FERTILITY CONTROL IN COYOTES: IS IT A POTENTIAL MANAGEMENT TOOL?

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ABSTRACT: Fertility control in wildlife is emerging as a potential management tool. Published research on feral horses, deer, rodents, and rabbits suggest an effective agent producing reversible infertility in these species could be developed. Furthermore, anecdotal reports suggest that infertility can be induced in a greater array of species. In this paper, the authors review methods of fertility control being studied for application in wildlife and focus on their studies designed to evaluate the effectiveness of fertility control agents in coyotes (*Canis latrans*). Immunocontraception using porcine zona pellucida (PZP) is currently the most promising method of fertility control in coyotes the authors have studied. This is consistent with results from other species. However, the vital question of whether any fertility control agent can reduce livestock losses due to coyote predation will require more research.

KEY WORDS: *Canis latrans*, coyotes, fertility control, GnRH, immunocontraception, PZP

Proc. 18th Vertebr. Pest Conf. (R.O. Baker & A.C. Crabb, Eds.) Published at Univ. of Calif., Davis. 1998.

INTRODUCTION

The search for alternative methods of managing nuisance wildlife has intensified in recent years. This is largely a result of stricter controls on traditional management techniques (i.e., use of chemicals), an expanding human population encroaching on wildlife habitat, the adaptability of some wildlife species to urban and suburban environments, the inability to manage such populations by traditional methods (e.g., hunting white-tailed deer [*Odocoileus virginianus*] and Canada geese [*Branta canadensis*], and trapping coyotes), and changing public attitudes toward lethal control. An alternative strategy for dealing with nuisance wildlife that has received considerable attention is fertility control. The authors' objectives are to review the current research on fertility control, and discuss some issues that may influence the use of fertility control methods in wildlife management. They also present preliminary results produced by the organizations that contribute to the goal of increasing understanding of reproductive physiology and behavior in carnivores, and producing a contraceptive system, using the coyote as a model.

METHODS OF FERTILITY CONTROL

Fertility control research can be broadly categorized under three general strategies: 1) surgical/chemical sterilization; 2) endocrine perturbation; and 3) immunocontraception. Each method has a unique set of advantages and disadvantages that influences the practicality of use in managing wildlife damage.

Surgical Sterilization

Surgical sterilization has been used successfully in domestic companion animals for many years, and with captive wildlife in zoos and research facilities. The primary advantage of this technique is that one treatment renders the animal permanently incapable of reproducing. While this is an advantage in domestic species and in captive wildlife, permanent sterility is sometimes considered a disadvantage of surgical sterilization for populations of wild animals. Concerns over permanent sterility in wildlife include a loss of genetic information from a population; permanently altered behavior patterns; the impractical implementation in wild populations; difficulties in capture and handling large numbers of animals; anesthesia; post-operative care; and cost of implementation.

While these concerns may be valid, surgical sterilization has been used effectively in several cases to manage some wild populations (Kennelly and Converse 1997). Several populations of feral cats were managed effectively with surgical sterilization (Neville 1983; Neville and Remfry 1984). These examples demonstrated that a wild population could effectively be managed with surgical sterilization when most healthy adults could be captured. Although the initial costs of this control method were high, the authors estimated that long-term costs would be lower than other control methods because only monitoring and periodic castration was necessary.

Bailey (1992) demonstrated that surgical sterility of introduced red fox (*Vulpes vulpes*) onto Alaskan islands

occupied by arctic fox (*Alopex lagopus*) could reduce adverse effects on native avifauna. The two fox species are not sympatric and, after nine years, the arctic foxes were extirpated from the islands and only a few red fox remained on one of the islands.

Brooks et al. (1980) and Kennelly and Lyons (1983) demonstrated that surgical sterilization could effectively control reproduction in beaver (*Castor canadensis*). Converse and Kennelly (1994) also successfully applied the technique to Canada geese. However, surgical sterilization was unsuccessful in controlling red-winged blackbird (*Agelaius phoeniceus*) production (Bray et al. 1975). Kennelly and Converse (1997) implied that effective use of surgical sterility is limited to species that are monogomous.

