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Fertility Control in Wildlife Management: A Review

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Introduction

The history of fertility control and chemosterilization as a management tool for the control of free-roaming wild and feral, and captive exotic animal populations is a relatively short one, and the fraternity of scientists who have created this short history is a small one. It is the purpose of this opening paper to "set the stage", that is, to review just what has been accomplished in the field and provide the background and context for the many papers which follow.

Until man's intervention became a serious factor, animal populations were kept within the limits of their food supplies and habitats through predation, starvation, disease, a variety of physiological controls upon reproductive success and, sometimes, migration. These often delicate balances have been severely disrupted by human intervention and two of the more obvious results have been elimination of predator species and a loss of critical habitat. Thus humans, caught in the whiplash of their own ignorance, have had to gradually take on the responsibility for managing present wildlife populations.

Historically, wildlife populations have been kept within the limits of food supplies and habitats through controlled hunting, poisoning, trapping, and sometimes relocation. A variety of social and political factors are now threatening to reduce the effectiveness of these traditional methods and uncontrolled population increases among some species are occurring throughout the world. In certain cases, such as the elk and bison herds of Yellowstone National Park, the protection afforded by refuges has resulted in severe overpopulation and degradation of habitat. In another example, feral horses have overpopulated their ranges in the western United States as a result of well-meant but poorly conceived legislation. Certain zoo animals, even though their wild free-roaming relatives are endangered, now reproduce so efficiently in captivity that we are simply running out of room to place their offspring. The most notable of these are the large cats.

Controlled hunting, although successful in most cases, is coming under increased public scrutiny. Legislative interference with deer hunting seasons has already occurred in a number of states despite growing populations. From a purely biological viewpoint, hunting does not insure natural selection either. Trapping, particularly with leg-hold devices, is extremely unpopular among certain segments of society and legislation against steel traps has already been passed or is pending in many states and over 60 countries. Even in regions where trapping is reasonably well-accepted, decreasing fur prices have resulted in

ıcreasing populations of predatory animals such as coyotes and foxes, and among ıecies as the skunk and raccoon, which carry and spread dangerous diseases such ı rabies and Lyme disease. Live-trapping and relocation of overpopulated species expensive and only works when sufficient suitable alternative habitat exists, a ıation which is almost impossible to find.

Poisoning overpopulated animals is distasteful, often dangerous to humans, d notoriously nonspecific. Most poisoning programs require state and federal rmission, something which is becoming difficult to obtain. For example, the e of strychnine has been prohibited by the Environmental Protection Agency in states and it is doubtful that the two remaining states, Montana and Wyoming, ll be permitted to use this poison for much longer. It is noteworthy that the use strychnine for eleven years in Montana has not reduced the incidence of rabies re; in fact, it has increased (Schatzow, 1986). The shortcomings of poisoning multiple and serious. First, the target animals are destroyed in a s-than-humane fashion, healthy animals along with diseased ones, in the case predation, the innocent along with the guilty, and in the case of scavenging, ıply the unlucky. Second, population reduction is only temporary and each new eding season results in new increases. Third, poisons kill nontarget species ıgdal et al., 1986).

The concept of fertility control as a means of controlling wild and feral cies has received little attention to date, despite a significant backlog of ıarch predicting success. This is surprising, since the technology associated ı fertility control in humans is impressive and its application to wild, feral and ıive exotic species is fundamentally sound. Furthermore, the compounds ilable for use in humans were first tested on other animals. Nonetheless, the ıcept is largely untested, and skeptics, who abound, consider the approach rre. In consideration of this situation, the remainder of this paper will focus the history and benefits of fertility control and chemosterilization in wild, , and captive exotic species. Emphasis will be placed on topics which are not essed in other papers in these proceedings.

Canidae

use of antifertility compounds in wild canids was prompted by the discovery 953 that mismated domestic bitches would resorb early embryos if given the ıetic estrogen diethylstilbestrol (DES) (Jackson, 1953). Linhart (1963) ıosed the use of orally delivered steroids to control reproduction in the red fox *ves fulva*), an animal implicated in the spread of sylvatic rabies. A year later, urt and Enders (1964) demonstrated that female foxes force-fed 50 mg of from nine days before mating to ten days post-mating became infertile. The apparently acted by causing implantation failure or early embryonic ption. The same dose of DES had no apparent effects upon male foxes.

While suppression of fertility among captive animals was shown to be possible, the first problems of application in the field soon became apparent. Linhart (1964) tested bait acceptance by foxes, using eight different bait types during winter months. Bait acceptance by foxes was sporadic and nontarget species such as farm dogs, crows, and skunks took baits as often as foxes. Despite these problems, contraception in foxes appeared possible. Oleyar and McGinnes (1974) attempted to inhibit reproduction in both red and gray foxes (Urocyon cinereoargenteus) in Virginia, with DES-drugged baits. Ground beef baits loaded with 50 mg DES were readily taken by gray foxes but less so by red foxes. Data subsequently obtained from trapped foxes demonstrated that fertility was significantly reduced in the gray foxes but not in the red foxes.

