State of the Animals 2000

Fertility Control in Animals

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INTRODUCTION: FROM MORTALITY CONTROL TO FERTILITY CONTROL

For most of the century we have just left behind, the energies of the government agencies charged by law with managing wildlife were dedicated to building the size and productivity of game populations. Under a utilitarian philosophy of wildlife conservation, this dedication made sense, and in its time, was arguably a highly progressive view of wildlife (Dunlap 1988).

In the U.S., state game management went far to reverse the wildlife catastrophe that was the 19th century. In those years, hunting and trapping for commercial markets drove Carolina parakeets and passenger pigeons extinct and nearly extirpated bison, elk, deer, beaver, egrets, waterfowl, songbirds, and any other furred or feathered creature that could make a meal or adorn a hat (Tober 1981). Predatory birds and mammals were shot on sight, because of the threat they posed to domestic livestock and poultry, and because they were believed by some to be genuinely evil (Dunlap 1988). (These attitudes still linger, and many of these species, such as gray wolves and grizzly bears, still confront them in their path to recovery.)

Through an aggressive program of re-introduction, habitat management, and restrictions on killing, the state wildlife agencies succeeded in restoring populations of deer, elk, beaver, otter, waterfowl, and other game and "fur-bearer" species (Gilbert and Dodds 1992). The lynchpin of this effort was recreational hunting and trapping, which furnished funding (through license sales and Pittman-Robertson grants), volunteer labor, and a dedicated political constituency.

At the beginning of the 21st century, this neat system is unraveling. The reasons are numerous: demographic changes that are producing an ever-shrinking and ever-aging population of hunters and trappers (hunters now represent only 7% of the total population in the U.S.) (U.S. Fish & Wildlife Service 1997); growing public appreciation of "non-game" species, which have been neglected and even harmed by management for game species; and changes in public values from utilitarian views to moral views of wildlife (Kellert 1985; Dunlap 1988). But the biggest challenge to the system may be arising from the failure of the state agencies to respond effectively to the problems associated with dense populations of deer, geese, and other species, especially in urban and suburban communities. Confronted with problems associated with wildlife overabundance, the system designed to increase game populations is floundering.

This seems a contradiction. How could a system founded on hunting and trapping — in short, on killing — find itself unable to control wildlife populations, and solve problems associated with abundant wildlife? First, public hunting on deer and other "big game" species traditionally focused on removing male animals, leaving behind populations streamlined for reproduction. Cultural attitudes, as well as regulations, have discouraged the killing of females. Second, many of the most severe wildlife conflicts arise in locations that are effectively unhuntable, such as parks, research campuses, and suburban neighborhoods. Third, killing of some species, such as wild horses, is simply unacceptable to the public. Finally, the public's tolerance of invasions of their parks and backyards by armed strangers is declining, while its sympathy for wild animals and interest in solving wildlife problems without killing is rising.

While the public is searching for new, humane approaches to solving conflicts with wildlife, the state wildlife agencies persist in recommending hunting and its variations. In part, this is because wildlife agencies in some states, such as New York, are required by law to promote recreational hunting (Marion 1987). But more pervasively, most state agency personnel have strong cultural and political links to the hunting and trapping community, which is (somewhat irrationally) hostile to the concept of non-lethal management of wildlife (Kirkpatrick and Turner 1995; Hagood 1997). The flip side of the wildlife agencies' advocacy of hunting and trapping is their reluctance to pursue or encourage research into other approaches. So the public is turning elsewhere for solutions.

There are really only two choices for actively managing the size of animal populations, reducing the birth rate or increasing the death rate. (Local population size may also be controlled by movement of individuals in and out; but when the size of animal populations concerns us, movement of individuals merely relocates the concerns. We are not absolved of our responsibility for animals simply because they go somewhere else.) Killing certainly can reduce and even destroy wildlife populations, if enough animals of the right description are removed from the population. And until the last decade of the 20th century, fertility control for wildlife was not seen as a feasible option.

But everything changed between 1988 and 1989. The successful use of a remotely deliverable immunocontraceptive on free-ranging wild horses at Assateague Island National Seashore, Maryland, opened a new universe of possibilities for the humane, non-lethal control of wildlife populations.