Little research has been conducted on surgical sterilization in wild canids. Mech and Fritts (1993) vasectomized five wolves (*Canis lupis*) and released them in northern Minnesota. They concluded that vasectomized wolves maintained pair bonds and territories, suggesting this method may be effective at reducing predation on livestock. Till and Knowlton (1983) demonstrated that adult coyotes (*Canis latrans*) reduced predation on livestock when the pups were removed from dens. They concluded that, in some situations, predation on livestock was driven by the presence of pups; when adults need to feed pups, they select larger prey items. These studies suggested that if reproduction in wild canids could be controlled while leaving territorial behavior intact, livestock losses could be reduced. This reduction might result if wild canids did not use larger prey sizes to support offspring, and the adults maintained territories, thereby preventing intact canids from immigrating into the area. National Wildlife Research Center biologists are currently testing this hypothesis. During December 1997 and January 1998, wild coyotes from about seven packs in northeastern Utah were captured. Packs were randomly assigned to either a treatment or control group. All animals in treatment groups received either a tubal ligation or vasectomy. Control group animals received a sham surgery, which consisted of the same anesthesia and surgical protocols except the oviducts and vas deferens were left intact. All animals were released where they were captured within 24 hours. Over the next three years, territorial, reproductive, and predatory behavior of these animals will be monitored to determine if surgical sterilization without removal of gonads influences these factors.

Endocrine Regulation

Steroids. Hormonal control and regulation of fertility in vertebrate species has primarily been accomplished through the use of steroids (Kirkpatrick and Turner 1991; Asa 1997). Progestogens and androgens successfully surpress normal ovarian cyclicity in domestic canids and felids, and in captive wildlife. However, use of progestins reportedly increases growth of the uterine lining and, consequently, induces hyperplasia, pyometra, and neoplasia in canids and felids, in addition to mammary development and post-therapy lactation (Asa and Porton 1991). Androgens also have undesirable effects, the most significant being external masculization. These effects, expense, and requirement for regular administration, are reasons steroids are generally considered impractical for use in wild populations.

Melengestrol acetate implants are the most used contraceptive in zoos (Porton et al. 1990). This steroid has also been used in oral forms with varying success (Asa 1997). Experiments to control fertility in coyotes have been conducted using steroid compounds such as diethylstilbestrol, mibolerone, and prostaglandins (Balser 1964). Although oral formulations would make these and other progestins (e.g., medroxyprogesterone acetate, levonorgestrel, megestrol acetate) more suitable for use in wild populations, the side effects previously discussed would still be expected. Additionally, oral presentation of these products could affect non-target species both directly via consumption of the compounds in baits, and indirectly if predators or scavengers consumed animals which had taken steroid-laden baits.

GnRH and Agonists. Recent efforts in endocrine regulation of fertility have focused on gonadotropin-releasing hormone (GnRH). A non-steroidal hormone, GnRH would have the advantage of no secondary toxicity because it is rapidly metabolized into amino acids. Gonadotropin-releasing hormone, a key regulator of reproduction in male and female mammals (Figure 1), is released by the hypothalamus in the brain and travels through a portal blood system to the anterior pituitary at the base of the brain. Gonadotropin-releasing hormone stimulates the anterior pituitary to release lutenizing hormone (LH) and follicle-stimulating hormone (FSH) in both females and males. These hormones subsequently influence the release of progesterone and estradiol in the female, and testosterone and estradiol in the male.

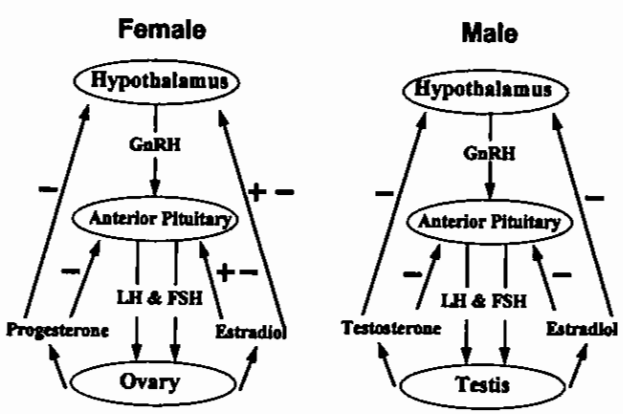

Figure 1. The mammalian hypothalamic-pituitary-gonadal axis in males and females (adapted from Becker and Katz 1997).

Gonadotropin-releasing hormone and its agonists have been used in male Hawaiian monk seals (*Monachus schauinsland*) (Atkinson et al. 1993) and African elephants (*Loxodonta africana*) (Brown et al. 1993). Single injections of GnRH in males of these species decreased blood testosterone levels and, subsequently,

aggressive behavior. However, prolonged administration of GnRH in cattle and red deer (*Cervus elaphus*) has resulted in stimulation of both pituitary and testicular function (Melson et al. 1986; Lincoln 1987).

Continuous administration of GnRH has inhibited ovulation in several species due to a negative feedback response by the hypothalamus (Vickery et al. 1989; Herschler and Vickery 1981; McNeilly and Fraser 1987; Montovan et al. 1990). However, Becker and Katz (1995) were unsuccessful in inhibiting LH secretion by the anterior pituitary with continual infusion of an GnRH analog. They suggested more research is needed to determine the usefulness of GnRH as a technique for regulating reproduction. Becker and Katz (1997) suggested that variation in response of the hypothalmic-pituitary-gonadal axis may be due to the choice of agonist, dose, treatment regimen, reproductive status, and species. Furthermore, they point out that the practicality of using GnRH as a contraceptive is dependent on the development of long-acting, time-release agonist that can be delivered remotely. Such an agonist, though, is currently unavailable.

