October 1993

Research and Field Applications of Contraceptives in White-Tailed Deer, Feral Horses, and Mountain Goats

Robert J. Warren

Richard A. Fayrer-Hosken

Lisa I. Muller

L. Paige Willis

Robin B. Goodloe

Research and Field Applications of Contraceptives in White-Tailed Deer, Feral Horses, and Mountain Goats

Robert J. Warren, Richard A. Fayrer–Hosken, Lisa I. Muller,

L. Paige Willis, and Robin B. Goodloe

Abstract: This paper reviews our applications of long-acting implantable steroids and immunocontraceptives in selected wild ungulates. We implanted captive white-tailed deer does with levonorgestrel but did not successfully prevent conception. We also evaluated antisperm immunocontraceptives delivered remotely via biobullet. Does immunized with plasma membrane proteins isolated from deer or porcine sperm showed persistence of antisperm antibody titers for 5 months, but these titers did not cause infertility. Our research also has included applications via biobullet of antigonadotropin-releasing hormone (GnRH), antisperm, and antiporcine zona pellucida (ZP) vaccines in female horses. Although the biobullet was effective in delivering immunocontraceptives at distances of $\leq$25 m, the anti-GnRH vaccine did not significantly reduce foal production in treated mares. In separate experiments, our treatment of captive mares with the antiporcine ZP vaccine resulted in high antibody titers and caused infertility in most mares for 2 years. Federal scientists have experimented with implanting melengestrol acetate (MA) in free–ranging, exotic mountain goats following capture by helicopter. Treated goats demonstrated lower reproductive rates than controls goats; however, this technique was time-consuming and expensive. Practicality and feasibility are of primary importance when considering the application of contraception in wildlife management. Ideally, these contraceptives should cause long-term infertility or sterility and should be remotely deliverable to improve their potential applicability in wildlife population management.

Keywords: Biobullet, contraception, feral horse, fertility control, immunocontraception, mountain goat, remote delivery, white-tailed deer

Introduction

Recently, wildlife managers have had to consider controlling populations of wild and feral ungulates by nonlethal means (Warren 1995). Public opposition, legislative mandates, human safety concerns, or budgetary limitations often make the application of traditional methods of hunting, controlled shooting, poisoning, or trapping-and-relocation programs unacceptable management alternatives. Therefore, interest and research in wildlife contraception has increased dramatically in the past decade.

This paper will review our research and other published applications of contraceptives in white-tailed deer *(Odocoileus virginianus)*, feral horses *(Equus caballus)*, and mountain goats *(Oreamnos americanus)* with the assumption that these methods must be practical, safe, and time and cost effective to be useful in wildlife management. We believe that two primary contraceptive tools have potential applicability in these species: long-acting, implantable steroids and immunocontraceptive vaccines. Most of our work in this area has focused on development and evaluation of these wildlife contraceptives and evaluation of delivery-method efficacy.

White-Tailed Deer

Need for Control

White-tailed deer have become so overabundant in many areas of the United States that they now represent a significant problem for natural resource managers. Warren (1991) reviewed the historical causes of this problem and presented an ecological justification for control of overabundant deer populations in national parks. In addition to ecological concerns, overpopulated deer herds also represent a public health and safety risk and cause significant economic losses in the form of crop damage, damage to landscape plantings, and damage from deer–vehicle collisions (Conover and Decker 1991, Curtis and Richmond 1992).

While regulated public hunting can effectively control deer populations (Behrend et al. 1970), it cannot be used as a management technique in some areas (e.g., national or State parks and urban or suburban areas). Hence, there has been great public interest in contraception as a technique for controlling deer populations in these areas. But before they will be accepted by wildlife managers for routine use in deer population control programs, contraceptives must

be safe, effective, easily administrable, and, ideally, capable of lasting the reproductive lifespan of the doe (Matschke 1980).

Contraceptive Steroids

Oral administration of the synthetic progesterone melengestrol acetate (MA) (Roughton 1979) or the synthetic estrogen diethylstilbestrol (DES) (Harder and Peterle 1974) can inhibit ovulation in female deer, but these contraceptives are not practical because they require daily oral exposure. Microencapsulation of DES can extend the effective treatment interval to 30 days, but these high doses are not readily eaten by deer (Matchke 1977a).

Subcutaneous steroid implants can increase treatment intervals to several months or years, but these techniques require costly trapping and handling of individual deer. Silicone tubing implants containing MA and DES have successfully reduced reproductive rates in deer for 1 to 2 years (Bell and Peterle 1975). Matschke examined fertility control in deer with Silastic® implants of DES and a synthetic progestin (DRC–6246). Calculated release times for DES were 1–2 years v. 3 years for DRC–6246 (Matschke 1977b); however, suppressed reproduction in the field lasted only 2 years before depletion of DRC–6246 occurred (Matschke 1980).

Implants containing MA have caused infertility in nonpregnant captive deer for 2 years (Plotka and Seal 1989). When the implants were applied to pregnant does during winter, however, pregnancy was not terminated, and the implants had to be removed. Plotka and Seal recommended that pregnant deer not be treated with MA implants unless pregnancy is terminated. It is unfortunate that these contraceptive steroid implants cannot be used in winter during pregnancy because at that time deer generally are easiest to bait, capture, and treat.

Levonorgestrel (LNG) is an implantable progestin that provides effective, long-term (>5-year) contraception in humans (Diaz et al. 1982). Contraception of deer for >5 years from one treatment may justify the time and cost associated with capturing and treating individual deer and hence increase the potential for providing a practical technique for contraceptive management of deer populations.