During this same period of time Cheatum and Hansel (1967) investigated the efficacy of several different reproductive inhibitors in captive red foxes over four breeding seasons. Three of the compounds tested proved effective. Various mixtures of clomiphene isomers [1-(p-beta-diethylaminoethoxyphenyl)-1,2 diphenyl-2-chloroethylene] given weekly in doses of 300 mg throughout the breeding season did not interfere with the occurrence of estrus or mating but prevented pregnancies in all vixens receiving the drug. The data suggested that clomiphene may have impaired fertilization, but the mechanism of action was not described. Chlormadinone acetate (6-chloro-6-17-acetoxyprogesterone) administered orally every four, seven, or ten days prevented estrus in most vixens until the feeding regime was halted.

Diethylstilbestrol given in meat baits on the day of mating or ten days thereafter, in doses of 100 mg prevented implantation in vixens. However, if the DES was administered in tallow, rather than the meat, it lost its efficacy. This suggested that the choice of bait was important in the delivery of synthetic steroids to carnivores.

The study of Cheatum and Hansel (1967) also demonstrated that a synthetic estrogen related to DES, mestranol [17-alpha-ethynyl-3-methoxyestra-1,3,5(10)-trien-17-beta-ol], (MES) was an effective reproductive inhibitor. No foxes fed MES for five days after mating produced pups. Although most first feedings were readily accepted, the vixens only nibbled at subsequent drugged feedings. Thus, it appeared that MES could not be disguised for prolonged administration to foxes and probably not to coyotes either. This bait acceptance problem with MES would surface again in rodents.

One of the most important features of the Cheatum and Hansel study was that it included an attempt to inhibit male fertility. Until this time, all attempts at fertility control in wild canids had focused upon the female. Spermatogenesis in male foxes was inhibited by feeding them a mixture of DES and chlormadinone acetate in meat baits at weekly intervals for four weeks, beginning the first week in December. Five weeks after drug administration was discontinued, spermatozoa were present in the seminiferous tubules but not in the epididymides. No

ignificant impairment of spermatogenesis was observed with either of these ompounds alone at the same dosages.

At about the same time as the above studies, Balser (1964) attempted to ontrol reproduction in female coyotes (*Canis latrans*), with DES. Initial aboratory tests had shown that DES given just before or after mating inhibited nplantation in coyotes just as it had in foxes. Tallow baits (Brushman et al., 967) filled with 100 mg of DES were air-dropped in certain sections of New lexico. Female coyotes were caught several weeks later in these areas, and pproximately 75% of these females showed implantation failure or signs of fetal aorption.

There were however, limitations in the effectiveness of DES baits for hibiting fertility in coyotes. First, DES ingestion had to be timed relatively ecisely with the animals' reproductive cycle for success. This problem was mpounded by the fact that coyotes did not take non-living baits with any gularity during the breeding season. Second, there also appeared to be some oblem in the absorption of the DES in tallow baits. Finally, Balser (1964) and nhart et al. (1968) reported that coyotes that did take the DES-drugged bait peared to remain sexually active longer than usual and were thought to be producing later in the season.

Following Balser's work with coyotes, research on contraception in canids as redirected to domestic dogs. Taking advantage of advances in reproductive docrinology, Simmons and Hamner (1973) placed silicone rubber implants ntaining testosterone or androstenedione subcutaneously in female beagles. The ches were kept in a constant state of anestrus for 420 to 840 days and when the plants were removed, normal fertility was restored. Estrus was clearly ppressed in these dogs but this study did not explain the mechanism of action. e most probable explanation was that the androgenic steroids interfered with the pothalamic-pituitary axis, blocking the release of luteinizing hormone (LH) and licle stimulating hormone (FSH), and inhibiting follicle stimulation and/or ulation. Unfortunately, in addition to producing antifertility, the androgenic roids caused both physical and behavioral masculinization of the female, a ndition unacceptable to dog owners.

At about the same time Storm and Sanderson (1969a) tested the ectiveness of an oral progestin, medroxyprogesterone acetate (Provera) on otive female red foxes. Each fox received 25 mg of provera/day for four or ht days during the breeding season and the number of litters was significantly uced. Shortly thereafter, other investigators explored the use of oral progestins controlling fertility in canids. Melengestrol acetate, an oral progestin closely ated to Provera was given to domestic bitches in doses of 200 µg or more per ', and estrus was completely inhibited for a treatment period of 243 days dkolowski and VanRavenswaay, 1976). The positive results obtained with lengestrol acetate led to the first progestin approved for commercial use in gs. This compound, megestrol acetate (Ovaban, Schering Corp., Kenilworth,

NJ) is an effective oral contraceptive in the bitch, highly reliable, and with few side effects (Wildt and Seager, 1977). In the Netherlands, another synthetic progestin, proligesterone (14 alpha, 17 alpha-propylidene-dioxy-progesterone) was tested in dogs and found to suppress estrus in 97% of the bitches fed the compound (VanOs and Oldenkamp, 1978). Despite these successes with domestic dogs, no significant field applications of these drugs have occurred with wild canids, even though fox-related rabies outbreaks have since occurred in various sections of the United States.

