurements are taken

Conclusions

In conclusion, positive reinforcement training is gaining stature among animal managers and veterinarians as a useful tool for enhancing animal health and husbandry. The applied use of positive reinforcement techniques provides the means to proactively address a wide range of medical conditions and to develop and implement an effective program of preventative medicine. These benefits make training a valuable part of any animal management program and have significant implications for overall animal care and welfare.

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The Use of Psychoactive Drugs in Great Apes: Survey Results
American Association of Zoo Veterinarians Conference 2001
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Abstract

A survey was sent to zoologic institutions housing gorillas questioning the use of psychoactive drugs to control aggression. Survey results, as well as a brief discussion of the types of drugs used for behavior modification, are presented.

Introduction

In recent years, psychoactive drugs have been a rapidly expanding component of modern veterinary practice for domestic animals as well as laboratory animals.[1] It is important to remember that the use of these drugs is extra-label and the pharmacologic, toxicologic, and behavioral effects seen may vary greatly from animal to animal. Because many of these drugs have side effects on multiple systems, a complete physical examination is recommended before commencing treatment. A complete behavioral analysis should also be performed, and a set of targeted problem behaviors clearly identified. Oversimplification of a complex behavioral problem may lead to errors that may be dangerous.

All psychoactive drugs are thought to have their effects through five main neurotransmitters in the brain. These neurotransmitters are acetylcholine, dopamine, norepinephrine, serotonin, and γ-aminobutyric acid (GABA). It is important to know which neurotransmitters are affected by each drug class in order to understand the possible related side effects.[6] Acetylcholine is produced from choline and is inactivated by anticholinesterase. Cholinergic receptors have numerous behavioral and physiologic effects that should be understood before initiating treatment with this class of drugs. Many psychoactive drugs affect acetylcholine producing anticholinergic side effects. These may include dry mouth, dilated pupils, GI stasis, and cardiac side effects, which may be of particular concern in captive gorillas.[3] Dopaminergic neurotransmission can occur by at least five subtypes of dopamine receptors, located both pre and post-synaptically. Dopaminergic antagonists may produce behavioral changes without the side effects of cortical depression. Norepinephrine is the precursor of epinephrine and a central neurotransmitter. Norepinephrine agonists are stimulating and increase arousal through several mechanisms, including the reticular activating system. Serotonin (5-hydroxytryptamine) is produced in the brain from tryptophan. There are at least nine serotonin receptor types, both pre and post-synaptically, and all with different behavioral effects. Serotonin is thought to be an important neurotransmitter in the regulation of sleep, pain, aggression, thermoregulation, appetite, and sexual behavior. Gamma-aminobutyric acid (GABA) is an inhibitory neurotransmitter produced from glutamate and is widely distributed throughout the brain. It is thought to have numerous behavioral and metabolic effects.

Psychoactive Drug Groups

Most psychopharmaceuticals used fall into the following four groups: antidepressants, mood stabilizers, antipsychotics (neuroleptics), and anxiolytics.

Antidepressants are generally organized into three classes: the tricyclic antidepressants, the selective serotonin-reuptake inhibitors, and the atypical antidepressants.[6] The antidepressants tend to have a wide range of behavioral effects and can be used to treat other psychologic disorders as well as depression. **Tricyclic antidepressants**: The tricyclic antidepressants are labeled for use in human medicine to treat depression, but also have been noted to have additional usefulness in treating panic disorders and agoraphobia.[6] They have long half-lives, a narrow therapeutic index, and there is a considerable risk of toxicity when overdosed. These antidepressants appear to block norepinephrine and serotonin presynaptic neurotransmitter receptors in the brain, reducing norepinephrine and serotonin turnover, thereby increasing their actions. Tricyclic antidepressants can have numerous side effects including cardiovascular side effects, which can be of particular concern in great apes.[3] Other side effects seen include anticholinergic effects. **Selective serotonin-reuptake inhibitors (SSRI)**: have a wide therapeutic index with a low incidence of side effects. In human medicine, they have been used to treat depression, obsessive-compulsive disorders, eating disorders, and panic disorders.[6] The SSRI enhance central serotonin by blocking presynaptic input at serotonin receptors. They may also act through an increased output or increased post-synaptic receptor sensitivity. They rarely produce sedation and the most commonly seen side effects are gastrointestinal signs, including anorexia, nausea, and diarrhea. Anxiety, agitation, and insomnia have also been seen in humans.[6] **Atypical Antidepressants**: contain drugs that are different from both tricyclic antidepressants and selective serotonin-reuptake inhibitors.

Mood stabilizers include compounds that are dissimilar in make-up that have been used in human medicine to treat bipolar disorders, reduce impulsivity, emotional reactivity, and aggression.[7] These drugs show some promise in great apes due to their effectiveness on aggression; however, careful monitoring of blood levels and side effects are needed.

Antipsychotics (neuroleptics or major tranquilizers) have been used in human medicine for many years.[6] They tend to have marked effects on behavior with a low risk of toxic side effects. These drugs all act as dopamine antagonists and block dopamine receptors in the basal nuclei and the limbic system. They can produce behavioral quieting and decreased emotional reactivity with or without some sedation. The antipsychotics are subdivided into low-potency and high-potency drugs. Low-potency drugs tend to require higher doses and, therefore, tend to have more side effects such as increased sedation, cardiovascular effects, and anticholinergic effects but with a lower chance of producing extrapyramidal side effects. The high-potency drugs require relatively lower doses, have fewer side effects but have an increased incidence of extrapyramidal side effects. Some side effects seen when using antipsychotics include sedation, anticholinergic effects, and cx-adrenergic blocking effects. In humans on high-potency antipsychotics there is also a risk of extrapyramidal motor side effects such as Parkinsonism, dystonic reactions, akathisia, and rarely, neuroleptic malignant syndrome and tardive dyskinesia.