Despite the potential for this deer contraceptive, two studies with LNG implants in captive white-tailed deer have shown this device to be ineffective. In the first study, Plotka and Seal (1989) implanted five does with a single homogenous silicone rod containing 200 mg LNG, and three of the five does became pregnant. Plotka and Seal did not measure LNG concentrations, so the lack of contraception may have been related to the shape and matrix of the implant, both of which can affect steroid hormone release (Robertson et al. 1983).

White et al. (1994) also tested LNG implants in deer but used the technique as it is applied in humans (i.e., 216 mg of LNG sealed inside six small silicone tubes). White's team compared six v. nine LNG implants (containing a total of 216 v. 324 mg of LNG) in adult v. fawn does. Fawns were included to determine the effects of LNG implantation on puberty attainment. Despite significant release of LNG from both doses of implants, three of five implanted adults and one of two fawns that survived 2 years after implantation became pregnant.

Norgestomet (NGM) is a synthetic progestin that has been applied successfully as a contraceptive in white-tailed deer (Kesler, this volume) and black-tailed deer (Odocoileus hemionus) (Jacobsen et al. 1995). This hormone originally was marketed for synchronizing estrus in domestic livestock. Antech Laboratories, Inc. (Champaign, IL), has complexed 42 mg of NGM into silicone rods and loaded it into biobullets (Kreeger, this volume) for remote delivery (Kesler, this volume). In both species of deer, NGM was nearly 100-percent successful in preventing pregnancies but it was effective for only 1 year (Jacobsen et al. 1995; Kesler, this volume). Therefore, annual treatments would be required to maintain control over deer reproduction. This requirement would limit the applicability of this contraceptive technique primarily to smaller populations and small areas where there is substantial control over the deer herd.

Immunocontraceptives

The basic principle of immunocontraception is to produce endogenous antibodies against a particular protein or peptide involved in the reproductive process. Sufficiently high antibody titers disrupt the function of the protein and cause contraception. Infertility is maintained as long as antibody titer levels remain high. However, fertility can resume after exposure to the antigen has ceased and the antibody titers decrease (Primakoff et al. 1988). For white-tailed deer, the proteins that have been evaluated as immunocontraceptive antigens have been the oocyte ZP and spermatozoa plasma membrane proteins.

Immunocontraceptives have numerous advantages over contraceptive steroids that may make the former more effective and efficient for use in deer. Immunocontraceptives can be delivered remotely, which makes them more feasible for field application than methods that require capture and immobilization of individual deer. Also, a protein-based vaccine likely would be deactivated if ingested orally by nontarget organisms, in contrast to the persistent tissue residues that often characterize the synthetic steroids. Digestion of the vaccine after oral ingestion also probably would prevent unintentional transfer to carnivores or humans.

Turner et al. (1992) successfully used porcine zona pellucida (PZP) antigen in an immunocontraceptive for white-tailed deer. Turner's team vaccinated white-tailed does with 5,000 heat-solubilized porcine zonae pellucidae (64.3 µg protein) emulsified in 0.5 cm^3 Freund's Complete Adjuvant and delivered remotely in a 1-cm^3 self-injecting dart. Booster injections of PZP emulsified in Freund's Incomplete Adjuvant were given 3–6 weeks after the initial injection. Six months after onset of the injection scheme, the does were bred to a healthy buck of known fertility. None of the ZP-treated does but six of seven (86 percent) of the control does produced fawns.

The requirement of multiple booster injections limits the practicality of using this contraceptive vaccine in free-ranging deer populations. However, recent advances in research with PZP include micro-encapsulation of the booster vaccinations, which

allows release of the booster over a period of weeks or months so that only 1 vaccination/year is required (J. F. Kirkpatrick, pers. comm.; Stevens et al. 1992).

Several different sperm proteins also have been considered for use in immunocontraceptive vaccines (Naz and Menge 1990). Antisperm vaccination may cause infertility in the male or female. In the male, antisperm antibodies may cause an autoimmune response to the sperm, thus resulting in infertility (Mathur et al. 1988). Treating bucks in a free-ranging deer population with an antisperm vaccine would have limited effect on the reproductive rate of the herd because deer are polygynous breeders. However, applying an antisperm vaccine may be more practical if males and females do not have to be distinguished prior to treatment.

In the female, antisperm antibodies may cause agglutination of sperm (reviewed in Shulman 1986), reduced penetration of sperm through the cervical mucus (Clarke 1988), or altered sperm binding to the zona pellucida (Naz et al. 1992). Antisperm vaccines also may be "self-boosted" (i.e., additional exposure and boosting of the immunity against sperm may occur with each insemination). Some women with spontaneous sperm-antibody titers have reduced titers following the use of condoms, which probably function to prevent boosting from sperm in the vagina (reviewed in Shulman 1986). Thus, if antisperm vaccines are self-boosting, they may be more practical for field application than multiple booster vaccinations of antiporcine ZP vaccines.

Very little research exists on the use of antisperm vaccines in deer. To date, our research laboratory has presented the only data available on antisperm vaccines for deer (White et al. 1993). We developed antisperm vaccines using anterior acrosomal sperm plasma membranes from deer, bull, and boar sperm. These vaccines were injected into adult does, from which blood samples were collected for antibody titer analysis. High antisperm antibody titers occurred in does injected with antisperm vaccines made from all species tested. However, antibody recognition of deer sperm was greatest in those does injected with either deer or boar sperm. Despite high antibody titers that

persisted for at least 11 months after immunization, the does treated in this preliminary trial became pregnant.