At this point attention returned to androgenic steroids. The synthetic androgen mibolerone (17-beta-hydroxy-7 alpha, 17-dimethylester-4-ene-3-one) given orally to domestic bitches for 240 days suppressed estrus and probably ovulation for the entire test period without the objectionable masculinization seen earlier with testosterone (Sokolowski and Zimbelman, 1976). Nine years later this same drug was given to five captive female timber wolves (*Canis lupis*) in doses of 6 µg/kg/day for 2 to 22 months (Gardner et al., 1985). There was a complete suppression of estrus and the only discernable side effect was increased aggression directed toward cage-mates. During this same period, the Carnation pet food company conducted extensive experiments with mibolerone. In one of the larger tests, 600 privately owned dogs in eight states were placed on mibolerone without the benefit of veterinary examinations; fertility inhibition was almost 100% and no untoward side effects were noted (Lloyd Miller, Carnation Research Laboratories, personal communication). Ultimately the FDA licensed the drug for prescription by veterinarians. Effective fertility inhibition requires 30 µg/day, a condition unlikely to be met in many wild populations.

In 1976, two independent studies took a different approach to the control of coyote reproduction. Gates at al. (1976) and Thompson (1976) attempted to produce chemosterilization in male coyotes through the administration of cadmium chloride ($CdCl_2$). Captive males were given from 2 to 24 mg/kg orally. In both studies there was no decrement in spermatogenesis. The failure of CdCl2 to produce chemosterilization in male coyotes was puzzling, considering the previously documented permanent damage to the testes of dogs (Sankaranarayana et al., 1973) and a wide variety of other mammals.

Still another approach to canine fertility control was taken by Al-Kafawi et al. (1974). This team attempted to immunize dogs against their own LH with injections of human chorionic gonadotropin (hCG). This experiment failed because canine gonadotropins did not cross-react with anti-hCG antibodies, but the concept was promising. A year later Faulkner et al. (1975) reported varying degrees of success in immunizing dogs against LH through the use of antibodies that were considerably more specific for canine LH. More recently, Vickery et al. (1984) successfully suppressed fertility in male dogs with repeated injections of a GnRH agonist. The agonist, [D-Nal(2)6-GnRH] was administered intramuscularly in doses of 10 µg/kg, and testis volume, ejaculate volume, sperm count, and sperm motility all declined for periods as long as 172 days. Libido

as depressed but could be restored with testosterone implants. Following this ork, Hasson et al. (1985) immunized male dogs against their own gonadotropin leasing hormone (GnRH) with GnRH-conjugated to human serum globulin. asma testosterone, LH and sperm counts were all significantly decreased.

Vickery et al. (1985) suppressed estrus in dogs with nafarelin 5-D-(2-napthyl)-alanine] GnRH), a potent GnRH agonist analog. Using a bcutaneous osmotic pump, 2, 8, or 32 µg were delivered daily and completely ppressed estrus for up to 18 months. While successful in captive domestic dogs, is approach has little usefulness in wild populations of foxes or coyotes. evertheless, the approach may be useful with zoo animals or larger free-roaming ecies where capture is not a problem.

Finally, Allen (1982) field tested DES, in sugar-coated ground fat baits, in 1 foxes in North Dakota. Each bait contained 50 mg of DES. Average bryonic litter size was reduced from 4.6 among control foxes to 3.0 among xes taking at least one bait.

Felidae

early as 1963 it had been demonstrated that synthetic progestins could suppress rus in female cats (Harris and Wolchuck, 1963). The precise form of the mpound and dose were refined, and by 1976 the progestin megestrol acetate was utinely administered to domestic cats to suppress estrus (Burke, 1977). egestrol acetate was next applied to feral cat populations in England with ccess. In these field tests, McDonald (1980) gave an initial dose of 5.0 mg in at baits, followed by 2.5 mg weekly, to dockside feral cats. Only one cat of ven received its dose each week; the other six were more or less erratic in their ndance. Five cats had no pregnancies, one disappeared, and one produced four rmal kittens. Five of the cats were later euthanized and necropsy results dicated no cases of mammary tumors or uterine pyometria. Two years later, mfry (1978) repeated the experiment in Scotland. Of 15 females treated, only ir had litters. The drug is available commercially, in Europe, under the name arid (Glaxo Drugs, Research Triangle Park, NC).

Another synthetic progestin, medroxyprogesterone acetate, has been used Denmark, since 1971, for controlling feral cats (Leo-information, 1976). lutex (Leo Laboratories) as it is known commercially, was administered weekly doses of 2.5 to 5.0 mg to 504 female cats. Of these, only 20 (4.0%) became gnant. Less than 1 % showed signs of mammary tumors or pyometria. lowing this, Kirkpatrick (1986) used both medroxyprogesterone acetate and gestrol acetate in a feral cat control study in Billings, Montana. Of eleven ales which regularly took baits containing 5 mg of steroid, only two produced ers. Five of eight control females became pregnant.

Critics of this approach to fertility control in cats point to the issue of rine pyometria and mammary tumors associated with ingestion of these drugs.

Current evidence indicates that synthetic progestins do cause these two conditions, and most evidence supports a rate of incidence of < 1.0%. However, when used to control feral cats, these problems must be put into proper perspective. Dr. Tom Wolski, of Cornell University, in an unpublished three-year study of feral cats reported that 50% of kittens do not survive to weaning, only 33% live to age one, and dog attacks and death of the mother were the major reasons for kitten mortality. It is unlikely that any contraceptive drug will be free from all side effects, but each approach must be measured against the magnitude of the problem. A 1.0% rate of mammary tumors or pyometria may be considered insignificant in the light of Dr. Wolski's data.