THE HISTORY OF WILDLIFE FERTILITY CONTROL

The history of wildlife fertility control and its application to the management of free-roaming and captive wildlife populations is relatively short, perhaps no more than 50 years. Until the late 1980's, wildlife contraception was a "boutique" subject among scientists and wildlife managers. This is a bit surprising because the technology developed for contraception in humans has been impressive and its application to wildlife is fundamentally sound, at least in a pharmacological context. The various compounds developed for use in humans were first tested in animal models. The resistance to new approaches in wildlife management, which played a significant role in the slow pace of development and interest in wildlife contraception stem from a variety of social, cultural and economic factors, are discussed below.

The history of wildlife contraception can be oversimplified by examining the technological approaches, and more specifically the nature of the chemicals, hormones, and other compounds applied to various animals. Chronologically, these can be classified as (1) nonhormonal chemicals, (2) steroid hormones, (3) nonsteroidal hormones, (4) barrier methods, and (5) immunocontraceptives.

This oversimplification is compounded by the various permutations of chemical agent, delivery system, and specific species. For example, a contraceptive can be delivered (1) orally, (2) by surgically-placed implant, or (3) by hand-injection or (4) by remotely delivered dart. Dart delivery systems have changed dramatically in the past 25 years and have improved significantly the ability to treat free-roaming animals at greater ranges; thus, dart-delivered drugs were not an early priority for scientists looking into this field. Finally, the historical development of wildlife contraceptives had to take into account whether the animal (1) was small and easily live-trapped, (2) was usually wary and unapproachable, (3) was in a captive setting, (4) could be induced to take baits, or (5) was classified as a food animal by the U.S. Food and Drug Administration (FDA).

Nonhormonal compounds have been used most extensively in birds. Some of the compounds used were classified as fungicides and seed disinfectants (Arasan®, DuPont Co.) (Elder 1964) or anticholesterol agents (22,25-diacholesterol dihydrochloride, later marketed as Ornitrol®, G. D. Searle and Co.) (Wofford and Elder 1967). In both cases, fertility was inhibited but toxic effects made this approach unacceptable. Most other compounds used for birds (thiotepta and triethylene melamine) had similar shortcomings (Davis 1959, 1962). In general, the nonhormonal compounds were abandoned because of their accompanying toxic effects. While some degree of contraception, and in a few cases sterilization, could be achieved, the administered dose had to be very precise. This was not possible with oral delivery in wildlife. Additionally, the mechanisms of action were poorly understood and it is unlikely that any of these compounds could have passed the rigorous regulatory requirements of today's FDA or Environmental Protection Agency (EPA).

Other nonhormonal compounds were derived from plant products, and based on historical evidence that Native Americans used certain plants for contraceptive purposes. A comprehensive review (Farnsworth and Waller 1982) listed 50 plant families that have documented antifertility effects in males and females. Despite some controlled tests with lab animals (Cranston 1945; Barfnect and Peng 1968), a few wild species of rodents (Berger et al. 1977) and occasional interference with fertility in humans (Shao 1987), few investigators have attempted to exploit these naturally occurring substances to control reproduction in wildlife. This area remains a fertile subject for interested scientists.

Research into the use of steroid hormones for wildlife fertility control became common in the 1960's and 70's and was based on the research originally directed at human fertility control (Pincus et al. 1958). In general, steroid hormones work as contraceptives by feeding back upon the hypothalamus and/or pituitary and depressing gonadotropic hormones, thereby reducing or eliminating ovulation or spermatogenesis, or by changing the speed with which the ovum moves through the oviducts. Diethylstilbestrol (DES, a synthetic estrogen) was introduced into bait and fed to foxes (*Vulpes vulpes*) (Allen, 1982; Linhart and Enders 1964; Cheatum 1967; Oleyar and McGinnes 1974) coyotes (*Canis latrans*) (Balser 1964; Brushman et al. 1967), white-tailed deer (*Odocoileus virginianus)* (Harder 1971; Harder and Peterle 1974), and black-tailed prairie dogs (*Cynomys ludovicianus*) (Garrott and Franklin 1983) with significant contraceptive effects. Another steroid, mestranol, which is closely related to DES, was fed to red foxes (Storm and Sanderson 1969), small rodents (voles, rats and mice) (Marsh and Howard 1969; Howard and Marsh 1969; Storm and Sanderson 1970), and cats (Burke 1977) with some contraceptive success, but bait acceptance decreased quickly. At about the same time, oral medroxyprogesterone acetate (MPA) was tested in red foxes (Storm and Sanderson 1969). Shortly thereafter, other investigators explored the use of oral progestins for controlling fertility in domestic canids. Oral melengestrol acetate (MGA) was highly effective in inhibiting fertility in dogs (Sokolowski and VanRavenswaay 1976) and a related compound, megestrol acetate (MA) was approved for commercial use in dogs (Ovaban®, Schering Corp.) (Wildt and Seager 1977).