Anxiolytics have antianxiety properties and include benzodiazepines, azapirones, barbiturates, and antihistamines. Most of their use in great apes appeared to be as pre-medications before stressful events such as anesthesia, transport, or introductions. The benzodiazepines and azapirones were the most commonly used and will be discussed. **Benzodiazepines**: in human medicine, drugs in this category have been used to treat anxiety, panic disorders, epilepsy, and insomnia.[7] Because benzodiazepines can have paradoxical effects due to disinhibiting suppressed behaviors, their use to treat aggression should be carefully weighed. Benzodiazepines are believed to act by binding γ-aminobutyric acid (GABA) receptors in the central nervous system. Their anxiolytic properties seem to result from GABA like activity in the cerebral cortex and the limbic system. Some side effects that may be observed when using benzodiazepines include sedation, cortical depression, and muscle relaxation. There is little effect on the respiratory or cardiovascular system, although they may potentiate respiratory depression produced by other sedatives. Benzodiazepines have amnesic properties and may interfere with learning conditioned responses. **Azapirones**: buspirone was reported in great apes and is a non-sedating antianxiety drug that takes approximately one week to initial effect. It has an antianxiety effect gained by blocking serotonin pre-synaptic and post-synaptic receptors. Buspirone causes down regulation of serotonin receptors and also acts as a dopamine agonist in the brain. This drug lacks sedative, muscle relaxant, or anticonvulsant activities and does not impair motor function. **Other Drugs** have been used in veterinary medicine to treat behavioral problems such as barbiturates, antihistamines, narcotic antagonists, and progestin hormones.[7] Beta-blockers reduce signs of fearfulness in humans and have helped in one gorilla case. Androcur and deslorelin implants have also shown promise in aggression problems (Table 1).

Survey Results

A summary of all of these survey results is presented in Table 1. Doses, dosages, and results are listed as given. All animals listed are adults unless otherwise specified.

Table 1. Results of survey

Drug	Dose given	Dosage range	Animal	Drug class	Reason given	Response	Side effects seen
Androcur			Male chimp, male spider monkeys	Anti-androgen	Aggression	Good	None

Alprazolam (Xanax)	0.25 mg SID	0.0024 mg/kg (combined with Prozac 0.2 mg/kg)	Adult female gorilla	Anxiolytic	Anxiety	Good	None
Atenolol	50–75 mg SID	0.48–0.7 mg/kg SID	Adult female gorilla	P blocker	Anxiety	Mixed	None
Buspirone (Buspar)		0.1 mg/kg BID	Adult male gorilla	Anxiolytic	Anxiety	Good	None
Clonazepam (Klonopin)	1–1.5 mg BID		Adult female gorilla	Anxiolytic	Self-mutilation	Fair	None
Deslorelin implants			Lion-tailed macaques	GnRH antagonist	Aggression		? Long-term effects on fertility
Diazepam (Valium)	2.5–10 mg SID/BID		Bonobos	Anxiolytic	Sedation	Mixed	Titrate to effect
	20 mg BID		Female gorilla		Anxiety		Drowsiness at higher doses
	1.25–2.5 mg		All ages of gorillas		Pre-med		Depression
	30–60 mg		Gorillas		Intros	Mixed	
		0.25 mg/kg	Gorillas		Premed/sedation	Good	
		0.2–0.6 mg/kg	Gorillas all ages		Premeds	Good	
Fluoxetine (Prozac)	10–40 mg SID		Adult female gorilla	Anti-depressant	Self-mutilation	Poor	Got worse
		0.3–0.6 mg/kg SID	Juvenile male gorilla		Anxiety	Good	
		0.12 mg/kg starting	Male gorilla				
	20–80 mg SID				Aggression/combined with Haldol	Poor	Lethargy and diarrhea
Haloperidol (Haldol)		0.1 mg/kg	Gorilla	Anti-psychotic	Anxiety		No effect
	1–4 mg TID (increased over 4 days)		Female gorilla		Anxiety	Slight improvement	
	3.75 mg BID then SID		Male gorilla		Post-op	Calm but picked sutures	Drowsiness
	2.5 mg IM	Combined with diazepam	Female gorilla		Post-op	Good	Drowsiness
	15–20 mg		Male gorillas		Intros	Calm but still aggressive	
	10 mg		Juvenile male		Intros	No effect	
	0.5 mg BID		Female gorilla		Anxiety	Good	
	10–50 mg SID	0.06 mg/kg to start	Male gorilla		Aggression	Poor	Lethargy at high dose
Lorazepam (Ativan)	3 mg BID	0.2 mg/kg	Female gorilla	Anxiolytic	Anxiety, group intro	Good	Lost fear, too playful
Midazolam (versed)	5–10 mg 12.5 mg 70 mg		Gorillas gorillas female gorilla	Anxiolytic	Pre-med Pre-med Pre-med	Mixed	Excitation
Naltrexone	50 mg SID		Female gorilla	Narcotic antagonist	Self-mutilation	Poor	None
Paroxetine (Paxil)	20 mg SID	0.2 mg/kg	Female gorilla	Anti-depressant	Anxiety	Good	None
Quetiapine (Seroquel)			Male gorilla	Anti-psychotic	Aggressive to females	Fair	None
Risperdal	4mg SID x 14 days, then increased by 2 mg q 4 days to 12 mg BID		Male gorilla	Anti-psychotic	Aggression	Mixed	Sedation, GI
Sertraline (Zoloft)	50–100 mg SID		Female gorilla	Anti-depressant	Self-mutilation	Good	Drowsiness, anorexia
	100 mg SID		Female gorilla		Self-mutilation	Good when combined with Clonazepam	
		0.5–2.2 mg/kg SID	Male gorilla		Aggression	Poor	
Thioridazine (Mellaril)	200 mg SID		Male gorilla	Anti-psychotic	Facilitate breeding	Mixed	Drowsiness at high doses
	80 mg BID x 7 days 90 mg		Male chimp		Aggression	Good, switched to generic	Drowsiness at higher dose

	BID x 7 days 150 mg BID x 7 days (maintenance at 100 mg BID)					liquid for better acceptance and cheaper	
	50–350 mg SID 200 mg SID		Male gorilla				
	100 mg BID		Male chimp		Aggression		
Zuclopenthixol Dihydro-chloride	0.2–0.4 mg/kg BID		Gorilla	Antipsychotic	Intros and transport	Very good	

CONCLUSIONS

While the use of behavior modifying drugs may aid in the resolution of a problem, environmental management and behavioral modification are also needed in most cases. Veterinarians must understand the ethical issues surrounding how and when to use these drugs in order to maximize their effectiveness. Survey results indicate that as a whole, psychoactive drugs used in great apes to try to curb aggression have not been successful. This could be due to several things including, but not limited to, misdiagnosis of behavioral problem type, multifactorial causes, incorrect dosing, inconsistent observations, and short treatment times. Certainly, more research is warranted in this field.

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Training and Enrichment in a Zoological Setting
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Introduction

Historically, the word 'training' conjures up images of lions jumping through hoops or parrots riding a bicycle on a tight wire. However, at Disney's Animal Programs the word 'training' cannot be used without the word 'enrichment'. These two processes now go hand in hand and will allow animals to exhibit their natural array of behaviors and assist, in turn, the veterinarians in medical procedures. This talk will focus on training zoo animals for veterinary procedures. However, the act of training can also enrich an animal's life by providing positive enriching environments.