Seal et al. (1976) using injectable medroxyprogesterone acetate (1.0 gram initially followed by 0.5 gms three months later) or melengestrol acetate in silastic implants (500 mg) achieved long-term suppression (two years) of estrus in captive African lions (*Panthera leo*), tigers (*Felis tigris*), leopards (*Panthera pardus*), and jaguars (*Panthera onca*). When the implants were removed, fertility was restored. Steroid fertility control is currently being applied in free-roaming female lions in Etosha National Park in Namibia, and this topic will be covered in detail by Drs. H. H. Berry and H. J. L. Orford later in these proceedings. In the initial studies depot progestins in silastic implants were placed in female lions in an effort to slow reproduction (Chadwick, 1983).

Gardner et al. (1985) used oral mibolerone in captive jaguars, spotted leopards, and lions. Actual doses of the drug ranged from 6 to 19 µg/day and suppression of estrus was successful in all three species. Side effects included refusal to eat at higher dose levels and masculinization in some of the lions. One female lion grew a mane.

Chan et al (1981) utilized an immunological approach to fertility control in cats. They homogenized feline ovaries and raised rabbit antibodies against them. The antibodies, when administered to pregnant cats, caused some fetal resorption but results were generally discouraging. Once again, as in dogs, nonspecificity of the antibody appeared to be the problem.

Cervidae

The increase in ungulates such as deer and elk, in refuges where hunting is either not permitted or impossible has stimulated research of chemical contraception in these animals. As early as 1968 attempts were made to regulate reproduction in Yellowstone's northern elk herd (*Cervus canadensis*). Greer at al. (1968) administered DES intramuscularly to 36 pregnant cow elk between December and March. Doses of 75-200 mg terminated pregnancy in 30% of the treated animals. Following this, Harder, (1971) and Harder and Peterle (1974) fed DES to female white-tailed deer (*Odocoileus virginianus*) before and during pregnancy. In both cases, with doses of 50-100 mg/day, there was significant fetal loss. The

ntramuscular approach was more effective but clearly impractical in animals as ecretive as white-tailed deer.

A year later, Bell and Peterle (1975) implanted both synthetic estrogen and rogestin in white-tailed does during pregnancy. The silastic implants contained , 50, 100, o0r 150 mg of melengestrol acetate, or 75 mg of DES. The calculated ormone release ranged from 0.02 to 12.58 mg/day. The implants were clearly aperior to injected steroids; pregnancy rates were significantly reduced among oes treated with either hormone. Matschke (1977a), in an attempt to regulate production in white-tailed deer in Mammoth Cave National Park, Kentucky, dministered DES orally to does in an encapsulated form. Doses of 500-1000 mg ncapsulated in a modified gelatin interrupted pregnancy in a high percentage of ases. However, poor acceptance by the does, the need for very high doses, and ost-abortion pregnancies led Matschke to conclude the approach was not ractical. Matschke (1977b) then tried two synthetic progestins, MGA (17 pha-acetoxy-6-methyl-16-methylene-4,6, pregnadiene-3,20-dione) and DRC 6246 7 alpha-allyl-17-beta- hydroxy-3-oxoestra-4,9,11-triene). Does were given 50 g and 1.0 g daily oral doses of these drugs, respectively, during the breeding ason. Although does accepted both compounds without reservation, neither one evented or delayed conception. Matschke (1980) hypothesized that not enough the steroids accumulated in the body fat of deer to bring about prolonged tion. Next, Matschke (1977c, 1980) placed subdermal implants containing DES d the progestin DRC-6246 in 23 sexually mature female deer. Daily release tes for the steroids averaged 193 µg of DES and 93 µg of DRC-6246. Nine of e experimental does died from handling-related stress and none of the remaining perimental does became pregnant. While the experiment proved that fertility uld be inhibited pharmacologically, the impracticality of capturing the animals d the resulting stress was a distinct shortcoming to this approach. Matschke 976) also tried a mechanical birth control device in deer. The device was nufactured from silastic and anchored in the vagina of the doe, and designed prevent intromission and ejaculation by the male. The devices failed to vent pregnancies and this approach was abandoned.

Roughton (1979), realizing the impracticality of implants in deer, fed -1.0 mg of melengestrol acetate daily to does during the breeding season. production was completely inhibited, there were no untoward side effects, and tility was later restored. To be effective however, the drug had to be given ly, a requirement that is difficult to meet in wild populations.

More recently attention returned to implants. Jay Holcomb, of the Marin unty (CA) Wildlife Center, is attempting to suppress fertility in white-tailed r on Angels Island, near San Francisco with subdermal silastic implants taining melengestrol acetate (Levenson, 1984). Dr. Richard Avanzino will be senting a detailed picture of this work and the results in a later paper in these ceedings.

In a similar experiment, U. S. Seal (Personal communication) placed subdermal silastic implants containing 800 mg of melengestrol acetate in 25 feral goats (*Capra hircus*), in Texas. The 25 experimental nannies, plus another 25 control females were placed with 5 billies. After two years no kids have been born to the treated goats.

Rodentia

The concept of chemical fertility control for managing pest rodent populations was originally put forth by Howard (1967). Marsh and Howard (1969) fed 0.05% mestranol baits to wild rats (*Rattus norvegicus*) and observed an immediate and significant reduction in pregnancies. Poor bait acceptance of the steroid gave short-lived results. Following this study, Howard and Marsh (1969) and Storm and Sanderson (1970) expanded this line of research to include voles (*Microtus pennsylvanicus, Microtus californicus*, and *Microtus montanus*) as well as rats. Again, rats did not accept mestranol baits well, and doses had to be reduced to 0.005% before voles would accept baits regularly. Reproduction was inhibited in the voles, and pups receiving mestranol through the mothers' milk never developed sexually, becoming irreversibly sterile.