Feral Horses

Need for Control

Feral horses occupy extensive areas of public land in the United States. Historically, these herds were controlled by local citizens who captured wild horses for use as beasts of burden, in pet food, and as rodeo stock. In 1971, the Wild Free-Roaming Horse and Burro Act (Public Laws 86–234 and 92–195) specifically eliminated these uses and required Federal agencies to control feral horses through capture and adoption (Wagner 1983). The adoption program has been very costly and unsuccessful. The cost of capture and adoption of each feral horse ranges from $300 (Turner and Kirkpatrick 1986) to more than $1,800 (Godfrey and Lawson 1986). In 1985, the Federal Government spent more than $5 million to remove and maintain up to 18,000 feral horses and burros through the "Adopt-a-Horse" program (Boyles 1986). Many of the horses captured were older stallions and were not in demand by potential adopters (Slade and Godfrey 1982). Clearly, alternative techniques for managing feral horse populations are needed.

Public sentiment and interest in feral horses is extremely high. This fact has led to the tremendous amount of political support this species has received. Visitors to national wildlife refuges and national parks that contain feral horses are very interested in observing these animals. Yet the agencies charged with managing these herds are faced with a dilemma: how to control the feral horse populations so as to minimize the effects of overgrazing on native vegetative communities and still meet public interest needs and/ or comply with the Wild Free-Roaming Horse and Burro Act in a manner that is logistically and fiscally feasible.

Garrott (1991) and Garrott et al. (1992) evaluated the potential and economic feasibility of fertility control for managing feral horse populations. Based

on their simulation analyses, Garrott and coworkers concluded that contraceptives could reduce substantially the number of horses that would have to be removed from Federal lands each year. Thus, fertility control may represent an effective alternative for feral horse population control that may be more economically feasible than maintenance and placement of excess horses in the Adopt-a-Horse programs.

Contraceptive Steroids

The harem breeding structure of feral horses, in which a dominant stallion breeds most of the mares in a particular harem, permits the use of male-based wildlife contraception management programs for this species. Turner and Kirkpatrick (1982) administered a microencapsulated form of testosterone propionate (MTP, given intramuscularly) to feral stallions. Foal counts were reduced to 0.07 foal/mare for MTP-treated bands compared to 0.37 for mares in control bands. The investigators also observed no differences in stallion behavior parameters, such as scent marking in response to mare elimination marking, mounting, or copulation. The primary advantage to this type of treatment was that the fertility of an entire herd could be controlled through the treatment of a single stallion. Disadvantages included the fact that immobilization of the stallion and multiple injections were required, resulting in high cost and hard work.

In a subsequent study, Kirkpatrick and Turner (1987 unpubl.; also cited in Turner and Kirkpatrick 1991) used MTP to treat feral stallions in a different population, each with a harem of proven fertility. In this study, the stallions were treated remotely instead of being immobilized. During the 5 years prior to treatment, harem fertility rate ranged from 42 to 50 percent; the year after MTP treatment, the fertility rate averaged 28.9 percent, compared to 45.4 percent for control harems during the same year. This method of contraception would require annual treatments and probably would be less effective in bands having sexually mature subordinate stallions or a high degree of movement by mares between harems.

Feral mares also have been treated with chemical contraceptives. Plotka et al. (1988) used silicone implants with estradiol and/or progesterone to inhibit

ovulation. Plotka's team observed greater levels of serum progesterone and estradiol for at least 21 weeks in treated mares but no reduction in ovulation or conception. In a subsequent study, Plotka et al. (1992) used silicone implants containing ethinylestradiol, estradiol 17–beta, or progesterone. The higher dosages of ethinylestradiol resulted in contraceptive rates of at least 88 percent for 3 years, with an estimated efficacy period up to 5 years. Contraception occurred regardless of route of implant delivery (subcutaneous, intramuscular, or intraperitoneal).

In another study, microencapsulated norethisterone (MNET, a synthetic progestin) was administered by remote delivery to six feral mares of proven fertility (Kirkpatrick and Turner 1987 unpubl., Turner and Kirkpatrick 1991). No contraceptive effect from this treatment was detected, which supported the results of Plotka et al. (1988) for progesterone.

Applications of microencapsulated steroids have a number of practical limitations. The microencapsulated suspension tends to settle out and clump if not delivered within 10 minutes of mixing (Turner and Kirkpatrick 1991). In addition, remote delivery of the suspension via barbless or microbarbed darts, which ultimately fall out of the animal, represents a potential for environmental contamination from lost or unrecovered darts. The method also necessitates careful calculation of velocity and trajectory in order to prevent rebound of the dart (Turner and Kirkpatrick 1991).

Immunocontraceptives

For feral horses, the proteins that have been evaluated as immunocontraceptive antigens have been hormones, the oocyte zona pellucida, and spermatozoa plasma membrane proteins. The only hormone used as an antigen for equine immunocontraception thus far has been luteinizing hormone-releasing hormone (LHRH, also referred to as gonadotropin-releasing hormone or GnRH). This hormone is a decapeptide released from the hypothalamus. The immunogenicity of peptides generally is low; therefore, LHRH must be conjugated to a larger protein to increase the response by the immune system.

Safir et al. (1987) used LHRH conjugated to human serum albumin (HSA) and combined with Freund's Complete Adjuvant as an immunocontraceptive vaccine to inhibit ovulation in captive mares. After multiple booster injections, three of five mares immunized against LHRH failed to ovulate for at least 5 months (duration of the study), whereas five of five untreated control mares ovulated. Inhibition of folliculogenesis and ovulation was related directly to LHRH antibody titers.