Enrichment

Enrichment can be defined as a process for improving or enhancing animal environments and care within the context of their inhabitants' behavioral biology and natural history.[1] It is a dynamic process in which changes to structures and husbandry practices are made with the goal of increasing behavioral choices available to animals and drawing out their species-appropriate behaviors and abilities, thus enhancing animal welfare.[1] More information on this process can be found at www.animalenrichment.org.

The enrichment framework developed at Disney's Animal Programs provides a process to ensure that our enrichment program meets the needs of the animals, and provides them with the opportunity to experience enhanced animal welfare. Animal welfare involves both the physical health of the animals (e.g., preventing and treating illnesses and injuries), as well as their psychological well-being. As an important aspect of welfare, an animal's psychological well-being is influenced by whether it can:

- Perform its highly motivated behaviors
- Respond to environmental conditions using its evolutionary adaptations
- Develop and use its cognitive abilities
- Effectively cope with challenges in its environment

Training

The words 'animal training' often conjures up images of animal side shows, where animals were trained to complete a variety of unnatural acts for our entertainment. Training now has a different context which includes "training" animals to exhibit a variety of natural behaviors for husbandry, education, and yes, entertainment purposes.

Animals continually gather information and respond to it. This process may be described as learning. A similar definition might be that learning is a change in behavior that occurs as the result of practice. Whether we are aware of it or not, as animal caretakers, we influence what animals in zoos and aquariums learn. In other words, as caretakers, we are teaching or training our animals all the time. Sometimes we are aware of what we're teaching or training; we make conscious efforts to "train" animals to exhibit a variety of behaviors for husbandry, education, and entertainment purposes. Sometimes we influence (train) animals' behavior inadvertently through our actions, our husbandry routines, or through other stimuli present in the captive environment. In effect, animal care staff is always training and they need to be aware of that fact. Training is all about associations. The key to an optimal captive environment is to facilitate animals' opportunities to make associations that enhance their wellbeing.

Setting Up A Training Program

A well-planned, consistently delivered training process is critical to the success of any program. To achieve this type of program, many facilities utilize a framework that is taught in American Zoo and Aquarium Association's (AZA) course, Managing Animal Enrichment and Training Programs, called the "**spider**" model. Steps in this framework include Setting goals, Planning, Implementation, Documentation, Evaluation, and Re-adjusting. More information on this process can be found at www.animaltraining.org. It is beneficial to start a training program by determining the overall behavioral goals (i.e., detailing the specific behaviors to be trained). This is the first step in the **spider** process, setting goals. During this goal development process, it is important to include all parties involved with the management of the animals. This may include meeting with and seeking feedback from keepers, veterinary staff, nutritionist, behavioral husbandry staff, curators, and managers. Goals should be based on the needs of the staff. For example, a veterinarian would like a blood sample from the animal. The goals in this case would then be to train an animal to enter a crate and desensitize to a blood draw. The next step is planning. Having everyone on the same page with clearly laid out plans, assignments, and timelines helps to facilitate a smooth process. Defining roles and creating clear avenues of communication among all participants is also important. This can be accomplished through regularly scheduled team meetings, a consistent method of documentation, and continual communication among all staff involved in training. Planning also includes creating a training plan, a step by step guide for how trainers are going to shape the behavior. Training plans are meant to just be a guide, a way for the trainer to think through the process before they start training an animal. Creating a training plan also creates a historical document for future reference. One way to write a plan is to establish what the final behavior will look like and then break down the behavior into a series of small steps. These small steps are called "successive approximations". The next several sections will discuss other considerations when starting a program.

Selecting and Shaping Behaviors

It is possible to train reptiles for a variety of behaviors. In order to select the most effective and appropriate techniques and behaviors for the species, it is necessary to consider the following:

1. **The animal's natural history** – it's important to consider the animal's predispositions. For example, it may make more sense to ask an arboreal animal to station off the ground/on a perch.
2. **The animal's individual history** – it's important to consider the early rearing/life experiences of the animal being trained. For example, an animal that's imprinted on humans may be trained substantially differently than a wild-caught animal brought in as an adult.
3. **The animal's function or "role" in your collection** – the animal may be in the collection as part of a breeding program or part of an education program. The type of training and your level of interactions with that animal may differ depending on the function this animal serves in your collection.

When selecting shaping techniques the above must also be considered as well as the safety of both the staff and the animal. Two shaping techniques that work well with reptiles are baiting and targeting. Baiting is when a trainer uses food to lure an animal. Tongs or forceps can be utilized to hold the food as an extension of the trainer's hand. Targeting can also be used effectively with reptiles. The animal must be previously trained to touch a body part to the target, for example a crocodilian can be trained to touch the end of its snout to a buoy. Once this behavior is reliable, the target can be a very useful tool to get an animal to move from one location to another or into a crate.

Facility

When beginning a training program, it is best to start training in an area that is safe for the animal care staff and the animal. An area where trainers can have access to the animal safely is usually the night quarters, holding area. Training can also be done in crates, chutes, or even open exhibit areas. Because all facility designs are different, training staff will have to be creative and utilize the space available. For safe access to an animal for behaviors such as blood draw, it is recommended the animal be trained to enter a crate which allows safe access to body parts. It is important to remember that a fancy, expensive facility is not necessary to accomplish a successful training program, just a creative mind.

Reinforcement

A critical component to positive reinforcement training is finding reinforcement or reward for which an animal is willing to work. Often food reward is offered because most animals respond positively when given food. However, in many mammal species, physical contact like scratching or brushing may also be used as a reward.

In most cases, when using food as a reward, the animals' regular diet can be used for training. Dividing the animal's diet into smaller portions can provide great opportunities for more training sessions. It is helpful to have a bucket or a waist pack containing diet near the trainer, so that reinforcement can be easily retrieved and delivered in a timely manner. Delivery of meat reinforcement can occur by placing a food item on tongs and passing it through the barrier or by tossing meat over or under the barrier. Hand feeding is not recommended with carnivorous species. It can be a safety issue for the keeper, and can also cause the animal to become focused on and aggressive toward the trainer. With respect to herbivores and grazers, care must also be taken as there are many rhino keepers missing the end of a finger from an accidental bite. Often placing the food in a reward in a plastic cup and then dumping on the ground after the training is complete will form the association.

Record Keeping

It is important for trainers to keep records of all sessions. Trainers can go back and look for patterns in the information which helps keep consistency among team members, and leaves a historical record for others. For examples of documentation methods go to www.animaltraining.org

Case Studies

The following are examples of training programs with crocodiles, Komodo dragons, giraffe and gorillas to name a few.