Brooks and Bowerman (1971) and Mischler et al. (1971) evaluated a new powerful estrogenic compound, 17 alpha-ethynylestradiol-3- cyclopentylether, later known as quinestrol. This compound was shown to be more effective than mestranol for antiovarian treatment in rodents. Doses as low as 10 µg completely inhibited reproduction, but once again poor bait acceptance in rats made the approach impractical.

Presently only one drug has been successfully tested as an antifertility agent in rodents and carries FDA approval for that use. Ericsson (1975) fed Norway rats alpha-chlorohydrin (3-chloro-1,2-propanediol). The drug was lethal in both sexes if ingested in high enough quantities (LD_{50} = 164 mg/kg body weight) but also caused permanent sterility in male rats at sublethal doses. The drug causes a blockage at the head of the epididymis, which prevents spermatozoa from leaving the testis, as well as interfering with sperm glycolysis. The sterilized rats are otherwise healthy and mate normally, although without results. The drug, now marketed commercially (Epibloc, Pestcon Systems, Inc., Alhambra, CA) is microencapsulated in a vinyl resin-based wall material, and bait acceptance has not been a problem. Because it can be toxic and its antifertility effects are permanent, alpha-chlorohydrin has limited use in wildlife management, but clearly is useful in controlling certain pest rodent species.

It has been known for almost 50 years that certain plants contain estrogenic substances which act as reproductive inhibitors, yet few investigators have attempted to utilize these naturally occurring substances to control reproduction in wildlife. Cranston (1945) fed an ethanolic extract of the *Lithospermum ruderale* root to mice. This plant had historically been used by Indians of the

athwest to inhibit fertility. Litter production decreased by 50% among mice nsuming the extract 10 days before and 10 day during breeding activity. rfknect and Peng (1968) prepared ethanolic extracts of the plants *Prunus arginata*, and *Lonicera ciliosa*, and fed them to laboratory mice as 1-2% of the t. Again, litter production was reduced by about 50%. It is interesting that both se plants were used by Indians of the northeast for contraceptive purposes. 'ger et al. (1977) extracted seven ethanolic fractions from winter wheat sprouts fed them to *Microtus montanus*. Five of the fractions caused significant actions in uterine weights and two fractions, p-coumaric acid (PCA), and ydroxy-3-methoxystyrene (4-VG) caused significant reductions in litters.

Recently, Garrett and Franklin (1983) successfully inhibited reproduction lack-tailed prairie dogs (*Cynomys ludovicanus*) in Wind Cave National Park 'eeding DES-treated oats (0.11% active ingredient). Reproductive inhibition almost 100% effective, and there was total reversibility when drug treatment withdrawn.

One of the largest rodents, the beaver (*Castor canadensis*) can cause tantial damage when it inhabits populated areas. Brooks et al. (1980) ıpted to control beaver populations by surgically neutering either the male or emale of family pairs. Production of litters was significantly reduced, without pting either behavior or social organization. While the logistics of surgical ring make this an unreasonable approach in some species, there is clearly a for this technique in certain instances and with certain species.

Equidae

ewed interest in fertility control in free-roaming species has resulted from amatic increases in feral horse populations in the western United States the past 15 years. Legislation and social pressure have prevented scale destruction of these animals, and relocation has proven prohibitively sive and ineffective. Despite the widely publicized Adopt-A-Horse m, feral horse populations grew from an estimated 17,000 animals in 1970, r 50,000 animals by the end of the decade. Interest in controlling this tion of free-roaming equids first emerged in 1972, and in 1977 the Bureau d Management, the agency responsible for managing feral horses in the ı U.S., sponsored the first fertility control research in feral horses. The esearch to limit fertility focused upon the stallion, and attempted to exploit erm-like social structure of feral horses. To test the concept, Kirkpatrick ner (unpublished data) vasectomized two feral stallions and followed their or the following two years. No foals appeared among the mares in these nd the stallions exhibited normal sexual behaviors. Kirkpatrick et al. and Turner and Kirkpatrick (1982) reported successfully inhibiting ction in feral horses by lowering sperm counts and reducing sperm motility ons. A microencapsulated form of testosterone propionate (mTP) was

injected into 10 immobilized stallions, in doses of 3.0 to 10 grams, several months before the April-June breeding season in Challis, Idaho. The polymer (DL-lactide) coating, developed by Southern Research Institute (Birmingham, Alabama), permitted a sustained release for up to six months. The stallions' behavior was unaffected and breeding took place, but there was an 83% reduction in foal production. Previous controlled experiments with domestic stallions indicated that the drug caused oligospermia and an impairment of sperm motility (Turner and Kirkpatrick, 1982). Additionally, Kirkpatrick et al. (1982) demonstrated that repeated injections of testosterone cypionate and single injections of quinestrol could also cause oligospermia in stallions, although these two drugs have not been field tested to date. Remote delivery of mTP to stallions, at doses of approximately 3.0 grams of active drug has also been attempted on Assateague Island, MD, with a reduction in foaling rates of approximately 45%. Dr. John Turner describes the use of mTP in stallions in more detail in a later paper in these proceedings. This same drug is currently being tested in a captive zebra stallion at the Woodland Park Zoo, in Portland, OR.

