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AZA Wildlife Contraception Center Programs

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ABSTRACT: Controlling reproduction is a responsibility facing both zoo and wildlife managers, and contraception is one of their options. However, management goals and parameters affecting administration of contraceptives vary considerably for free-ranging and captive wildlife. Captive breeding programs consider the entire captive population but manage at the level of the individual. Not only must they focus on the genetic value of individual animals, but each birth results in an animal that will require resources and occupy limited space for its lifetime. Thus, captive programs dictate that contraceptive be virtually 100% effective, safe, and reversible. This contrasts with management of most free-ranging animals, where reproductive rate of the population, not each individual, is the measure of success. The other notable distinction is ease of delivery in captive populations, perhaps the greatest challenge with free-ranging animals. Captive animals are always accessible, are individually known, and can be monitored. Yet, despite these differences, zoo and wildlife biologists can benefit from collaborative efforts, especially when they target the same species. In particular, trials with captive animals can provide more definitive results than comparable studies with free-ranging animals. In addition, we all face the problems inherent in programs that represent a limited commercial market. Improved communication and exploring the potential for collaborations may accelerate our progress.

KEY WORDS: captive breeding, contraception, fertility control, population management, zoos

INTRODUCTION

Genetic and reproductive management are critical components to endangered species recovery programs in modern zoos. American Zoo and Aquarium Association (AZA) Species Survival Plans (SSP) have been established to manage individuals of each endangered species in all accredited AZA institutions as one genetic population. Computer programs use studbook records to analyze parentage and relationships in making recommendations for reproduction among individual animals. Those pairings are accomplished most commonly by shipping animals among institutions, a form of managed “dispersal”, or by shipping semen for artificial insemination.

Another serious consideration regarding reproductive recommendations is the ultimately limited number of individual animals that can be properly housed and managed at each zoo. Although visitors want to see animal babies when they go to a zoo, the fact remains that all zoos, no matter their budget, are limited at least by space in the number of animals they can accommodate while still providing for their well-being for a lifetime. To fail to limit the number of offspring produced is considered irresponsible.

Because modern zoos also are committed to maintaining animals in groupings that reflect their natural social systems, it is also often necessary to prevent reproduction among animals in the group. Most institutions prefer using reversible contraception rather than physical separation, so that family groups do not need to be disrupted. In fact, in a recent survey, we found that 167 of the 215 AZA institutions have reported using contraception. Those who have not include, for the most part, aviaries and aquariums. Contraception has been employed primarily to control reproduction in mammals, with little application to other taxa such as bird, reptiles, and fish. In contrast, although the media give much more coverage to cases involving assisted reproduction techniques such as artificial insemination and embryo transfer, the fact is that very few zoos use those techniques, whereas a vast majority use contraceptives on a daily basis in many mammalian species.

Contraceptive application began officially in zoos in the U.S. in 1975, with the pioneering work of Dr. Ulysses Seal with lions (Seal et al. 1976). He compared the two best-known contraceptive products of the time, melengestrol acetate (MGA) and medroxy-progesterone acetate (MPA), now best known as the active ingredient in the commercial product Depo-Provera® (Pfizer). His results demonstrated fewer side effects for MGA, so he began producing and supplying MGA incorporated in silastic implants to the zoo community. Those implants were used primarily in lions (Panthera leo) and tigers (P. tigris), two of the most common and prolific species in zoos at that time.

However, with time and with the implementation in the early 1980s of genetic management, contraceptives were needed for other taxa as well. Increasingly, questions arose regarding dosages and details of application. Responding to the growing need for information and monitoring, the AZA Contraception Advisory Group was established in 1989 with Ingrid Porton, Saint Louis Zoo curator, and I appointed as chair. The Group, consisting of reproductive physiologists, veterinarians, and curators, reviewed information on contraceptive use in various taxa and prepared recommendations. They also established the Contraception Database and instituted an annual survey that queried all accredited zoos about their use of contraceptives in any species. From these surveys analyses could be conducted to assess efficacy and to identify any problems with application.