Summary

These are just a few examples of how zoo animals can be trained to facilitate medical care. These techniques can be applied to a multitude of species and sizes of mammals, reptiles and birds. It is important to remember when designing a training program that knowledge of the species' natural and individual histories is critical to understanding the needs and capabilities of the animal. A good partnership between the veterinarians and animal care staff is also crucial to the success of any training program. The responsibility lies with us to continually strive to learn more in order to better care for captive animals, including reptiles. Training can have a huge impact on an animal's welfare and, although it may require an investment of time and effort, it often pays off in an improved quality of life for the animal.

Resources

1. www.animalenrichment.org: Disney's Animal Enrichment web site
2. www.animaltraining.org: Disney's Animal Training web site

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Treatment of an Asian Elephant (*Elephas maximus*) with Fluoxetine
2016 Joint AAZV, EAZWV, IZW Conference

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ABSTRACT

A 51-year-old female Asian elephant (*Elephas maximus*) was examined due to a recent increase in aggression towards keepers and herd mates. She also regularly exhibited many behaviors considered to be associated with anxiety or stress in elephants such as frequent trunk sucking, "tongue play" and repetitive rubbing on the bars of her pen. She was housed with two other elephants in a partly wooded 15-acre paddock with a barn, in which the elephants were confined at night and during the coldest winter months. Historically, haloperidol had been used intermittently to decrease her aggression with varying degrees of success reported by different keepers and veterinarians. At the time of evaluation by a veterinary behaviorist, she had been receiving haloperidol for approximately 4 months with an increase in dose approximately 3 months earlier. At the conclusion of the visit, the haloperidol dosage was decreased slowly over a period of several weeks and fluoxetine begun at a low dose of 0.25 mg/kg and increased slowly over a period of 2–4 weeks.[1] Within 2 months, fluoxetine was being administered at 1 mg/kg daily with minimal effects on appetite and a slight decrease in aggressive and anxiety related behaviors. Over the following months, anxiety related behaviors and aggression continued to decrease, and blood counts and serum chemistry profiles repeated at 6 months and 1 year demonstrated no abnormalities likely to be associated with the administration of fluoxetine. This case suggests that fluoxetine is safe and may be useful at managing aggression associated with anxiety in Asian elephants.

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Use of Buspirone to Manage Undesirable Behavior in Three Species of Carnivores
American Association of Zoo Veterinarians Conference 2005
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Abstract

Occasionally captive nondomestic carnivores exhibit undesirable behaviors that may range from aggression to self-mutilation. These behaviors have been mitigated by a variety of methods including the addition of new enrichment items to their environment, or the use of anxiolytic agents.[1-3] The use of buspirone in three species of carnivores: a raccoon (*Procyon lotor*), a badger (*Taxidea taxus*), and an African lion (*Panthera leo*), lessened or solved the behavioral problems exhibited by these animals without noticeable side effects.

Case 1

A neutered 5-year-old male raccoon weighing approximately 9.5 kg developed a habit of barbering the fur of the rear third of its body, its tail, as well as barbering the hair of its brother's coat. While this behavior did not pose any health problems, it did result in an abnormal appearance to these exhibit animals. Initially the raccoon was given additional enrichment items with treats routinely hidden within the exhibit in an effort to break their barbering habit. Bitter apple chew deterrent was placed on the fur of both animals and had no effect on the barbering. When these methods proved unsuccessful the raccoon was treated with buspirone (buspirone hydrochloride, Par Pharmaceutical Inc., Spring Valley, NY, USA) 0.26 mg/kg PO BID to manage the behavior. During the first month of treatment, the animal stopped barbering its sibling; however, it continued to barber the lower third of his body and tail, but at a reduced amount. After 1 month of treatment, the buspirone dose was increased to 0.53 mg/kg PO BID. It stopped barbering its body while on the higher dose, but continued to barber the tail, never allowing the hair to grow back. In an attempt to stop the tail barbering, the buspirone was discontinued and amitriptyline (AstraZeneca Pharmaceuticals, Wilmington, DE, USA) 10 mg PO SID was given for 23 days which appeared to cause the barbering of the tail to worsen with excoriations evident for the first time. The amitriptyline was discontinued, and no other drug regimens were started. The excoriations on the tail healed but the animal continues to barber the hair on its tail. The buspirone appeared to help to extinguish the barbering of the body hair and the hair of the other raccoon; however, it did not completely extinguish the behavior of tail barbering in this animal.

Case 2

A spayed female badger weighing approximately 11 kg had a lifelong history of apparent anxiety attacks which generally were manifested by loud screaming and obvious agitation. Over the years the worst episodes of this behavior resulted in the animal biting at sides of its body causing excoriations to the skin. Diazepam (Valium, Roche Pharmaceuticals, Nutley, NJ, USA; 0.7 mg/kg PO SID) was given to manage the more severe episodes. The lesser episodes had been controlled fairly well with the addition of enrichment to the animal's exhibit. Over a 10-year period, the episodes grew worse in both intensity and duration. The typical side effects of the valium (inactivity and a tendency to sleep most of the day) were suboptimal for this exhibit animal. After a particularly severe set of episodes the diazepam appeared to have little effect and was discontinued in favor of a new anxiolytic drug, buspirone, which was given at a dose of 0.45 mg/kg PO BID. After 3 weeks of treatment the episodes of self-mutilation ceased, and the animal appeared content and playful most of the day. The buspirone appeared to effectively control the aberrant behavior in the badger, and the animal was maintained on the drug twice daily for over 18 months with no obvious side effects.

Case 3

A 17-year-old intact male lion weighing 183 kg housed with a female lion periodically exhibited very aggressive and possessive behavior towards its mate and its surroundings. This behavior occurred 2–3 times each year, with each episode lasting from 2 to 14 days. These events appeared to occur sporadically but were occasionally precipitated by large noisy crowds of people. The male often refused to eat or drink, and if on exhibit, would not allow his mate to eat, drink or leave the exhibit area. The male was treated with 0.11–0.33 mg/kg diazepam PO BID. whenever these aggressive episodes occurred. The diazepam did not provide a reliable steady behavioral state and the lion would either appear too aggressive or too groggy. The episodes could be controlled with just a few days of diazepam treatment if the problem was recognized in the morning and the lion was kept in the night quarters for treatment. However, if the lion was allowed into the exhibit during the time when one of the aggressive episodes occurred, it frequently refused to come into the holding area, refused to allow the female in, and sometimes could not be administered medication for many days. These periods could last for up to 2 weeks. The animal would be maintained on 0.11–0.33 mg/kg diazepam PO BID until it was no longer displaying possessive behavior as determined by the keepers when they arrived in the morning. Based on the animal's behavior, the diazepam dose could be lowered or it could be discontinued. Because of the inconsistencies produced by the diazepam treatment, the treatment plan was changed to buspirone. The optimal dose of buspirone for this animal appears to be 0.16 mg/kg PO in the morning and 0.11 mg/kg PO in the evening. The lion has been maintained on this dose since May 2004. The lion exhibits all of its normal behaviors with no aggressive or possessive behavior seen. Because there have been no noticeable side effects to the buspirone, there is no plan to discontinue the drug at this time. Treatment of the male with buspirone has improved the quality of life for both the male and the female lion.