Concern over band infidelity by mares and the potential ineffectiveness of treating stallions led to two different attempts to reduce fertility in mares with steroids. In a project still in progress, Vevea et al. (1987) placed subdermal implants containing various doses of estradiol (E) and progesterone (P) in captive feral mares. Temporary decreases in behavioral estrus occurred among mares receiving 8 g E, 12 g P + 4 g E, or 8 g P + 8 g E, but plasma hormone levels decreased and behavioral estrus appeared among these mares by five weeks after treatment. The investigators suggested that mares increase their clearance rates of these steroids after administration. Dr. E. D. Plotka describes this project in more detail in a later paper.

In another study, Kirkpatrick and Turner (1987), using remotely delivered darts, administered a microencapsulated synthetic progestin, norethisterone (mNET) to six feral mares on Assateague Island, MD. This progestin, which has been used successfully to inhibit fertility in women, was given in a dose of approximately 2.0 g. All six mares receiving the progestin foaled a year later, a highly improbable event among Assateague mares, which suggests that the mNET actually enhanced fertility. The enhanced fertility strengthens the theory of Vevea et al. (1987) that steroid administration to mares increases their clearance rates. Despite a wide range of results using steroids in stallions and mares, the logistics of placing subdermal implants or delivering up to four darts in feral horses suggests new directions for attacking the overpopulation problem in feral horses.

The most promising new approaches are immunological in nature. Liu et al. (in press) at the University of California at Davis has developed a vaccine which causes passive immunization in mares to the zonae pellucidae of ova and the preimplantation embryo. In an initial test, the vaccine, utilizing porcine zonae emulsified with Freund's adjuvant, caused infertility in nine of ten captive feral mares. In four domestic mares given the vaccine, antibody titers remained high

ight months after inoculation. These mares returned to estrus and became nant the following year, demonstrating the reversibility of the approach. ough a minimum of two injections is necessary for the initial infertility effect, antigen recognition has occurred, it is likely that a single booster inistration will suffice in subsequent years (Liu, personal communication). patrick, Liu and Turner will initiate field tests of this vaccine in March of . In a paper later in these proceedings, Dr. Robin Goodloe will report on ber immunological approach, developed at the University of Georgia and g tested on barrier island horses on the east coast (Bratton, 1986).

In still another approach to contraception in horses, John Hughes and Peter (Personal communication), at the University of California at Davis have loped an equine intrauterine device. They placed IUDs into six fertile mares e spring of 1986, and turned the mares out with a fertile stallion. The stallion d with the mares and all were served numerous times, when in estrous. None e IUD mares conceived and all six control mares conceived and carried foals rm. In April, 1987, the six mares with IUDs were recovered, the IUDs ved, and the mares turned out with a stallion. All six conceived at their first s and all are presently pregnant. This approach, while having the lvantage of requiring capture, is simple enough to use with large numbers of mares which can be turned back out after insertion of the device.

Miscellaneous Mammals

dd that two common small mammals, the skunk (*Mephitis mephitis*) and the on (*Procyon lotor*), which are implicated in serious diseases such as Lyme se and rabies, and which adapt well to urban areas have not been the target eater efforts in the area of fertility control. The only serious attempt to it fertility in skunks was made by Storm and Sanderson (1969b) almost 20 ago. They used diethylstilbestrol-loaded baits but were unable to ficantly reduce reproduction. Nelson and Linder (1972) studied bait ptance by both skunks and raccoons, but without actually using a osterilant. Egg baits were loaded with demethylchlortetracycline (DMCT), npound which concentrates in bone and serves as a marker. Nine months animals were collected and examined for the presence of DMCT. Among ons and skunks collected, 87% and 29% respectively, possessed the marker. e the presence of the marker indicated that the animal had taken a bait, it ded no data regarding the frequency of bait acceptance. Despite those raging beginnings there has been little activity in this area.

Aves

Controlling reproduction in the common feral pigeon (*Columba livia*) has challenged wildlife biologists for more than 20 years. Elder (1964) demonstrated that provera (an oral progestin), Arasan (a common fungicide and seed disinfectant), and the anticholesterol agent SC-12937 (22,25-diacholesterol dihydrochloride) (Searle & Co., Chicago) all brought about reversible inhibition of ovulation in pigeons. In more refined follow-up studies, Wofford and Elder (1967) fed SC-12937 in wheat (0.1% by weight) to pigeons. It was calculated that each pigeon consumed about 0.3 g of the drug over an 11 to 16 day period. In rural areas and small towns, reproductive inhibition ranged from almost 100% to 89% for 3 to 7 months. In large cities, reproductive inhibition fell to 10%, primarily because of the large numbers of birds and crossing over of treated and untreated pigeons. Lofts et al. (1968) found that SC-12937 inhibited meiosis in the pigeon testis. Additionally, the drug interfered with sertoli cell function and produced atrophy of Leydig cells, with subsequent loss of sexual behaviors. In the female, clutch size was reduced significantly (Sturtevant and Wentworth, 1970). However, this latter study also produced evidence that the decrement in reproductive function in SC-12937-fed pigeons was as much due to debilitating illness caused by the drug. In several other studies (Becker, 1966; Murton et al., 1972; Schortemeyer and Beckwith, 1970; Woulfe, 1970) the toxic effects of SC-12937 were clearly demonstrated and as a humane reproductive inhibitor the drug was found to be lacking. Despite the evidence that showed SC-12937 to be toxic and the cause of high mortality rates, the drug was registered by the U. S. Department of Agriculture and produced commercially under the name of Ornitrol. Its use remains illegal in Great Britain.