During the same period Dr. Linda Munson, now at the University of California-Davis, was investigating potentially deleterious effects in wild felids. Information from
lions and tigers treated with MGA or MPA implicated these hormones in pathology of uterine and mammary tissue. Both consist of synthetic progestins that achieve contraception via negative feedback on the hypothalamus and pituitary, but the resulting rather high levels of synthetic progestin appear to over-stimulate uterine endometrial and mammary tissue (Munson et al. 2002). Although progestin-based contraceptives had been used safely for years in humans, Dr. Munson found that felids responded very differently to these same compounds, emphasizing the importance of considering species differences in developing, evaluating, and recommending contraceptives for wildlife. Because safety is a critical concern for captive animal treatment, Dr. Munson’s Contraceptive Health Surveillance Program was incorporated into the Contraception Advisory Group.

Our Contraceptive Database on efficacy and reversibility, coupled with Dr. Munson’s database on the health effects of contraceptives, provides comprehensive information that forms the basis of the recommendations we produce and update at least annually. Those recommendations appear on our website (www.stlzoo.org/contraception) and are available for download by biologists around the world as well as providing a service to the zoo community. Database information is also compiled for Food and Drug Administration reports and used for retrospective analyses of minimum effective dosages and reversibility in addition to safety and efficacy.

By 1999, the growth of the program managed by the Contraception Advisory Group prompted the AZA to designate the program an AZA Center to be hosted by the Saint Louis Zoo and to be directed by Ingrid Porton and me. The Center’s Advisory Board continues to have veterinarians, reproductive physiologists, and curators, but now also includes an endocrinologist, nutritionist, medical doctors, and representatives of the pharmaceutical industry and our commercial partners. This expansion in expertise reflects the expansion in activities of the Center. We coordinate research trials of promising new methods and work to bring them to market, monitor the use of all methods in zoos, and advise managers and veterinarians in the choice and administration of contraceptives for their particular applications.

**METHODS**

**Synthetic Progestins**

Table 1 lists the contraceptive products commercially available at the present time. The MGA implant (now available through Wildlife Pharmaceuticals, Ft. Collins, CO) is still the most commonly used contraceptive in zoos in the U.S., and historically, MPA as Depo-Provera injections has been the second-most common. These progestin-based products have proven effective in all mammalian taxa treated to date, except for equids and possibly other Perissodactyls, although systematic studies have not been conducted in all species (Asa and Porton 2005). However, another synthetic progestin, altrenogest (Regu-Mate®: Hoechst-Roussel) has been shown effective in horses (Equus caballus) and likely works in wild equids as well.

Other commercially available contraceptives that are progestin-based are occasionally used in zoos. Norplant® (Wyeth-Ayerst) implants are sometimes preferred over MGA implants due to their smaller size, which can make them simpler to use in small species such as marmosets and tamarins (Callitrichidae). Ovaban® (Schering-Plough) pills approved for use in domestic dogs have been used in wild carnivores such as bears (Ursidae) that can be fed a treat containing a pill each day. An interest in oral delivery of contraceptives led to the development of two additional products specifically for captive wildlife. Purina Mills, LLC, agreed to add MGA to its most popular herbivore diet (Mazuri ADF-16), so that ungulates could consume their contraceptive medication along with their daily food ration. To provide an orally delivered product that could be added to any diet, Wildlife Pharmaceuticals now offers MGA in solution. In addition, many zoos use commercially available birth control pills, formulated for women using a combination estrogen and progestin, but almost exclusively in great apes.

In general, the progestins appear to be reversible, but systematic analyses have been conducted only for golden lion tamarins (*Leontopithecus rosalia*; Wood et al. 2001) and tigers (Chuei 2005). Concern has been raised regarding progestin reversibility in some primates, but the results in one study involved very few animals and provided only conjecture about fertility from uterine biopsies (Murnane et al. 1996) and the other did not distinguish females in which implants had been removed or left in place after 2 years (De Vleeschouwer et al. 2002).