The use of these and similar oral steroid hormones in wildlife was restricted by problems with bait acceptance, providing frequent and effective doses, and environmental concerns, especially effects on non-target species (all these steroids pass through the food chain). This changed the focus of wildlife contraceptive research to more narrowly targeted delivery systems. These and similar steroid hormones were administered via injection or surgically-placed implants in wapiti (*Cervus elaphus*) (Greer et al. 1968), large exotic species of cats (Seal et al. 1976), deer (Bell and Peterle 1975; Levenson 1984), and wild horses (*Equus caballus*) (Plotka and Vevea 1990; Kirkpatrick et al. 1982). Once again significant contraceptive effects were achieved in these species, but several new problems arose. First, the application of these steroids to free-roaming wildlife required relatively large doses of the compounds, negating the use of remote delivery via darts. This in turn meant that each animal had to be captured before it could be hand-injected or given a surgical implant. This was impractical with most species, because of the stresses associated with capture, the frequency with which the steroid had to be administered, and the large doses that had to be administered. Unknown at the time, but evident in later years, were the various pathologies that resulted from long-term use of these steroids, particularly among (but not restricted to) felids (Buergelt and Kollias 1987). These molecules also have profound effects upon behavior of treated animals, something that would be undesirable in valued wildlife species.

Norplant® implants containing levonorgestrol were effective in striped skunks (*Mephitis mephitis*) (Bickle at al. 1991), and raccoons (*Procyon lotor*) (Kirkpatrick, unpublished data), which could be easily captured in live traps in urban settings, but these two species were clearly an exception to the practical application of injectable or implant steroids to larger species.

Wildlife contraceptive research with nonsteroidal hormones has been largely confined to agonists and antagonists of gonadotropin releasing hormone (GnRH) (Becker and Katz 1997).

Normally GnRH signals the pituitary to secrete the gonadotropins luteinizing hormone (LH) or follicle stimulating hormone (FSH) which are both necessary for normal function in the ovaries and testes. The agonists and antagonists of GnRH block the effects of GnRH on the pituitary by one of several mechanisms. These compounds have been used successfully to inhibit fertility in dogs (Vickery et al. 1984,1985; Inaba et al. 1996), monkeys (*Macaca* spp.) (Fraser et al. 1987) and a variety of other species as well. To date, however, these compounds have been short-lived in their effects, and require large doses for extended effectiveness.

Mechanical birth control devices have been tested in white-tailed deer (unsuccessfully), horses (successfully) and a variety of zoo animals (with mixed results), but the logistics of application to free-roaming wildlife are prohibitory in most species. These methods have included IUD-like barriers for the deer (Matschke 1980) and horses (Daels and Hughes 1995), and silastic vas deferens plugs in the zoo animals (Porton et al. 1990). More comprehensive reviews of the history of wildlife contraception exists (Kirkpatrick and Turner, 1985, 1991).

More recently, immunocontraception, or vaccine-based fertility control, became a reality in wildlife. Immunocontraception is based on the same principles as disease prevention through vaccination. Humans and other animals are vaccinated against diseases by injecting dead or attenuated disease bacteria or viruses, or molecules which are harmless but similar to toxins that these disease organisms produce. The stimulated immune systems produce antibodies against some essential event or structure in the reproductive process.

There are a variety of immunocontraceptive vaccines under development, including vaccines against brain reproductive hormones such as GnRH (Hassan et al. 1985; Ladd et al. 1988, 1989; Bell et al. 1997) and LH (Al-Kafawi et al. 1974), and vaccines against sperm

(Primikoff et al. 1988; Herr et al. 1989) and egg (Florman and Wassarman 1985), which in turn prevent fertilization. One of the first immunological approaches was a vaccine against the zona pellucida of the mammalian egg, which was patented as an anti-fertility agent in 1976 by R. B. L. Gwatkin for Merck & Co., Inc. (Skinner et al. 1996). In 1988, this vaccine was applied to wild horses with great success, and since that time other experiments with anti-sperm vaccines have been initiated. The success with the porcine zona pellucida vaccine (PZP) has opened the door to a practical approach to wildlife fertility control and will be discussed in greater detail below.