Field application of an LHRH immunocontraceptive vaccine has been evaluated in feral horses. Goodloe (1991) used a vaccine composed of LHRH (15 mg immunogenic activity) conjugated to keyhole limpet hematocyanin (KLH) and mixed with one of two adjuvants, either alum (AP) or Ribi ImmunoChem's triple adjuvant (TA; 100 mg each monophosphoryl lipid A, trehalose dimycolate, and Bacillus Calmette–Guerin cell-wall skeleton). Initially, captive domestic mares were given the vaccine as a means of monitoring antibody titer levels. Vaccines were prepared in a microencapsulated form for the first year of study in captive mares; biobullet delivery was used for the second year. The microencapsulated vaccine was designed to release one dose immediately upon injection, one dose in 2–3 months, and a final dose in 6–9 months. The microencapsulated vaccines could not be delivered via biobullet because of its limited payload capacity (300 mg).

During the first year of the study using microencapsulation, the vaccine with the TA adjuvant produced higher antibody titers than did the vaccine with the AP adjuvant (Goodloe 1991). Three of the four mares treated with the TA form of the vaccine ovulated an average of 111 days after initial treatment, compared to a mean of 44 days for control mares. Thus, this treatment delayed but did not significantly inhibit ovulation. Microencapsulated vaccine also resulted in swelling or an abscess at the injection site of each mare.

During the second year of study, the same mares were boosted remotely with a single biobullet. Although it did not stimulate antibody production sufficient to inhibit ovulation, this mode of vacination did not result

in abscess formation. Overall, there were no significant differences between treatment and control mares in terms of date of first ovulation, number of ovulations, or percentage of mares that became pregnant.

Goodloe (1991) applied the same vaccine via biobullet followed by one booster injection 2–3 months later and a second booster injection an additional 8 months later to 21 feral mares on Cumberland Island, GA. The field study further substantiated the results from the captive mares: foal production did not differ between treated and untreated mares.

The differences in success between the studies by Goodloe (1991) and Safir et al. (1987) could be due to either the type of adjuvant or conjugate used, or to the number of booster vaccinations given. However, both studies indicate that LHRH-based immuno-contraceptive vaccines may be expected to produce infertility for at most a single breeding season, which obviously limits the practicality of this method of contraception for routine use in feral horse population management programs.

The oocyte ZP also has been used as an immunogen for contraception in horses. Liu et al. (1989) used a series of four vaccinations (given at 2- to 4-week intervals) with heat- solubilized porcine ZP (64.3 µg) and either aluminum hydroxide gel or Freund's Complete Adjuvant. Ten feral mares were vaccinated and released into their natural territory, known to contain fertile stallions. Eight months later, the mares were recaptured, and their pregnancy status was determined by rectal palpation. Four domestic mares also were treated and monitored in captivity. Contraception occurred in 12 of the 14 (86 percent) fertile mares studied.

Subsequently, Kirkpatrick et al. (1990) evaluated the applicability of this porcine ZP vaccine to feral horse populations on Assateague Island, MD. The investigators selected sexually mature mares with known breeding histories; 26 mares were treated with the porcine ZP vaccine, six control mares were injected with phosphate buffer and adjuvant, and 11 mares served as untreated controls. The vaccine contained 5,000 heat-solubilized porcine zonae pellucidae (64.3 µg protein) emulsified with equal

volumes of Freund's Complete or Incomplete Adjuvant. An initial and two booster vaccinations were delivered remotely using self-injecting plastic syringe darts tipped with barbless needles.

Of the 26 porcine ZP-treated mares, 3 developed abscesses at the injection site after the third vaccination (Kirkpatrick et al. 1990). At the time of initial injection, 14 of the 26 mares (57.6 percent) were pregnant, and all these gave birth to live foals 1–3 months after the final injection. Similarly, two of the six control mares produced live foals that same year. In the year after vaccination, the foaling rate for mares treated with porcine ZP was significantly lower the year after treatment (3.8 percent) compared to the 2 years prior to treatment (53.8 percent). In addition, foaling rates were significantly lower for the 26 mares treated with porcine ZP in the year after treatment (3.8 percent) when compared to foaling rates for the six control mares (50 percent) or the 11 untreated mares (45.4 percent).

Kirkpatrick et al. (1990) had difficultly in relocating all mares they initially injected. Of those that were relocated, some had become very wary and could not be given booster vaccinations. Subsequent work by this research team has focused on developing a one-shot injection in which a booster vaccination is micro-encapsulated (J. F. Kirkpatrick, pers. comm.).

Kirkpatrick et al. (1991) continued this study and gave booster vaccinations to 14 of the original 26 mares treated with porcine ZP approximately 1 year following the initial treatment. Foaling data collected in the subsequent year indicated that foals were produced by 1 of 14 (7 percent) boosted mares, 3 of 6 (50 percent) control mares, and 7 of 16 (44 percent) untreated mares. During a third year for the same study, Kirkpatrick et al. (1992) treated 10 of the mares boosted during the second year with another identical vaccination. None of the 10 mares boosted for a third consecutive year became pregnant, as opposed to 11 of 20 (55 percent) control mares. The researchers also used intensive visual observations and urinary analysis to monitor behavioral estrus and ovarian function for seven of the treated and four of the control mares. Based on these analyses, only two of the

seven treated mares demonstrated ovulatory cycles. The lack of cyclicity was thought to be due to altered ovarian function as has been shown to occur in other species given a similar vaccine (Skinner et al. 1984, Dunbar et al. 1989).

Thus, the porcine ZP vaccine has been shown to be very effective as an immunocontraceptive in feral horses. However, the formulation of porcine ZP vaccine used by Kirkpatrick et al. (1990, 1991, 1992) has certain characteristics that may limit its practical applicability in the field. Use of Freund's Complete Adjuvant in the vaccine is a distinct disadvantage. Most approved veterinary vaccination protocols do not permit the use of Freund's Complete Adjuvant in any applications other than small-scale, experimental trials. Therefore, a porcine ZP vaccine containing this adjuvant probably will not be approved for routine use in feral horse population-control programs. In addition, because Freund's Adjuvant cannot be lyophilized, a vaccine incorporating it must be administered as a liquid in a syringe dart as opposed to the biobullet.