At this point attention turned to another drug for controlling pigeons. Sturtevant (1970, 1971) incorporated mestranol into grit and fed pigeons approximately 183 µg/day. Fertility was reduced by 26% to 67%. Even F1 males hatched from treated adults had significantly depressed fertility. Further, there was no evidence of debilitating toxicity.

Other bird species also stimulated research into fertility inhibitors. Davis (1959) demonstrated that testis weights and spermatogenesis could be reduced in starlings (*Sterna vulgaris*) by feeding the compound triethylene melamine (TEM). He then suggested that the broad concept of population control through chemical gametocide be applied to wildlife management (Davis, 1961). Following up on the concept, Vandenbergh and Davis (1962) showed that TEM could inhibit reproduction in breeding populations of red-winged blackbirds (*Agelaius phoeniceus*). Testis weights were reduced in TEM-treated males, and meiosis was also inhibited; however, the drug's extreme toxicity became apparent. Despite the shortcomings, research with TEM continued. Messersmith (1971) tested the compound on Kent Island, MD. In this study fertility was clearly reduced in red-winged blackbirds, but mortality was not studied.

More recently attention has turned to the antifertility agent thiotepa [tris
azirdinyl) phosphine sulfide] which acts by interfering with nucleic acid
ntbesis. Potvin et al. (1982a,b) fed blackbirds 2.5 - 3.58 mg/kg and reduced
itis weights by 90%, and hatching rates by 50% or more. Despite this success,
s drug caused toxicity at higher levels and the LD50 was determined to be about
2 mg/kg. Attention has returned to SC-12937 and LaCombe and Cyr (1985) fed
d-winged blackbirds cracked corn with 0.1% active drug. While reproductive
fects were similar to those seen in treated pigeons, the birds lost weight during
: course of the study and showed the same debilitating effects seen previously.

One of the shortcomings of male fertility control in blackbirds is
omiscuity by females of a harem. To test the effectiveness of male fertility
ntrol Bray et al. (1975) vasectomized males and examined the fertility of eggs.
rtility was markedly reduced - up to 88% depending upon the distance the
sectomized male's territory was from other territories. It was concluded that
ale chemosterilization was feasible.

Ornitrol has also been used to control reproduction in the common sparrow
asser domesticus), a bird associated with the amplification phase of equine
cephalitis. Mitchell et al. (1979) fed 0.1% Ornitrol in canary seed, to a colony
11 male and 12 female sparrows for a period of two months. Hatching success
as 0 % among treated sparrows versus 64% in controls. Hatching success
ached pretreatment levels among treated birds 4-5 weeks after withdrawal of
nitrol. Two treated sparrows died during the experiment but the cause of death
as not determined.

Discussion

actly what does the history of research on fertility control in wild and feral
imals tell us? First, we can identify the research gaps which exist in this field.
cond, it becomes obvious that research in this area has not kept pace with
odern contraceptive developments. Recent advances in chemical contraception
ve been impressive (Kirkpatrick and Turner, 1985) and later in these
oceedings we will hear about some of these advances in detail. In the 1960s,
nen interest in chemical fertility control in wild and feral species first occurred,
e number of available contraceptive chemicals was relatively small and delivery
stems were limited as well. Today some 25-30 different commercial injectable
d oral contraceptive steroids are available, and several new long-acting
ogestins show great promise. Drs. Wayne Bardin and Lourens Zaneveld will be
scussing some of these compounds later in these proceedings. Another exciting
vance is the development of biodegradable encapsulation processes to permit
ng-term sustained release of injectable contraceptive agents (Beck et al., 1980).
eyond steroids, entirely new doors are opening through which to attack fertility
wild species. The Nobel Prize-winning work of Andrew Schally and Ralph
uillemin on peptide releasing hormones in the hypothalamus offers new promise.

Synthetic analogs of gonadotropin-releasing hormone (GnRH) have been administered by injection and have been extremely effective in blocking ovulation in several species (Schally, 1983). Dr. Brian Vickery discusses advances in this particular area later in these proceedings.

One of the most exciting possibilities for fertility control in wild and feral species lies in immunology, a subject which will be presented later by Dr. Alan Hunter. Still another potentially useful, but largely unexplored approach is using natural products from plants that interfere with reproduction. A recent review (Farnsworth and Waller, 1982) listed 50 plant families, genera, and species that have documented antifertility effects in males and females. Using some of these plants, particularly in managing reproduction in herbivores, deserves further consideration.

One of the more obvious research needs is bait acceptance by small mammals. Research results thus far make it clear that the control of rodent, canine, and other small animal fertility is an easy proposition if resistance to bait acceptance can be overcome. Encapsulating steroids in a disguised and acceptable medium may represent a profitable direction for new research. For example, Calanchi (1976) made 5-mg doses of steroid palatable to human patients by microencapsulating them. Previously the drugs had been unacceptable in uncoated 200 µg doses.