The biology of the PZP vaccine is at once both simple and complex. An extracellular matrix known as the zona pellucida (ZP) surrounds all mammalian eggs. The ZP consists of three major glycoprotein families, one of which, ZP3, is thought to be the principal sperm receptor in most species (Prasad et al. 2000). The PZP vaccine itself is derived from pig eggs. When this vaccine is injected into the muscle of the target female animal, it stimulates her immune system to produce antibodies against the vaccine. These antibodies also attach to the sperm receptors on the ZP of her own eggs and distort their shape, thereby blocking fertilization (Florman and Wassarman 1985).

THE ART AND SCIENCE OF WILDLIFE IMMUNOCONTRACEPTION

Prior to the application of the PZP vaccine to wildlife, the failure to achieve practical results and the dangers associated with steroid hormones led to a re-examination of the problems and needs related to wildlife contraception. It became apparent by the late 1980's that research in this area was proceeding without a standard by which to evaluate each new approach. Thus, an idealized standard was created (Kirkpatrick and Turner 1991). It included:

1. Contraceptive effectiveness of at least 90%.

2. The ability for remote delivery, with no or minimal handling of animals.

3. Reversibility of contraceptive effects (more important for some species than others).

4. Safety for use in pregnant animals.

5. Absence of significant health side-effects, short- or long-term.

6. No passage of the contraceptive agent through the food chain.

7. Minimal effects upon individual and social behaviors.

8. Low cost.

While some of these standards are more or less arbitrary, they at least provided reasonable guidelines for discussions and planning for new wildlife contraceptives. When these standards were developed, they were built exclusively around wild horse contraception, and did not address all problems associated with diverse species and settings. For example, the challenge of deer contraception, even in urban areas, raised the issue of a one-inoculation form of the vaccine that would provide at least one and perhaps several years of contraception from that one application. The use of the raw native form of the PZP vaccine requires two inoculations the first year, which can be very difficult with wary species like deer. A one-inoculation form of the vaccine could improve the efficiency in significant ways. The challenge of elephant contraception, where doses of vaccine must be 10X larger than standard wild horse or deer doses raised the need for the development of a synthetic form of the vaccine. The process of producing the native PZP vaccine is laborious and the number of doses that can be produced in a year is limited at this time by the production process. Thus, a synthetic form of the vaccine would expand the application of wildlife contraception beyond present logistical restrictions, and eliminate some of the regulatory concerns raised by the use of natural products.

The mere availability of a good physiological immunocontraceptive does not insure its effective application to wildlife. Obviously the first step in the development of a wildlife contraceptive is to test its efficacy in captive animals, or domestic counterparts. But once this has been done and physiological efficacy determined, strategies for application to free-roaming species must be developed. It is a large leap from inoculating a deer in a pen and inoculating a wild free-roaming deer; yet another leap is required from administering the vaccine in the field to controlling a wildlife population.

Actual application to free-roaming species requires a variety of delivery and access strategies. Immunocontraceptives can be currently be delivered by intramuscular injection, thus an animal must either be given the vaccine by hand injection or by a dart. The limit of two delivery systems requires therefore at least two access strategies. Hand injection requires physical capture of the target animal and this in turn increases stress for the target animal, increased danger for the person(s) doing the work, and increased expense. In some settings, such as zoos, access is not as much of a problem, but even here it is not always possible to hand-inject animals without causing some degree of capture-related stress. In the case of western wild horses, where hundreds are rounded-up at a time for entry into adoption programs, it is relatively easy to hand-inject animals as they pass through a chute.

For most other species of wildlife, the only remaining delivery system is by dart. It is intuitive that this approach has both advantages and disadvantages. The most obvious advantage is eliminating the need for stressful capture of animals. The small volume of vaccine necessary to immunize an animal (1.0 cc) permits the use of very small and light darts, which increases the effective range of darting and which decreases the chances of injury to the target animal. The disadvantages include being required to approach the animal to within 50 m or less, keeping track of which animals have already been inoculated and which ones haven't, and the labor-intensive nature of the endeavor.

Despite the fact that inoculation of free-roaming wildlife with a contraceptive vaccine is at best difficult, a significant degree of success has been achieved under field conditions. A brief review of what has been accomplished through 1999 follows.