Antiprogestins. Antiprogestins (also called anti-progestogens) are derivatives of cholesterol molecules and have some of the properties of steroid hormones (Dence 1980; Teutsch et al. 1995). These compounds tend to be stable, which allows for oral delivery without degradation and loss of function in the digestive tract. It also prolongs the duration of stability in bait materials, an important consideration for field delivery systems. There are few reports regarding the use of antiprogestins in canids. When used in domestic canines, termination of pregnancy without negative side effects was reported (Concannon et al. 1990; Sankai et al. 1991). Baulieu et al. (1987) published the first papers dealing with the antiprogestin mifepristone (RU-486). This compound has since been used in a variety of species as a contragestive with up to 80% effectiveness following a single oral dose (Brogden et al. 1993). However, when used in conjunction with prostaglandins, the success rate reaches 100% (Brogden et al. 1993).

The authors are currently evaluating the effectiveness of mifepristone and an analog (RTI3021-003; Research Triangle Institute, North Carolina) as contragestive agents in coyotes. Initial results suggest that RTI-003 used alone is not an effective contragestive agent in coyotes. However, the effectiveness of RTI3021-003 in combination with misoprostol, a prostaglandin, and mifepristone combined with misoprostol is also being evaluated.

Immunocontraception

Immunocontraception uses an individual's own immune system to disrupt reproduction (Figure 2). This is accomplished through the administration of a vaccine that results in the production of circulating antibodies or cellular immune effector cells in the target animal. Unlike vaccines developed to protect animals from infectious agents, contraceptive vaccines must trigger an immune response to self-antigens. Thus, an individual's immune system must be trained to target antigens it normally would not.

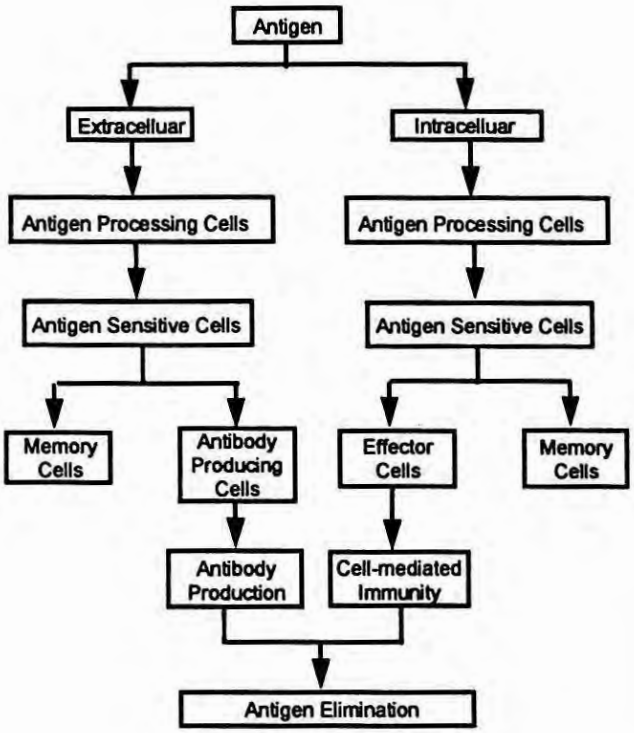

Figure 2. Essential features of the immune response (adapted from Tizard 1996).

Contraceptive vaccines studied to date can be classified as hormone-based vaccines and gamete-based vaccines. Hormone-based vaccines attempt to illicit an immune response against an individual's reproductive hormones. Studies have evaluated vaccines targeting GnRH, LH, and FSH (Thau et al. 1987; Mougdal 1990; Becker and Katz 1997).

Active immunization against GnRH has had some success in numerous domestic species (Clarke et al. 1978; Adams and Adams 1986; Awoniyi et al. 1987; Safir et al. 1987; Ladd et al. 1988; Baile et al. 1989; Adams et al. 1993). Circulating GnRH antibodies produced by immunization bound GnRH after it was released from the hypothalamus and before it reached the pituitary. Antibody-bound GnRH was ineffective at stimulating the release of LH and FSH, which resulted in impaired reproductive function. The effectiveness of these immunizations at suppressing reproductive function was positively correlated to the GnRH antibody titer (Lincoln et al. 1982; Safir et al. 1987; Baile et al. 1989).