Because of the above-mentioned concerns over the use of Freund's Adjuvant, Willis et al. (1994b) evaluated the use of an alternative formulation of the porcine ZP vaccine for horse contraception. The Willis team's formulation contained 200 µg of porcine ZP antigen and 500 µg of synthetic trehalose dicorynomycolate glycolipid (Ribi ImunoChem Research, Inc., Hamilton, MT) as an adjuvant. This porcine ZP vaccine formulation was lyophilized and packed into biobullets (Kreeger, this volume) for remote delivery to captive horses. Goodloe (1991) had previously documented the efficacy of this method for remote delivery of immunocontraceptives to free-ranging feral horses. Willis et al. (1994b) treated four mares with an initial and one booster vaccination separated by 1 month. Four control mares were injected with biobullets containing only the adjuvant. All mares were bled for antibody titer analysis and bred to a sexually mature stallion at each estrous period through two complete breeding seasons. The control mares had no titer levels and conceived during their first estrous period, in contrast to three of the four mares treated with porcine ZP, which had high antiporcine ZP titers and did not conceive. The fourth treated mare had lower titer levels and was fertile, but she too became infertile after administration of a subsequent booster vaccination.

Willis et al. (1994b) monitored antibody titer levels and infertility during the breeding season the year after initial treatment and, despite not having received a booster vaccination in the second year of this study, all of the treated mares continued to have high titer levels and were infertile. The greater potential duration of contraceptive effect apparent for this porcine ZP vaccine formulation may greatly improve its field applicability compared to other formulations that require annual booster vaccinations.

Sperm proteins also have potential for being used as antigens in immunocontraceptive vaccines, although relatively little research has been done in this area with horses. The most extensively characterized sperm immunocontraceptive thus far was developed by Naz et al. (1984). Naz and coworkers developed a monoclonal antibody (MA–24) in the mouse that specifically recognized a glycoprotein found only on the postacrosome, midpiece, and tail of sperm. This glycoprotein was termed fertilization antigen 1 (FA–1). FA–1 was determined to be nonspecies specific because the MA–24 antibody cross-reacted with sperm from mice, rabbits, rhesus monkeys, and bulls (Naz and Menge 1990). The MA–24 antibody apparently causes contraception by blocking sperm–egg binding. Treatment of sperm with either the MA–24 antibody or antiserum against FA–1 prior to insemination significantly reduced in vitro fertilization rates as compared to untreated sperm (Naz 1987). In addition, female rabbits immunized with purified FA–1 had significantly lower in vivo fertilization rates (14.7 percent) as compared to control rabbits (91.7 percent) (Naz et al. 1986).

The only research published to date in the area of sperm plasma-membrane protein immunocontraception in horses was done in our research laboratory (Willis 1993, Willis et al. 1994a). We developed antisperm vaccines using plasma membrane proteins from porcine and equine sperm. These vaccines were adjuvented with synthetic trehalose dicorynomycolate glycolipid, lyophilized, and administered via biobullet to two captive mares. Four mares served as controls

and received biobullets containing only the adjuvant. All mares were bred to a fertile stallion, and blood samples were collected for antibody titer analysis. High antisperm antibody titers were detected in the treated mares, but no significant differences occurred in conception: one of two treated mares became pregnant compared to three of four controls.

Mountain Goats

Need for Control

The mountain goat is a native species in some mountainous habitats in North America. However, there is debate over its status as a native species on the Olympic Peninsula of western Washington. National Park Service (NPS) scientists in Olympic National Park maintain that the mountain goats were artificially introduced into this park by humans in the 1920's (Moorhead and Stevens 1982). Conversely, Lyman (1988) argued that this species may have become locally extinct on the Olympic Peninsula prior to the first biological surveys in the late 19th and early 20th centuries. If Lyman is correct, mountain goats may not be exotics in the park.

The status (i.e., native or exotic) of mountain goats in this park is very important because NPS management policies encourage the elimination of exotic species that may threaten the survival of native species. Ecological research conducted in the park has shown that fragile alpine plant communities are being threatened by grazing pressure from mountain goats (Olympic National Park 1981 and 1987). Because of this concern, NPS began a capture-and-removal program in 1981 to reduce or eliminate mountain goats from the park (Houston and Stevens 1988, Carlquist 1990, Houston et al. 1991). This removal program has been very costly (as much as $900–1,000 per goat removed) (Houston et al. 1991). Therefore, NPS has experimented with fertility control as a more cost-effective means of controlling mountain goats in the park. Lethal removal of mountain goats, while acceptable and cost effective for control

of feral goats in some countries (Parkes 1990), is very controversial in the United States.

Contraceptive Steroids

In deciding which contraceptive techniques to evaluate, NPS scientists considered a number of criteria: ease of application in the field, safety to goats and humans, potential for treating a large proportion of the population, duration of efficacy, and cost. In an experimental evaluation of contraceptive and sterilization methods to control goats in Olympic National Park, Hoffman and Wright (1990) captured and placed silicone implants containing MA in the neck region of 11 female mountain goats. The investigators also captured five male goats in a different portion of the park and injected their epididymis with a sclerosing agent containing lactic acid (Chemcast™, BioCeutic Laboratories, Inc., St. Joseph, MO). The females were monitored in the field for a period of 5 years, during which the rate of kid production averaged 10 percent as compared to 68 percent for a similar group of untreated females in the park during the same time period. Comparative examination of the treated males 2 years after treatment confirmed blockage of their epididymides and sterilization. However, visual monitoring of the area occupied by the males for 2 years after treatment revealed no change in population size or the rate of kid production by females. Male-based contraceptive techniques obviously have limited potential for success in a wild, polygynous species. Hoffman and Wright (1990) concluded that the techniques they tested might have potential for controlling the numbers of mountain goats in the park. However, the requirement that goats had to be captured for treatment made these techniques very expensive and limited their widespread operational application over a larger portion of the park. In addition, captures by helicopter, which were mandatory for capturing mountain goats in the park, were discouraged in 1990 by the U.S. Department of the Interior's Office of Aircraft Safety after a risk assessment revealed that the goat capture procedures represented a significant human safety hazard (Tuler et al. 1992).