Wild Horses

Liu et al. (1989) first discovered that the PZP vaccine would inhibit fertility in domestic mares. Soon after, wild horses were first treated with the PZP vaccine on Assateague Island National Seashore, Maryland, and studies have continued for twelve years. The vaccine was delivered remotely, with small darts, and contraceptive efficacy was greater than 95% (Kirkpatrick et al. 1990). The vaccine was safe to administer to pregnant animals and did not interfere with pregnancies in progress or the health of the foals born to inoculated mothers. A single annual booster inoculation was sufficient to maintain the contraceptive effects (Kirkpatrick et al. 1991), and contraception was reversible after three and four years of treatment (Kirkpatrick et al. 1992, 1995a; 1996a). Finally, no changes occurred in the social organization or behaviors of the treated animals. In 1994, the National Park Service began the management of the Assateague wild horses with this method and after only three years, the herd reached zero population growth (Kirkpatrick 1995; Kirkpatrick et al. 1997). Applications of this immunocontraceptive approach are now being applied to large wild horse herds in Nevada (Turner et al. 1996a), and PZP trials with feral donkeys (*E. asinus*) in Virgin Islands National Park have been successful (Turner et al. 1996b).

White-tailed and Black-tailed Deer

In North America, populations of white-tailed deer and, to a lesser extent, black-tailed deer (*O. hemionus*) exploded during the last two to three decades of the 20th century. Although the causes of this population explosion are undoubtedly complex, it is generally attributed to the use of high-yield crops, the spread of deer-friendly suburbs (which offer deer a diverse menu of heavily fertilized ornamental shrubs and grasses, intermingled with disturbed "natural areas" such as small parks and woodlots), increasingly mild winters, the absence of natural predators, and recreational hunting practices ill-suited for controlling deer populations in suburbs. Accompanying the burgeoning deer populations and the sprawl of suburbs has been a rapid rise in conflicts between deer and people, most notably, deer-vehicle collisions, damage to crops and ornamental plants, undesirable impacts on some forest ecosystems, and association with tick-borne zoonotic diseases, most notably Lyme disease (Conover 1997; Rutberg 1997]). Consequently, there is enormous interest in finding new tools that will allow people and deer to coexist, and much public attention has focused on immunocontraception. In autumn 1997 alone, for example, The HSUS received requests for information on deer immunocontraception from people in more than 60 different communities across the U.S.

The 1988-89 demonstration that PZP could be remotely delivered to wild horses in the field at Assateague (above) spurred preliminary testing of PZP on captive deer. Effects on captive deer resembled those in wild horses; the two-shot vaccine protocol was highly effective, the vaccine could be delivered remotely, its effects were reversible after at least two years of treatment, and no health side effects were apparent (Kirkpatrick et al. 1997; Turner et al. 1992, 1995, 1996c, 1997; see also Miller et al. 1999). A subsequent trial with semi-free-roaming deer at the Smithsonian Institute's Conservation and Research Center, in Front Royal, Virginia, provided evidence that the vaccine could be delivered remotely under field conditions; while there was evidence that PZP treatments extended the mating season, treated females gained more weight than untreated females, presumably because they were spared the energetic costs of pregnancy and lactation (McShea et al. 1997). The initiation of a study at Fire Island National Seashore, New York, in 1993, began a series of field studies that explored the effectiveness and costs of different field techniques, tested vaccination schedules, and vaccine preparations, as well as investigating effects of PZP on behavior and survival (Kirkpatrick et al 1997; Thiele 1999; Walter 2000; Rudolf et al. 2000 [*several ms's are currently in review, and hopefully will be at least in press by the time this goes to publication*]. The Fire Island study was the first to show that biologically significant numbers of females could be efficiently and effectively treated in the field, with approximately 200 females a year under treatment by 1996. However, vaccine effectiveness in this study was lower than in previous deer studies, especially in the first year following treatment; this reduction in effectiveness can probably be attributed to incomplete or misplaced initial vaccinations (Kirkpatrick et al. 1997; *Naugle et al in review?;* Thiele 1999).

The first demonstration that immunocontraception reduced an unconfined deer population was accomplished at the National Institute of Standards and Technology (NIST). NIST, a 574 acre federal research facility within the city of Gaithersburg, Maryland, supported a deer population numbered at approximately 180 animals in 1993. By the time PZP treatments began in autumn 1996, the population had risen to approximately 250, and peaked at approximately 300 in autumn 1997 (Thiele 2000). By autumn 1998, however, over 90% of the NIST females were receiving PZP treatments, and the population had declined about 20% below peak levels by spring 2000 (HSUS, unpubl. data). Good access to deer for treatment, high population mortality (the majority due to vehicle collisions), and relatively low reproductive rate all contributed to the success of PZP in controlling this population.