Little research has been conducted on GnRH vaccines in wildlife. Studies on red deer (*Cervus elaphus*) have had mixed results (Lincoln et al. 1982; Ataja et al. 1992; Freudenberger et al. 1993). Ataja et al. (1992) found only a light suppression of LH and no reduction of testosterone levels. Alternatively, Lincoln et al. (1982) observed a significant decrease in testosterone combined with testicular atrophy and premature casting of antlers.

Becker and Katz (1997) suggested that variable results from GnRH immunizations may result from differences in carrier proteins used in vaccines, timing of primary immunizations relative to the reproductive season, and variability of individual animal immune responses to the vaccines.

The authors have conducted preliminary research on the use of GnRH vaccines to prevent reproduction in coyotes. They vaccinated five male and five female coyotes with 300μg of GnRH conjugated with keyhole limpet hemocyanin (KLH). The coyotes were boosted twice with 200μg injections of the GnRH-KLH vaccine at monthly intervals. Two of the females developed high antibody titers to GnRH and did not produce high levels of progesterone. Thus, it was assumed that these females did not ovulate or ovulated but did not maintain corpora lutea, which produce the progesterone required to maintain pregnancy. The remaining three females did not produce high GnRH antibody titers, or the antibodies were produced too late to prevent ovulation and a rise in progesterone. Of the five males vaccinated with GnRH, two developed high antibody titers, which resulted in a decrease of testosterone to levels observed prior to the breeding season. Three males had low antibody levels and either normal or only moderately reduced testosterone levels. It appears from this limited study that GnRH vaccines have some potential to control reproduction in coyotes; however, more research would be needed to evaluate the efficacy of such a vaccine. The problem of delivering such a vaccine in the absence of an orally active form seems particularly daunting.

The second group of contraceptive vaccines studied to date are gamete-based vaccines. These vaccines are designed to affect spermatogenesis, oocyte maturation, fertilization, and trophoblast development. Of these, vaccines directed at oocyte maturation, and specifically the zona pellucida (the glycoprotein matrix surrounding the mature mammalian egg), have received the most attention in wildlife (see reviews by Warren et al. 1997; Turner et al. 1997; Kirkpatrick et al. 1997). However, little research has been conducted on the use of such vaccines in predators.

The authors initiated research to evaluate gamete-based vaccines for fertility control in coyotes. In December 1995, female coyotes were injected with 300 μg of PZP, and boosted with 200 μg on PZP in January 1996. This initial study resulted in a reduction of mean litter size from 3.5 pups among control females, to 1.3 pups for vaccinated females. In December 1996, the same female coyotes were boosted again with 45 μg of PZP. This single, low dose boost was performed to evaluate if an annual boost would effectively keep litter sizes reduced. The results of this second year of research suggested that annual boosters of PZP were effective in maintaining reduced litter size; mean litter size during the second year was 3.8 pups/female and 2.6 pups/female for the control and PZP animals, respectively.

Although their earlier research on PZP demonstrated it was an effective immunocontraceptive for reducing coyote litter size, the authors initiated a second study to determine if more frequent boosting with PZP prior to the breeding season could eliminate litters entirely. In December 1997, they vaccinated five female coyotes with 300μg of PZP and boosted with 200μg four and six weeks later. In this experiment, females were euthanized and necropsied 30 days after the last observed breeding date. All control females were pregnant and the mean number of fetuses/females was 5.8, compared to zero fetuses in PZP vaccinated females. Thus, the PZP vaccine can be an effective immunocontraceptive in coyotes. The authors are currently conducting research that will elucidate the mechanism through which PZP reduces fertility, and will conduct research designed to develop an orally deliverable form of PZP.

CONCLUSIONS

The most effective means of resolving wildlife-human conflicts in many situations is to reduce wildlife populations by shooting, poisoning, or trapping. However, as the human population expands into wildlife habitat, lethal control options become limited and controversial. Thus, there is an increasing need to develop non-lethal control strategies that can be integrated into damage management programs.

Presently, relatively few cost-effective, non-lethal control options are available to managers. Fertility control could provide an effective addition to control programs. However, many hurdles must be overcome before fertility control becomes a viable alternative. These include, but are not limited to, the development of contraceptive agents that are orally deliverable, species specific, reversible, have few side-effects, and are cost effective (Sanborn et al. 1994).

Is fertility control a potential management tool for coyotes? Current research suggests that it has possibilities. Studies conducted to date on immuno-contraception suggest it has the potential for at least reducing litter size in coyotes. Further studies on antiprogestins will assess the value of these compounds in reducing litter size. Will litter size reduction significantly alter predatory behavior of coyotes on livestock? If productivity in a local population of coyotes is reduced, or eliminated, but the loss of livestock in the area is not significantly reduced, then a fertility control program would not be an effective management tool. The authors' research with surgically sterilized coyotes should provide an answer to this key question.

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