Immunocontraceptives

No published research is available on immunocontraceptives in mountain goats. Immunocontraception may have potential for application in Olympic National Park. However, logistical and fiscal limitations associated with fieldwork in this park will necessitate long-acting (preferably permanent) immunocontraceptives that can be delivered remotely via a biobullet or syringe dart shot from a helicopter. Field application of remotely delivered immunocontraceptives from a helicopter in the rugged, mountainous terrain of Olympic National Park likely represents the most difficult situation for contraceptive management of a wildlife population.

Conclusions and Practical Applicability

The above literature review demonstrates that several available contraceptive techniques are effective in individually treated deer, horses, and mountain goats. Additional literature on the application of contraceptives in other species has been reviewed by Bomford (1990) and Kirkpatrick and Turner (1991). Despite the success of some contraceptives in individually treated animals or in captive situations, management of wildlife populations with contraceptives may be infeasible if they are not practically applicable in the field. More research is needed to document that contraceptives can be effective when applied as a management technique at the population level. Garrott (1995) published results of a study that used computer simulations to consider the prospects of controlling wildlife populations with contraceptive techniques. However, nobody will know the true potential for contraceptive management until these techniques are tested under real-world conditions where feasibility of field applicability, interactions among ecological factors and processes, the potential population-level efficacy of treatments, and considerations of time and cost efficiency become paramount to the success or failure of any program for wildlife contraception.

A number of important practical questions exist relative to the potential applicability of contraception in wildlife management. Aside from the questions about the efficacy of the particular contraceptive agent, its duration of effect, and its safety to treated animals are important questions relative to the potential effects of the agent on the ecological food chain. In this regard, contraceptive vaccines likely will be safer than contraceptive steroids. Nonetheless, research is needed to determine the extent to which contraceptive vaccines may be effective after ingestion by nontarget organisms, including humans. Immunocontraceptives will not be approved by Federal and State regulatory agencies for routine field implementation in wildlife management programs until these potential secondary effects are documented as being environmentally insignificant.

Interactions among ecological processes will likely exert a great effect on the success of wildlife contraceptive-management programs. Reduced reproduction by females treated with contraceptives may provide greater chances for survival of offspring born to other untreated females in the population. In other words, there may be a compensatory increase in juvenile survival. Additionally, reductions in a particular population because of reduced reproduction could be offset by immigration of individuals from areas surrounding the treatment area.

Time and cost efficiency are extremely important issues when considering wildlife contraceptive-management programs. The contraceptive agents themselves may be economical, but the personnel and operating expenses associated with delivering contraceptives to significant proportions of individuals in a wildlife population likely will be cost prohibitive. State wildlife agencies obtain much of their funding from sales of hunting and fishing licenses and Federal aid funds for wildlife restoration (e.g., the Pittman–Robertson tax). Therefore, it may be inappropriate for these agencies to use these revenues for contraceptive management programs. Alternate State, Federal, municipal, or private funds probably will be required to support contraceptive management programs.

The nature of the wildlife management profession has changed greatly in the United States during the past few decades. Societal changes have altered the opinions and expectations of the public we serve. Wildlife biologists and managers are entrusted by the public with the responsibility of managing our wildlife resources. Nonlethal techniques for wildlife population management are increasingly demanded by the public in some situations. The potential for contraception to become a successful wildlife population management technique in certain publicly sensitive situations is great. Wildlife biologists have a professional obligation to consider all possible techniques for use in wildlife population management.

References Cited

Behrend, D. F.; Mattfield, G. F.; Tierson, W. C.; Wiley, J. E., III. 1970. Deer density control for comprehensive forest management. Journal of Forestry 68: 695–700.

Bell, R. L.; Peterle, T. J. 1975. Hormone implants control reproduction in white-tailed deer. Wildlife Society Bulletin 3: 152–156.

Bomford, M. 1990. A role for fertility control in wildlife management. Bull. 7. Canberra, AUS: Bureau of Rural Resources, Australian Government Publications Service. 50 p.

Boyles, J. S. 1986. Managing America's wild horses and burros. Journal of Equine Veterinary Science 6: 261–265.

Carlquist, B. 1990. An effective management plan for the exotic mountain goat in Olympic National Park. Natural Areas Journal 10: 12–18.

Clarke, G. N. 1988. Lack of correlation between the immunobead test and the enzyme-linked immunosorbent assay for sperm antibody detection. American Journal of Reproductive Immunology 18: 44–46.

Conover, M. R.; Decker, D. J. 1991. Wildlife damage to crops: perceptions of agricultural and wildlife professionals in 1957 and 1987. Wildlife Society Bulletin 19: 46–52.

Curtis, P. D.; Richmond, M. E. 1992. Future challenges of suburban white-tailed deer management. Transactions of the North American Wildlife and Natural Resources Conference 57: 104–114.

Diaz, S.; Pavez, M.; Miranda, P.; Robertson, D. N.; Sivin, I; Croxatto, H. B. 1982. A five-year clinical trial of levonorgestrel silastic implants (NORPLANT[3]). Contraception 25: 447–456.