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Use of Depot Leuprolide and Cyproterone to Control Aggression in an All-Male California Sea Otter (*Enhydra lutris nereis*) Colony
American Association of Zoo Veterinarians Conference 1998

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ABSTRACT

Male marine mammals in zoos and aquariums are sometimes maintained alone or in same sex groups for behavioral demonstrations, to prevent breeding, control aggressive behavior, or retain the genetic representation of animals for future reproduction. These management schemes may be complicated by undesirable behaviors (aggression, anorexia, and loss of operant training). While castration effectively minimizes these problems, anesthesia and surgery are required and it eliminates future reproduction.

Leuprolide acetate is a long-acting, but reversible, gonadotropin-releasing hormone (GnRH) agonist. Administration initially results in an increase in follicle stimulating hormone (FSH) and luteinizing hormone (LH) causing transiently elevated testosterone. A progressive suppression then occurs reducing circulating testosterone levels to those of a castrate. Leuprolide acetate has been previously demonstrated to suppress testicular function in Atlantic bottlenose dolphins (*Tursiops truncatus*).[2,3] Cyproterone is an orally administered testosterone receptor blocking agent. In addition to blocking androgen receptors, it exerts a negative feedback on the hypothalamic pituitary axis inhibiting LH secretion and consequently suppresses testicular testosterone production.

Four male California sea otters (*Enhydra lutris nereis*) were exhibited together at the Aquarium for Wildlife Conservation. As they matured, intraspecific aggression developed until eventually they could no longer be maintained as a compatible colony. During this study (July 1996–December 1997) parenteral leuprolide acetate in either a 1-month (phase 1)[1,4] or 4-month (phase 2) depot suspension, or oral cyproterone acetate (phase 3), were administered in succession to control aggression.

Four otters were included in phase 1.[1,4] One otter died of causes unrelated to the study and the remaining three otters were included in phases 2 and 3. Ages and weights of otters ranged from 3.5–6 years, and 20–34 kg, during the course of the study. Otters were manually confined in an otter restraint device for venipuncture and all injections.[5]

During phase 1 otters received 3.75 mg (0.11–0.19 mg/kg) of a 1-month depot formulation of leuprolide acetate IM at monthly intervals. Initiation of drug administration in each otter was staggered, so animals received 3–7 injections in a 6-month interval. In phase 2, otters were given 30 mg (0.9–1.1 mg/kg) of a 4-month depot formulation of leuprolide acetate administered either IM or SC twice at intervals of 3.5–4 months. Leuprolide was administered in the dorsal surface of a pelvic limb. In phase 3, otters were given 50 or 75 mg (1.5–2.3 mg/kg) cyproterone acetate PO, SID for 84 days.

Testicular lengths of two otters were measured before the initial treatment and at the end of each phase. Marked testicular atrophy occurred and was maintained in all phases. Pretreatment testicular length (mean ± SD) (53±3.5 mm) was significantly greater (paired t-test; $p<0.05$) than at the end of each phase (35±2.5 mm, 27.5±2.5 mm, and 26.8±2.6 mm for phases 1, 2, and 3; respectively). Mean testicular length in phase 1 was significantly greater (Tukey Honest Test, $p<0.05$) than in phases 2 and 3; there was no significant difference in testicular size between phases 2 and 3.

Testosterone levels were determined by radioimmunoassay before treatment and then monthly in phase 1; 3–5 times at 4–6-week intervals in phase 2; and 2–3 times 4–12 weeks after initiation of treatment in phase 3. Testosterone levels of the youngest otter were below the assay detection limit (<0.05 ng/ml) on all sampling dates. Pretreatment values for the two others ranged from 0.31–2.28 ng/ml. Testosterone levels in phase 1 decreased after 1 month of treatment (<0.05–0.19 ng/ml) and after 2 months of treatment all were undetectable. In phase 2, all testosterone levels except one (0.7 ng/ml) were below the assay detection limit. In phase 3, testosterone was below the assay detection limit on all sampling dates.

Despite the effectiveness of leuprolide at inducing testicular atrophy and testosterone suppression, with consequent reduction in intraspecific aggression, treatment was discontinued due to adverse injection site reactions. These consisted of anorexia and depression with moderate to marked injection site lameness, swelling, or sterile abscesses. Preventing or treating these reactions with either diphenhydramine (1.5 mg/kg PO, BID for 7 days) or flunixin meglumine (0.9 mg/kg PO, SID for 5 days) was not successful while carprofen (1.5–2 mg/kg PO, BID for 5–10 days) was a more effective treatment. Some otters were also treated with trimethoprim sulfa (33.6 mg/kg PO, SID for 10 days). No adverse effects were noted in phase 3.

Administration of depot leuprolide acetate or cyproterone acetate was successful in suppressing testosterone and controlling aggression in an all-male sea otter colony. This enabled otters to be maintained in a more compatible social group. Leuprolide was more effective than cyproterone in controlling aggression. Compared to castration, advantages of these medications include no requirement for anesthesia or surgery and reversibility. Disadvantages of leuprolide are the drug cost, injection site reactions, and the necessity for frequent animal handling. Cyproterone acetate is currently not commercially available in the United States but offers the advantage of oral administration with no animal handling required. These treatments have potential application for the control of male-associated undesirable behaviors in sea otters in zoos and aquariums. A trial with a long-lasting GnRH agonist implant (deslorelin) is currently underway.

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Use of Neupogen® (Filgrastim) in a Bottlenose Dolphin (*Tursiops truncatus*)
American Association of Zoo Veterinarians Conference 2008
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ABSTRACT

In December 2006 all the dolphins from L'Oceanogràfic were removed from their exhibit and separated into several other minor enclosures during pool remodeling. When the work was finished 3 months later, all the animals were placed back in the dolphinarium. During the previous week one young male dolphin (body weight was 126 kg) was already experiencing a social stress situation in his own small group. According to the unstable blood work, some relevant rake marks and the concern this animal was potentially immunocompromised, antibiotic treatment with amoxicillin + clavulanic acid (Augmentine®, Glaxo Smith Kline, Tres Cantos, Madrid, Spain) at 10 mg/kg PO BID was initiated and this animal was separated from the aggressive pool mate.