**Porcine Zona Pellucida Vaccine**

Despite the almost universal efficacy of the progestin contraceptives, the problem of potentially serious side effects remained, particularly for carnivores. Porcine zona pellucida vaccine, provided by Dr. J. Kirkpatrick to

| Table 1. Commercially available contraceptive products. |
|--------------------------------------------------------|
| **Generic Name** | **Product Name** | **Manufacturer or Supplier** |
| **Synthetic progestins** | | |
| Altrenogest | Regu-mate® oral solution | Hoechst-Roussel |
| Levonorgestrel | Norplant® implants | Wyeth-Ayerst |
| Medroxyprogesterone acetate | Depo-Provera® injections | Pfizer |
| Megestrol acetate | Ovaban® tablets | Schering-Plough |
| Melengestrol acetate | MGA implants Mazuri® ADF-16 with MGA | Wildlife Pharmaceuticals Purina Mills LLC |
| **GnRH agonists** | | |
| Deslorelin | Suprelorin® | Peptech Animal Health |
| Leuprolide acetate | Leuprolide injectable | Wildlife Pharmaceuticals |
| Leuprolide acetate | Lupron-Depot® | TAP Pharmaceuticals |

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the zoo community, is effective across all the ungulates except suids, but has not proven to be both effective and reversible in carnivores. Thus, although a considerable number of ungulates in U.S. zoos are treated regularly with the PZP vaccine, other options had to be explored for carnivores.

**GnRH Agonists**

The most promising alternatives to date have been the GnRH agonists. Several are now available in the U.S., deslorelin (Suprelorin®, Peptech Animal Health, Australia, available through the AZA Wildlife Contraception Center for research trials), and leuprolide acetate (Lupron Depot®, TAP Pharmaceuticals, and as an injectable implant from Wildlife Pharmaceuticals). Deslorelin has been used more extensively than the other formulations and has been successful in most species (Bertschinger et al. 2001, Munson et al. 2001). The major limitation of the GnRH agonists is that they do not down-regulate the hypothalamo-pituitary axis in male ungulates or marsupials (Penfold et al. In Press, Herbert et al. 2004), although they do appear effective in females of those species. The failure of the GnRH agonists to work in males of some species has been disappointing, but they are still a vast improvement over the progestins that have not been effective contraceptives in males at all. A further benefit is that no side effects have been reported for the GnRH agonists, save the changes that occur following ovariectomy of females or castration of males for the respective species.

**Reversible Vasectomy**

A rather different technique, reversible vasectomy, was recently accomplished for the first time in a wild species, the bush dog (Speothos venaticus), a wild canid native to South America (DeMatteo et al. 2006). Although this microsurgical approach will not replace the hormonal methods, it does offer an alternative for males, especially in cases where a future need for fertility is unlikely but possible.

**DISCUSSION**

There are several major differences in the criteria for contraceptives used in captive compared to free-ranging wildlife. First, delivery is much simpler in the captive situation, since the animals are easily accessible and identifiable, so repeated application, sometimes even daily, is possible for many animals. Also, they never enter the food chain so compounds used cannot affect humans. However, the zoo community has very high expectations of contraceptives. They want methods to be 100% effective, virtually 100% reversible, and with no side effects. They also require a variety of methods that offer delivery options to suit their particular species and situation. The applications can be summarized as: zoos treat genetically valuable individual animals, and wildlife biologists treat populations of animals.

Despite these differences, there are challenges that affect us both, primarily involving regulatory issues and the small size of our markets that limits opportunities for commercialization. Regular communication among our respective groups may facilitate these processes. In addition, the zoo community can offer a potential service to wildlife biologists needing to test new methods in a more controlled situation than that faced with free-ranging animals. We look forward to productive collaborations.

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