Dunbar, B. S.; Lo, C.; Powell, J.; Stevens, V. C. 1989. Use of a synthetic peptide adjuvant for the immunization of baboons with denatured and deglycosylated pig zona pellucida glycoproteins. Fertility and Sterility 52: 311–318.

Garrott, R. A. 1991. Feral horse fertility control: potential and limitations. Wildlife Society Bulletin 19: 52–58.

Garrott, R. A. 1995. Effective management of free-ranging ungulate populations using contraception. Wildlife Society Bulletin 23: 445–452.

Garrott, R. A.; Siniff, D. B.; Tester, J. R.; Eagle, T. C.; Plotka, E. D. 1992. A comparison of contraceptive technologies for feral horse management. Wildlife Society Bulletin 20: 318–326.

Godfrey, E. G.; Lawson, P. 1986. Wild horse management: an economic perspective. Journal of Equine Veterinary Science 6: 266–272.

Goodloe, R. B. 1991. Immunocontraception, genetic management, and demography of feral horses on four eastern U.S. barrier islands. Ph.D. dissertation. Athens, GA: University of Georgia. 150 p.

Harder, J. D.; Peterle, T. J. 1974. Effect of diethylstilbestrol on reproductive performance of white-tailed deer. Journal of Wildlife Management 38: 183–196.

Hoffman, R. A.; Wright, R. G. 1990. Fertility control in a non-native population of mountain goats. Northwest Science 64: 1–6.

Houston, D. B.; Stevens, V. 1988. Resource limitation in mountain goats: a test by experimental cropping. Canadian Journal of Zoology 66: 228–238.

Houston, D. B.; Schreiner, E. G.; Moorhead, B. B.; Olson, R. W. 1991. Mountain goat management in Olympic National Park: a progress report. Natural Areas Journal 11: 87–92.

Jacobsen, N. K.; Jessup, D. A.; Kesler, D. J. 1995. Contraception in captive black-tailed deer by remotely delivered norgestomet ballistic implants. Wildlife Society Bulletin 23: 718–722.

Kirkpatrick, J. F.; Liu, I.K.M.; Turner, J. W., Jr. 1990. Remotely-delivered immunocontraception in feral horses. Wildlife Society Bulletin 18: 326–330.

Kirkpatrick, J. F.; Turner, J. W., Jr. 1991. Reversible contraception in nondomestic animals. Journal of Zoo Wildlife Medicine 22: 392–408.

Kirkpatrick, J. F.; Liu, I.K.M.; Turner, J. W., Jr.; Bernoco, M. 1991. Antigen recognition in feral mares previously immunized with porcine zonae pellucidae. Journal of Reproduction and Fertility, Suppl. 44: 321–325.

Kirkpatrick, J. F.; Liu, I.K.M.; Turner, J. W., Jr.; Naugle, R.; Keiper, R. 1992. Long-term effects of porcine zonae pellucidae immunocontraception on ovarian function in feral horses (Equus caballus). Journal of Reproduction and Fertility 94: 437–444.

Liu, I.K.M.; Bernoco, M.; Feldman, M. 1989. Contraception in mares heteroimmunized with pig zonae pellucidae. Journal of Reproduction and Fertility 85: 19–29.

Lyman, R. L. 1988. Significance for wildlife management of the late quaternary biogeography of mountain goats (Oreamnos americanus) in the Pacific Northwest, U.S.A. Arctic and Alpine Research 20; 13–23.

Matschke, G. H. 1977a. Microencapsulated diethylstilbestrol as an oral contraceptive in white-tailed deer. Journal of Wildlife Management 41: 87–91.

Matschke, G. H. 1977b. Fertility control in white-tailed deer by steroid implants. Journal of Wildlife Management 41: 7331–735.

Matschke, G. H. 1980. Efficacy of steroid implants in preventing pregnancy in white-tailed deer. Journal of Wildlife Management 44: 756–758.

Mathur, S.; Chao, L.; Goust, J. M.; Milroy, G. T.; Woodley–Miller, C.; Caldwell, J. Z.; Daru, F.; Williamson, H. O. 1988. Special antigens on sperm from autoimmune infertile men. American Journal of Reproductive Immunology 17: 5–13.

Moorhead, B. B.; Stevens, V. 1982. Introduction and dispersal of mountain goats in Olympic National Park. In: Starkey, E.; Franklin, J.; Matthews, J., eds. Ecological research in national parks of the Pacific Northwest. Corvallis, OR: Oregon State University, Forest Research Laboratory: 46–50.

Naz, R. K. 1987. The fertilization antigen (FA–1) causes a reduction of fertility in actively immunized female rabbits. Journal of Reproductive Immunology 11: 117–133.

Naz, R.; Menge, A. 1990. Development of antisperm contraceptive vaccine for humans: why and how? Human Reproduction 5: 511–518.

Naz, R. K.; Alexander, N. J.; Isahakia, M.; Hamilton, M. S. 1984. Monoclonal antibody to a huyman germ cell membrane glycoprotein that inhibits fertilization. Science 225: 347–344.

Naz, R. K.; Brazil, C.; Overstreet, J. W. 1992. Effects of antibodies to sperm surface fertilization antigen–1 on human sperm–zona pelucida interaction. Fertility an Sterility 57: 1304–1310.

Naz, R. K.; Phillips, T. M.; Rosenblum, B. B. 1986. Characterization of the fertilization antigen 1 for the development of a contraceptive vaccine. Proceedings of the National Academy of Science 83: 5713–5717.

Olympic National Park. 1981. Environmental assessment: management of introduced mountain goats in Olympic National Park. Port Angeles, WA: Olympic National Park. 49 p.

Olympic National Park. 1987. Environmental assessment: management of introduced mountain goats in Olympic National Park. Port Angeles, WA: Olympic National Park. 72 p.