Zoo Animals

A third application of the concept of wildlife immunocontraception is the control of the production of "surplus" animals in zoos. Despite the often heard discussions of captive breeding efforts for endangered species, most zoo species breed quite successfully and the production - and more to the point, the disposition - of "surplus" animals is perhaps the largest single problem facing zoos worldwide. Beginning in 1990, the PZP vaccine was applied to various exotic species in zoos, beginning with Przewalski's horses (*E. przewalskii*) and banteng (*Bos javanicus*) (at the Cologne Zoo (Kirkpatrick et al. 1995b), and five species of deer at the Bronx Zoo (now the Wildlife Conservation Center) (Kirkpatrick et al. 1996b). Since that time the PZP vaccine has been tested in more than 90 species in more than 70 zoos worldwide (Frisbie and Kirkpatrick 1998). Today the PZP vaccine is reducing zoo births and providing some relief to the problem of surplus animals.

African Elephants

A fourth major application is underway in Africa. Devastated by the lucrative trade in elephant ivory, populations of African elephants (*Loxodonta africana*) were reduced to dangerously low numbers during the 1970's and 1980's. During that same period of time, elephant populations retreated to the sanctuary of national parks. Much land outside of these parks that was formerly elephant habitat is now under intensive agricultural use and in a sense, Africa's elephant populations are now trapped in the national parks. With the cessation of poaching, their numbers are increasing by as much as 5% per year. The paradox is that, in some areas, these elephants are now threatening the ecosystems of these national parks and their own health. In recent years this problem has been managed through culling — a euphemism for shooting. Four African nations currently kill elephants in order to keep populations within the carrying capacity of the parks. (Kruger National Park, in South Africa, killed between 300-700 elephants annually for 30 years, but suspended culling in 1995.) This is simply tragic, particularly for a species which is believed to understand the concept of death.

In 1995, preliminary experiments provided evidence that the PZP vaccine will work in this species. Several zoo elephants have been treated with the vaccine and while these are not breeding animals, we were able to determine that the treated elephants will produce antibodies against the vaccine. In October 1996, 21 elephants in Kruger National Park were captured, radio-collared and treated with the PZP vaccine in order to determine its contraceptive efficacy. In November 1996 and again in June 1997 the treated elephants were each given a single booster inoculation remotely, by means of a dart fired from a shooter in a helicopter. None of the animals were captured for these booster inoculations. This portion of the experiment proved that elephants need not be captured to administer the vaccine (Fayrer-Hosken et al. 1997). Results of this trial indicate that pregnancy rates in elephants were reduced from 90 % in untreated controls to approximately 37.5 % in treated animals. Based on the successful preliminary results, there may be a non-lethal solution for the wise management of these magnificent animals. Additional studies, designed to increase the efficacy of the vaccine in elephants were carried out in 1998. Results from this latest round of trials indicates that fertility was reduced by 75%, that there were no changes in behavior among the treated animals, and that the contraceptive effects are reversible, and that the reproductive system of the treated animals (uteri and ovaries) remain normal.

Other Species

In May 1997, ZooMontana, under contract to the U. S. Navy, began treating 30 water buffalo (*Bubalis bubalis*) on the island of Guam, with the PZP vaccine. Preliminary results indicate the experiment successfully and significantly reduced pregnancies in these animals. This in turn has led to a new five-year project by the U. S. Navy and the U. S. Fish and Wildlife Service to control the water buffalo on the naval base with PZP contraception. This project will lead to the important precedent of non-lethal control of wildlife by The Department of Defense.

On Point Reyes National Seashore in California, Tule elk (*C. elaphus nannodes*) are being treated with the contraceptive vaccine in a series of tests to determine if the herd can be managed in this way. Preliminary evidence already exists that elk can be successfully contracepted with PZP (Kirkpatrick et al. 1996b; Heilmann et al. 1998; Shideler, pers. comm.)

RESEARCH IN PROGRESS

Experience with the species described above provides a clearer picture of the needs for the future if wildlife contraception is to become a common management tool. Thus far the PZP vaccine appears to come as close to the optimum contraceptive agent when measured against the "ideal" wildlife contraceptive. So far, at least, its physiological actions appear to be sound and safe; it does not appear to pass through the food chain; and is not associated with immune responses to somatic tissues (Turner et al. 1997; Barber and Fayrer-Hosken 2000). However, the ideal wildlife contraceptive vaccine would require only a single inoculation in order to achieve several years of contraception. It would use adjuvants that have already been federally licensed for use in food animals, instead of the experimental or non-approved adjuvants currently in use, or use no adjuvants at all. The remote delivery system would in some manner mark the animal as well as inoculate it, so that it can be distinguished from untreated animals. Finally, the ZP antigen itself should be readily available in large and inexpensive quantities, suggesting a genetically-engineered or synthetic form of the vaccine. Some of the research which is currently being carried out with these goals in mind is described below.