Once in the dolphinarium, after 5 days of controlled regrouping of the entire original group, trauma from conspecifics resulted in new injuries, group isolation, and eventually shock of this juvenile dolphin.

The day of the crisis, although the animal was performing a show in the morning, at noon the dolphin was completely stuporous with tremors, became unable to swim and eventually unable to keep position in the water. Emergency support treatment was applied to stabilize the animal. Six hours later, he was able to swim without assistance, especially under the effect of pain relievers such as metamizole (Nolotil®, Boehringer Ingelheim España, Sant Cugat del Vallés, Barcelona, Spain) at a total dose of 1 g IM. The initial total leukocyte count was 2100 cells/µl with 94% neutrophils and 2% band cells (absolute leukopenia). Although there was an evident drop in ALKP, albumin, and iron, other relevant markers of inflammation such as ESR and fibrinogen were within normal ranges. A decision was made to institute among others, a more aggressive antibiotic therapy including amikacin (Biclin®, Bristol-Myers Squibb, Madrid, Spain) at 14 mg/kg IM SID) to cover the potential septic shock or septicemia.

Twelve hours after the initiation of the stabilizing therapy the WBC increased slightly up to 2720 cells/µl. Six hours later another blood sample showed a decrease to 1400 WBC/µl and another 6 hours later it fell to 1040 WBC/µl. At this point the animal had greatly improved in attitude, was swimming almost normally and was eating on its own. A decision was made to remove the clavulanic component of the antibiotic therapy and to decrease as much as possible, the metamizole as these two drugs have been previously described to potentially cause granulocytopenia and leukopenia in humans.[4,6] Additionally, dexamethasone (Fortecortín®, Merck Farma y Química, S.A., Mollet del Vallés, Barcelona, Spain) was used at a total dose of 30 mg IM to revert the shock. It was then substituted by progressive decreasing dosages of prednisone (Dacortín®, Merck Farma y Química, S.A., Polígono Merck, Barcelona, Spain). Finally, a recombinant human granulocyte colony-stimulating factor, G-CSF, the filgrastim (Neupogen®, Amgen Europe B.V., Breda, Holland) was administered at a total dose of 30 MU (0,0025 mg/kg) IM in an attempt to increase neutrophil production in this animal.

Twelve hours after the first filgrastim injection the WBC dramatically increased to 5160 cells/µl with 96,9% neutrophils and a band and proleukocite count of 76%. A second dose of the same amount of Neupogen® was administered 24 hours after the first one.

After these two filgrastim doses, the WBC kept gradually increasing during the next few days up to a maximum of 16400 cells/µl on the sixth day after the first administration. Meanwhile band cell counts kept decreasing, reaching normal values for this individual (1,7%) on the tenth day. The hemogram and blood chemistry was completely normal regarding baselines for this individual 19 days after the first filgrastim injection.

The viability of this initial increase of highly immature leukocytes to combat bacterial infection could be controversial. Furthermore, the potential host antibody production could inactivate the filgrastim in case of prolonged or successive treatments in allospecific patients. In this case there was no decline in the WBC series suppression after the treatment as described by other authors in other species.[1,2,5] In fact, they kept increasing during the 5 days following the second filgrastim dose. Additionally, in this particular case, filgrastim seemed to increase proliferation much faster than the previously reported experience in a killer whale (*Orcinus orca*),[3] rising up not only granulocytes but all other leukocyte populations and even red blood cell precursors.

In the authors' opinion, this case suggests that filgrastim is potentially useful to treat neutropenic bottlenose dolphins at a dose of 0,0025 mg/kg IM SID for 2 days, aiding to overcome infection especially in the event the bone marrow is not properly responding.

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Use of Neuroleptic Agents in the Control of Intraspecific Aggression in Great Apes
American Association of Zoo Veterinarians Conference 1993

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Neuroleptic drugs have been used frequently in human medicine to control schizophrenia, alter mood or attitude, or reduce behavioral abnormalities. Their use improves social adaptation and reduces belligerent, dominant, or aggressive behavior. The use of these drugs in zoo animals has generally been limited to ungulates since they show a higher incidence of capture-related stress and trauma.

Two intermediate-acting neuroleptic agents (haloperidol and thioridazine) were used in combination with an antiparkinsonian drug (biperiden) to control aggression and maladaptive behavior in gorillas and chimpanzees. The following are summaries of two cases.

Case 1

A 12-year-old, 65-kg, male chimpanzee (*Pan troglodytes*) who had been living in isolation for several years was donated to the Jerez Zoo. Introduction to an adult female who had recently lost her mate was attempted. Initial association through a barred door allowed visual, olfactory, and auditory contact. After a period of several weeks, the animals were allowed to interact without barriers. The male displayed constant aggression toward the female. The following treatment protocol was instilled in order to control the male's aggression (Table 1).

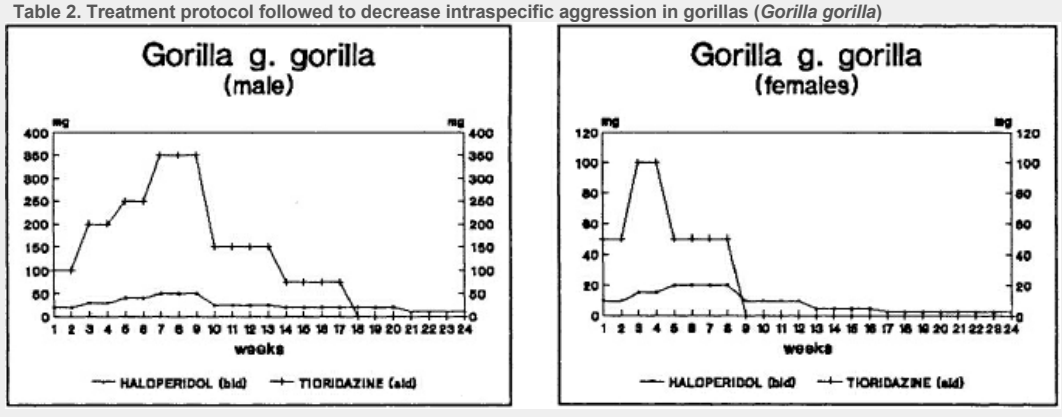
Table 1. Treatment protocol followed to decrease aggression in a chimpanzee (Pan troglodytes)

Drug	Dose	Frequency	Duration
Haloperidol Biperiden	20 mg PO 2 mg PO	SID SID	10 days 10 days
Haloperidol Biperiden Thioridazine	15 mg PO 1 mg PO 30 mg PO	SID SID SID	3 months 3 months 3 months

Case 2

An 11-year-old, 65-kg adult female lowland gorilla (*Gorilla gorilla gorilla*) was introduced to an established pair of adult handraised animals. The pair (one 14-year-old, 180-kg male, and a 13-year-old, 70-kg female) had been showing abnormal behavior (aberrant social behavior, coprophagia, and regurgitation followed by ingestion) for some time. The male displayed constant aggression towards the new female. In two cases, interaction resulted in severe injury, and the female had to be separated for some time. This group was considered important for breeding purposes. The following protocol was used in an attempt to control aggression as well as abnormal behavior (Table 2).