Parkes, J. P. 1990. Feral goat control in New Zealand. Biological Conservation 54: 335–348.

Plotka, E. D.; Eagle, T. C.; Vevea, D. N.; Koller, A. L.; Siniff, D. B.; Tester, J. R.; Seal, U. S. 1988. Effects of hormone implants on estrus and ovulation in feral mares. Journal of Wildlife Diseases 24: 507–514.

Plotka, E. D.; Seal, U. S. 1989. Fertility control in female white-tailed deer. Journal of Wildlife Diseases 25: 643–646.

Plotka, E. D.; Vevea, D. N.; Eagle, T. C.; Tester, J. R.; Siniff, D. B. 1992. hormonal contraception of feral mares with silastic rods. Journal of Wildlife Diseases 28: 255–262.

Primakoff, P.; Lathrop, W.; Woolman, L.; Cowan, A.; Myles, D. 1988. Fully effective contraception in male and female guinea pigs immunized with the sperm protein PH–20. Nature 335: 543–546.

Robertson, D. N.; Sivin, I.; Nash, H. A.; Braun, J.; Dinh, J. 1983. Release rates of levonorgestrel from Silastic® capsules, homogenous rods and covered rods in humans. Contraception 27: 483–495.

Roughton, R. D. 1979. Effects of oral melengestrol acetate on reproduction in captive white-tailed deer. Journal of Wildlife Management 43: 428–436.

Safir, J. M.; Loy, R. G.; Fitzgerald, B. P. 1987. Inhibition of ovulation in the mare by active immunization against LHRH. Journal of Reproduction and Fertility, Suppl. 35: 229–237.

Shulman, S. 1986. Sperm antigens and autoantigens: effects on fertility. American Journal of Reproductive Immunology 10: 82–89.

Skinner, S. M.; Mills, T.; Kirchick, H. J.; Dunbar, B. S. 1984. Immunization with zona pellucida proteins results in abnormal ovarian follicular differentiation and inhibition of gonadotropin-induced steroid secretion. Endocrinology 115: 2418–2432.

Slade, L. M.; Godfrey, E. G. 1982. Wild horses. in: Chapman, J. A.; Feldhamer, G. A., eds. Wild mammals of North America. Baltimore, MD: Johns Hopkins University Press: 1089–1098.

Stevens, V. C; Powell, J. E.; Lee, A. E.; Kaumaya, P.T.P.; Lewis, H. D.; Rickey, M.; Atkins, T. J. 1992. Development of a delivery system for a birth control vaccine using biodegradable microspheres. Proceedings of the International Symposium on Controlled Release of Bioactive Materials 19: 112–113.

Tuler, S.; Machlis, G E.; Kasperson, R. E. 1992. Mountain goat removal in Olympic National Park: a case study of the role of organizational culture in individual risk decisions and behavior. Risk Issues in Health and Safety 3: 317–340.

Turner, J. W., Jr.; Kirkpatrick, J. F. 1982. Androgens, behavior and fertility control in feral stallions. Journal of Reproductive Fertility, Suppl. 32: 79–87.

Turner, J. W., Jr.; Kirkpatrick, J. F. 1986. Fertility control as a management tool for feral horse populations. Journal of Equine Veterinary Science 6: 278–284.

Turner, J. W., Jr.; Kirkpatrick, J. F. 1991. New developments in feral horse contraception and their potential application to wildlife. Wildlife Society Bulletin 19: 350–359.

Turner, J. W.; Liu, I.K.M.; Kirkpatrick, J. F. 1992. Remotely-delivered immunocontraception in captive white-tailed deer. Journal of Wildlife Management 56: 154–157.

Wagner, F. H. 1983. Status of wild horse and burro management on public rangelands. Transactions of the North American Wildlife and Natural Resources Conference 48: 116–133.

Warren, R. J. 1991. Ecological justification for controlling deer populations in eastern national parks. Transactions of the North American Wildlife and Natural Resources Conference 56: 56–66.

Warren, R. J. 1995. Should wildlife biologists be involved in wildlife contraception research and management? Wildlife Society Bulletin 23: 441–444.

White, L. M.; Smith, P. M.; Miller, C. C.; Fayrer-Hosken, R. A.; Warren, R. J. 1993. Development of an anti-sperm immunocontraceptive for white-tailed deer *(Odocoileus virginianus)*. Abstract. Theriogenology 39: 339.

White, L. M.; Warren, R. J.; Fayrer–Hosken, R. A. 1994. Levonorgestrel implants as a contraceptive in captive white-tailed deer. Journal of Wildlife Diseases 30: 241–246.

Willis, L. P. 1993. Equine immunocontraception and oviductal fluid characterization. Ph.D. dissertation. Athens, GA: University of Georgia. 175 p.

Willis, L. P.; Heusner, G. L.; Sekhar, K.N.C.; Naz, R. K.; Fayrer–Hosken, R. A. 1994a. Development of an equine immunocontraceptive agent using sperm plasma membranes. Abstract. Theriogenology 41: 335.

Willis, L. P.; Heusner, G. L.; Warren, R. J.; Kesler, D. J.; Fayrer–Hosken, R. A. 1994b. Equine immunocontraception using porcine zona pellucida: a new method for remote delivery and characterization of the immune response. Journal of Equine Veterinary Science 14: 364–370.

References Cited—Unpublished

Kirkpatrick, J. F.; Turner, J. W., Jr. 1987. Chemical fertility control and the management of the Assateague feral ponies. Final report, Assateague Island National Seashore, Berlin, MD. [National Park Service contract CA1600–3–0005.] 36 p.

Directory of Personal Communication

Kirkpatrick, J. F. Deaconess Research Institute, 1500 Poly Drive, Billings, MT 59102.