A One-Inoculation Vaccine

The current vaccine requires animals to be treated twice before full effectiveness is achieved, with the second vaccination coming a few weeks before the breeding season. However, it is quite difficult to treat individual wild animals twice, and the time just prior to the breeding season is not always the most practical time for administering treatments. Consequently, research is focusing on the development and testing of a longer acting "one-inoculation" vaccine.

The first approach to a one-inoculation vaccine utilized microspheres formed from a lactide-glycolide polymer which is biodegradable after injection and non-toxic as it breaks down (Kreeger 1997; Turner et al. 1997). These microspheres can be engineered to release the incorporated vaccine at varying rates by means of altering the size of the spheres and the ratio of lactide to glycolide (Eldridge et al. 1989). In the first experiment with these microspheres, in wild horses in Nevada, a single inoculation achieved the same degree of contraception as two inoculations of the raw vaccine. However, the spheres clogged syringes, needles, and darts, and delivery was impractical (Turner et al., *in press?*). This led to experiments with small pellets, made of the same material but shaped to fit into the needle of a dart. When the pellets are injected into the muscle of the animal, along with a bolus of raw vaccine and adjuvant, they begin to erode, releasing the vaccine at one and three months. In an initial study with the pellets, antibody titers in domestic mares remained at contraceptive levels for close to a year, and in a small pilot study with wild mares, significant contraception was achieved (I. K. M. Liu and J. W. Turner, pers. comm.). Additional research is being carried out in an attempt to develop pellets which will release at nine months, thereby permitting two years of contraception from a single inoculation.

A second approach involves the packaging of the PZP vaccine in liposomes, which are formed from phospholipids and cholesterol in saline (Brown et al. 1997a). This preparation, which is being tested under the name SpayVac™ (NuTech, Halifax, Canada), has shown especially promising results for gray seals (*Halichoerus grypus)*, some of which remained infertile for at least six years after a single dose (Brown et al. 1996, 1997b). Published data concerning the effects of SpayVac™ n other species are limited at this time, but there is considerable interest in further testing, which is underway.

PZP, Adjuvants, and the Immune System

The PZP vaccine works in most mammalian species because the ZP molecule is similar, but not identical, among the many species of mammals. The drawback to this similarity across species is that PZP is not very good at causing antibodies to be formed. Thus, it must be given with a general immunostimulant known as an adjuvant. The adjuvant, when given with a specific vaccine, causes the body to make greater concentrations of antibodies against the vaccine, which in turn results in better contraception. The most effective available adjuvant, and the one employed in most previous PZP test, is known as Freund's Complete Adjuvant (FCA). In many species, however, FCA also causes localized inflammation and tissue damage, and may trigger false positive tuberculosis tests after injection (Hanly et al. 1997). Thus, the FDA and other regulators, as well as those concerned with animal welfare, discourage widespread use. Several new adjuvants are under study for use with the PZP vaccine, and success may lead to more relaxed regulation of the vaccine by the FDA.

Different adjuvants may target different immune pathways, which has important implications for both the mechanism and duration of action (Weeratna et al. 2000). PZP has been assumed to work through short-term activation of the humoral immune system. However, some adjuvants appear to activate the cellular immune system, which could lead to the destruction of target tissues, such as the ovaries. Preliminary experiments suggest that conjugation of PZP to other immunogenic molecules, such as keyhole limpet hemocyanin (KLH) or tetanus toxoid, may also activate the cellular immune system.

Activation of the cellular immune system against the ZP protein could lead to irreversible sterilants, as well as more effective contraceptives. The ability to cause sterilization rather than temporary contraception may represent a huge advantage with some species in some situations, such as white-tailed deer or companion animals.

Genetically-Engineered or Synthetic ZP Vaccines

Currently the PZP vaccine must be made as a natural product and the actual glycoprotein antigen is extracted from the zona pellucida of pig eggs. This means that production of the vaccine is very labor intensive and must rely on an adequate supply of pig ovaries from slaughter houses. It is unlikely that any given small laboratory operation can produce more than 15,000 65μg doses per year. That level of production can probably meet demands for wild horses, zoo animals and deer, but elephants (which currently require three 600 μg doses) and companion animals (which number in the hundreds of thousands or millions) will far exceed the ability to produce the native PZP (see also the discussion of ethics, below). Thus, there is a significant need to produce a synthetic form of the vaccine.