Table 2. Treatment protocol followed to decrease intraspecific aggression in gorillas (*Gorilla gorilla*)



The protocols were helpful in controlling aggression and decreasing physical aggressive interaction in both cases. Improvement in acceptance and cohabitation was noted during the introductory periods. In the animals showing aberrant behavior, however, the patterns were unchanged. As in human medicine, neuroleptics were found to be helpful tools for short periods of time. They must not be used as a permanent form of therapy.

Use of Positive Behavioral Techniques in Primates for Husbandry and Handling
American Association of Zoo Veterinarians Conference 1990
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Active Environments, Torrance, CA, USA

Operant conditioning is commonly thought of as the process that teaches pigeons to peck levers, rats to run mazes, bears to dance, and dolphins to leap. Whether you appreciate the product, the process is certainly a versatile one and, unbeknownst to most of us, a natural part of our everyday life. We use operant conditioning all the time, and it is used as frequently on us; we just aren't aware of it. Our lives are filled with various stimuli, reinforcers are handed out regularly, and responses are shaped, increased, and extinguished at an amazing rate. For example, in a conference room like this, generous and appreciative applause for a well-presented paper is a powerful reinforcer for increasing the likelihood that the speaker will return to present again. The amazing thing is that a process so powerful, and so simple, is rarely viewed as a method for accomplishing our goals.

Caring for zoo animals is no exception. Only the most adventurous keeper, one who likes to live on the edge, would publicly admit that he or she uses operant conditioning to bring the animals in at night. Even though placing the food dish in the stall, opening the outside gate, and allowing the animal to enter and eat, is exactly that. In a simple form, but training nonetheless. It is perhaps a little too simple, however, to maximize on the process. Because, in this context, those times the baboon or bear decides not to come in when the door opens, there is no series of steps to backtrack through to effectively problem solve and find solutions.

My point is that operant conditioning is a powerful, versatile, user-friendly tool that is rarely utilized to its full potential. I, and my partner Tim Desmond, came from the ranks of the professional fish-chuckers who make a living training dolphins to do those amazing spins and flips, killer whales to demonstrate pee slaps and lob tails, and sea lions to flipper walk with ease. Being able to train long chains of behavior and intricate movements gave us a sense of accomplishment, but also an insider's peek at the possibilities.

So we used positive reinforcement to train voluntary cooperation in veterinary procedures with cetaceans and pinnipeds. The presentation of tail flukes for drawing blood, inserting stomach tubes for contents sampling, and fecal tubes for uncontaminated fecal samples were trained and maintained at an extremely high rate of reliability. Animals were trained to lie still for ultrasound, and pinnipeds tolerated the lancing and cleaning of abscesses, needle biopsies on suspicious lumps, and the insertion of a 2-inch spinal needle for blood sampling. All this accomplished with a whistle, some fish, and the skill to apply them effectively.

Social interactions among animals were also prime areas of interest. Operant conditioning techniques, carefully applied, helped mitigate the negative consequences of dominance. Cooperation and positive social interactions could be increased and aggression decreased by training for these outcomes. Neurotic behaviors such as biting, frequent regurgitation, and swallowing foreign objects were handled from a behavioral perspective with encouraging results. We maximized on the power of operant conditioning by integrating it into a practical and comprehensive approach to animal care. In doing so, however, we also recognized its limitations.

An underlying premise of this approach is that every animal has individual motivators and outside pressures that influence its behavior. It is totally irrelevant how many pounds of food you offer a subdominant animal, if the dominant animal is waiting around the corner to kick his behind if he does what you ask. I guarantee you he is not going to do it. Despite these limitations, however, operant conditioning still remains a valuable tool that can be of great benefit to a sound animal management system.

Although much of the ground-breaking work with training has been done with marine mammals, the potential is there to work with almost any kind of animal, with varying degrees of success. Primates, as a group, offer great opportunities for positive reinforcement work, and a variety of projects have already been done, by ourselves and others. The following are just a few examples of novel situations where a behavioral approach was used.

The first project involved a group of 5 drills at the Los Angeles Zoo who were chosen for behavioral work because of several concerns. First, despite the presence of sexually mature animals, no breeding had occurred for over 6 years. In addition, observational studies of the drills conducted by the research department for 1½ years prior to the project showed very little affiliative behavior or positive social interactions between group members. Second, Sam, the dominant male, was overweight and control of his food intake, as well as that of the rest of the group, was very difficult. Third, Rocky, the sub-adult male, was shunned by the rest of the group. He appeared stressed a good deal of the time and on the verge of developing neurotic behavior. Fourth, the subdominant animals were inaccessible to the keepers for any handling or husbandry purposes because of the social dynamics within the group.

With this information, we designed and implemented a behavioral program to address these concerns, utilizing keepers with no prior training experience, working under our direction. Initial work focused on establishing feeding stations for each animal to control food intake. Feeding pairs were established where animals were fed side-by-side, with the dominant animal being reinforced heavily for allowing the subdominant animal to eat. We also introduced a round piece of wood as a target that they were to touch through the fence with their finger when it was presented. By moving it to different spots in their work area, their gross movements could be controlled and more physical activity was encouraged.

Next, we trained separation or gating behaviors. Four of the five animals were worked on gating in one or both of the holding areas off the main exhibit. At the same time, we worked on increasing Rocky, the subdominant male's positive social interaction with group members and with his trainers. We rewarded group members for allowing him to eat, and we engaged in a simplified form of grooming behavior with him.