There is a need for a different type of research too. The lessons learned over the past decades of research on human contraception must not be lost to those who wish to apply this technology to wild and feral species. Regardless of the safety or efficacy of a chemical fertility control agent, there are important public issues to be considered and political barriers that must be overcome before widespread success can be achieved. Wildlife - its preservation and particularly its management - is more often than not a highly charged emotional issue. Thus a final thrust for future research should be aimed at determining whether the public will accept fertility control in wild and feral species and how to change resistance to acceptance.

A compelling question then, is why, with increasing problems of wildlife management, hasn't fertility control for wild and feral species kept pace with available technological advances? There is no single clear answer to this question, but at least three factors can be identified. First, much of the early work in this field occurred in the 1960s and early 1970s, when available technology and our knowledge of reproductive physiology was limited, probably limiting successes. Skepticism grew out of this spotty beginning and it remains today. Past failures are not viewed in the context of either the limited technology then, or the advanced technology available now. A surprising proportion of the general public and an equally surprising segment of the scientific community simply find the concept bizarre. Wildlife management simply isn't done this way. Who among us, those who have worked in the field for any length of time, have not faced skepticism or outright ridicule? Finally, funding for this type of research is

emely limited. Federal agencies such as the NSF, NIH, EPA, the Department Agriculture, and even the Public Health Service have shown virtually no est in fertility control in wild and feral species. It is somewhat ironic that the ority of funding for this type of research, during the past 15 years, has come the Department of the Interior. Animal welfare organizations have provided ership in promoting this concept, but lack the financial resources to fund l research. Private foundations have shown some interest but have not been ng to invest in the research.

Why pursue fertility control as a wildlife management technique? Perhaps most compelling reasons for using fertility control are social. Simply, the oach is humane, and public acceptance is more likely than in the case of ng, poisoning or trapping. Not only is individual animal discomfort mized or eliminated, but there is an often-overlooked secondary humane t. Where hunting is forbidden by law and relocating animals is economically ysically unfeasible, overpopulation ends, inevitably, in disease and death tarvation. Fertility control is more likely to be permitted within such cted areas.

Chemical fertility control can bring long-term economic benefits as well, well-planned wildlife management programs will prevent unnecessarily large lation increases by attacking the heart of the problem - reproduction. ng, capture and sale, trapping, and poisoning really only address the toms of overpopulation, not the causes. It is the difference between ntion and cure. Certainly there are some wildlife populations already in s, and their numbers can only be decreased to an acceptable range by ished methods. Once this is done, however, the more cost-effective ology of fertility control can significantly reduce management costs.

Chemical fertility control is a flexible management tool, permitting a large y of control manipulations. With smaller mammals like skunks, and using ed baits, local populations can be controlled with some precision, rather than ting entire states or districts to a single approach. Where drugs can be red remotely to large animals, particular herds, bands, or even individuals e singled out. The reversibility of the drug action adds even more gement flexibility. A large and unanticipated winter kill, for example, can set by withdrawing the treatment for one or more breeding seasons. Since ng animals have not been permanently removed, population size can be d to safe levels.

There are important biological reasons why fertility control must be d for wildlife management. Removing an animal from the population by g, trapping, poisoning, or relocating is permanent; the genes are lost from ol forever. Because chemical contraception is reversible, its use within an gent management plan, and randomizing treatment recipients over a number ding seasons, keeps the gene pool intact. This may be extremely important

where dwindling habitat results in localized overpopulation of rare or endangered species.

Another obvious advantage is the ability to concentrate upon target species without serious damage to other animals. Delivering a bait to a particular species without having a variety of other animals ingesting the drug is probably impossible. However, through careful manipulation of drug types and dosages, effects on a nontarget species can be minimized. For example, a dose of a particular steroid that inhibits vole reproduction may well have no effect on foxes or eagles, however, more research is needed before this can be stated with certainty. Moreover, the peak breeding season for one species often varies significantly from that of another, which makes it easier to deliver baits without interfering with nontarget species. Red foxes, for example, breed from December to March, but skunks do not begin breeding until March (Asdell, 1964). Thus, a bait-delivered fertility control program could be tailored for skunks to avoid interference with fox reproduction. At very least, accidental ingestion will not kill nontarget species or, except for very young animals, cause irreversible fertility loss.

Finally, chemical fertility control affords an approach that, when properly evaluated, will not influence the social structure of the animal populations involved. Since sexually mature individuals are not actually removed, or for that matter even harrassed, the hierarchy of the population is not altered unwittingly by human intervention. It is the considerations such as these, above, that make it clear that no single person in a management program can implement wildlife fertility control for a given species. It will require the coordinated skills of the management group, addressing reproductive biology, behavior, social organization, pharmacodynamics, demography, and ecology attentive to interactions among species and habitats.

How can the concept be developed and implemented to a point where it helps wildlife? The future of fertility control in wildlife management does not rest as much with the scientific community as it does with other forces. It will be public opinion, our federal research-sponsoring agencies, wildlife managers who decide how their budgets shall be utilized, and animal welfare organizations which must bring contraceptive management from conceptual form to reality. The public must be brought to understand the nature of the subject, chances for success, the benefits, and most of all, the consequences of not pursuing this goal. The guidelines for research funding among federal, state, and private research-sponsoring agencies must be broadened to include this particular application of fertility control. The argument that this is "high risk" research may be true in some cases, but unless the risks are taken the answers will not be forthcoming. Finally, those in charge of wildlife management at all levels, must be willing to allocate resources to these new approaches.

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