The third phase involved reproduction goals. We concentrated on Sam and Nadine because they had previously produced offspring. Past observations had shown that Nadine's aggressiveness toward Sam often ended any mating attempts. Training consisted of stationing Sam and his trainer and Nadine with her trainer within close proximity of each other and just feeding them. Next, Sam's behavior of touching the wood target was shaped into him touching Nadine, and each was reinforced when contact was made. After several sessions, she began to present to him and he was placing both hands on her, approximating the mating position.

The second reproduction task was to train voluntary cooperation with artificial insemination procedures in the event that normal breeding did not occur. The females were trained to present to us by positioning their hindquarters right up to the fence. We then desensitized them to a smooth plastic syringe casing and later a rubber catheter tube being inserted into the vagina. This behavior would allow frequent insemination of the females without restraint or anesthesia.

The other part of the artificial insemination procedure was semen collection. Our strategy was to train Sam to masturbate on command in a specific location where the semen could be easily collected. We introduced a plexiglas plate that could slide under the fence in one of the holding areas, and trained him to sit on it. We observed and reinforced spontaneously occurring masturbation and worked on formal approximation of the behavior.

The Los Angeles Zoo Research Department continued observations of the drills during the project, outside of training sessions, and after the project ended. The results of the observations showed dramatic increases in every category of social interaction by the end of the project and beyond that time. In addition, aggressive behavior, although increasing on an absolute level, dropped from 34% to 25% of total social interaction. Since the project end, some work has resumed with the drills. Semen collection is now being pursued with Sam through the use of an artificial vagina. To date, 3 females have been inseminated using the tube insertion technique. No pregnancies have resulted as yet.

Operant conditioning techniques are being utilized for behavioral enrichment and husbandry purposes in an ongoing project at Monkey Jungle with a solitary male gorilla. Behavioral work was initiated with King because of his lack of social contacts and the limitations of his rather small, old-fashioned caging. The goals of the project are to increase his physical activity, increase socialization between King and his keepers, increase tolerance of environmental changes, create opportunities for non-invasive behavioral/cognitive research and train voluntary cooperation in husbandry procedures.

The work with King is being conducted by his keepers under the direction of Lisa Paciulli. He is worked twice a day for part of his normal diet. When work first started, King was quite responsive to the training, but spent equal time testing the trainer on just how much he could get away with. The disruptive behavior was dealt with in three ways. It was either ignored, responded to with a short-time out, or the keeper would simply leave and return later for a new session.

After over a year of training, King is a willing, enthusiastic, and quick learner. He is working on 26 behaviors, with 18 completed. The behaviors include natural ones—chest beat, climb, run, drum on lap; control behaviors—target, stay, come, follow, sit, stand, down, turn; enrichment behaviors—kiss, throw objects, retrieve objects, count; and husbandry

behaviors—nose swabs, open mouth for tongue depressor, position arm for blood sample, position for stethoscope, eye exam with flashlight, ear inspection and cleaning. These behaviors are worked regularly by the keepers, but King has also been desensitized to other individuals, like curators and veterinarians, being present and participating in the behaviors. In one case, an outside dentist was brought in and examined King's teeth, utilizing the open mouth behavior.

King is being physically exercised regularly. He climbs around the entire perimeter of his cage, and runs laps with the keeper. Plans are underway to conduct some cognitive work with him, including discrimination tests and puzzle boxes. A full complement of enrichment behaviors are always a part of the sessions, to keep them not only challenging, but just plain fun.

A third project of importance to this discussion was the work done at the Toledo Zoo by members of the staff and my partner Tim Desmond. The goal of the project was to successfully introduce a male gorilla into a family of females including adults, juveniles, and babies.

The introduction of Akbar into his family group bore an element of risk to all the animals. This risk could neither be accurately quantified nor eliminated. Under the best circumstances, training activity could only serve to reduce the probability of injury. It was with this understanding that a behavioral approach was incorporated into the strategy.

The basic game plan for the introduction included the following steps.

1. Have Akbar and the others spend a period of gradually increasing visual contact with one another, leading, in the later stages, to physical contact through cage bars.

2. Provide the animals with food and the keeper's attention during these periods of contact. Reward cooperation by reinforcing Akbar for allowing the females to eat and get attention. Praise and reward exploratory and gentle actions. Disapprove of any aggressive actions by Akbar.

3. Increase the reliability of Akbar's gating, which will be critical once he is in with the family.

4. Train Akbar to touch a "target"—a plastic bottle. Teach him to follow and come to this target. While it is unlikely that Akbar would respond to a target in a highly agitated state, he may respond shortly after an episode, or be diverted from another outburst before it happens.

5. While touching the target or the keeper's hand, establish the command "easy" and reward Akbar when he touches more gently than roughly. This easy command may be useful during the introduction when Akbar handles the youngsters.

With this work, and other logistical procedures in place, the introduction was attempted. Despite the wide array of posturing, threats, physical contact, deafening vocalizations, and mild to rampant chaos, the outcome was successful. By the end of the first day all was quiet, order was restored, and animals came out of it unscathed. What impact the behavioral work had on the outcome is difficult to assess. Several times during the day Akbar did respond by coming over to one of the doors and targeting on the bottle, including a few instances when he appeared to be in an agitated state. He handled the babies very gently while being told "easy", but that could also be his natural response.

Perhaps what is more important is the impact that training can have on the individual components of a process like this. For instance, through behavioral techniques, a concept like cooperation can be reinforced while aggressive acts are discouraged. The concept of being gentle and touching something "easy" can be taught and then accessed in a variety of ways. A simple behavior like touching a target provides a point of reference and aids in controlling movement. Behavioral enrichment can provide a more stimulating and challenging environment for the animals. It can also be used to make less desirable areas more tolerable, which in turn can positively effect gating. Finally, using operant conditioning techniques to train a basic behavior like gating between areas, may have the greatest positive impact on an animal management system than any other single behavior.

There are, of course, many other behavioral projects of note. Trainers at the Brookfield Zoo and the San Diego Zoo have successfully trained individual primates to voluntarily accept injections of insulin to treat diabetes, without restraint. Elements of training were used to aid in the introduction of Zoo Atlanta's gorillas, including Willie B., to their new *Gorillas of Camaroon* exhibit. Drills and other primates at the Philadelphia Zoo participated in a behavioral project to enhance handling, husbandry work, and socialization between group members.

Operant conditioning can be a valuable tool in manipulating the behavior of captive primates. Beyond that, however, it also provides a means of better understanding the social and environmental factors which influence that behavior. Training provides a classic exercise in the scientific method that allows us to formulate hypotheses about the behavioral habits of captive animals, test those hypotheses, and then make adjustments as needed. The innovative use of animal training techniques represents a significant and virtually untapped resource for the modern zoo.