A number of investigators have successfully cloned the protein backbone of the ZP molecules of several species (Harris et al. 1994; Prasad et al. 2000). Thus far, however, they have all been unsuccessful at producing a recombinant ZP with contraceptive effects, probably because of difficulties in glycosylating this backbone. This step is essential in order to impart adequate antigenicity to the antigen. Even several large pharmaceutical companies have failed in their attempts to produce a genetically-engineered form of the vaccine. Work continues on this project by several foreign companies and a number of research groups; among the most promising approaches involves conjugating short sequences of the ZP antigen to tetanus toxin or other non-specific immune system booster (Patterson et al. 1999; but see Kaul et al. 1996).

Delivery Systems: Marking Darts, Oral Delivery, and Transmissable Vectors

The ability to treat free-roaming wildlife remotely with darts and know which animals have been treated is essential in the course of most applications in wildlife management. To this end, a dart has been developed by Pneu-dart® that inoculates the animal with vaccine and which also leaves a small paint or dye mark on the animal at the same time. While this would not allow long-term individual recognition, it would allow darters to discriminate between treated and untreated animals, which is all that is needed when success is measured by impact on the population. At the present time, this dart works in a fairly reliable manner but only at relatively short ranges, and improvements are being pursued. The various dyes tested thus far have also fallen short of the mark. Deer in particular have a tendency to lick the dye off from the injection site. More permanent, non-toxic dyes must be found that will survive attention by the target animal and which will persist over at least a three to four week period.

It is intuitive that the ability to deliver contraceptives to wildlife orally, in baits, would be easier and more cost effective. However, for safety and ethical reasons, both the public and regulatory agencies are likely to demand that any oral contraceptive must be species-specific. This will be extremely difficult and expensive to accomplish, and little progress has been made. A second problem is that the PZP vaccine (or any ZP vaccine) is protein in nature and easily destroyed by the digestive process of most animals. A delivery system must be developed which permits the undigested protein of the antigen to pass into the lymph of the target animal's gastrointestinal system. Several strategies to accomplish this are available. One would be to insert a ZP vaccine into a non-transmissable bacterial or viral vector; this is the approach used for the oral rabies vaccine, which is incorporated into a *Vaccinia* (smallpox) vaccine (Bradley et al. 1997; Linhart et al. 1997; Miller 1997). A second method would be to incorporate the ZP vaccine into a microcapsule designed to be absorbed through the lymphoid tissue (or other route) in the digestive tract (Miller 1997). Until the species-specificity issue is resolved, however, solving the technical problems of oral delivery will not move the idea far toward management application.

Researchers working with the Australian government are seeking to engineer the genes for PZP and similar contraceptive molecules into transmissable, non-pathogenic viruses for use in controlling populations of introduced wildlife species such as European rabbits (*Oryctolagus cuniculus*) (Holland et al. 1997; Robinson et al. 1997). These viruses would be introduced into the wild populations, and then transmitted from animal to animal without further human intervention. While the approach is scientifically feasible, controlling the spread of the vaccine would be a serious problem, and such a vaccine would raise serious safety and environmental concerns in the U.S. and around the world (see The Ethics of Immunocontraception, below).

Abortifacients

At least two research groups are seeking to administer compounds that will cause abortion in recipient animals. This has already been shown to be feasible in deer, with prostaglandin-F2α delivered remotely via biobullet (DeNicola et al. 1997). By its nature, however, this method will require annual application, and a multi-year treatment will not be possible. Moreover, the social objections that will attend this method of wildlife control make it an unlikely solution to large-scale management efforts, especially if a safe and effective contraceptive is available.

IMMUNOSTERILIZATION FOR COMPANION ANIMALS

The invention of an immunosterilant for companion animals would be an extraordinary gift to the millions of dogs and cats worldwide who suffer and die each year for want of compassionate care and loving homes. In the U.S. alone, an estimated 6-8 million unwanted dogs and cats are euthanized in shelters each year, not to mention countless other stray, feral, and abandoned animals that live and die under the harshest conditions imaginable. And the situation for cats and dogs is far, far, worse in other spots around the globe. Although many other approaches are important — most notably educational outreach by animal shelters, in communities where there *are* animal shelters — only effective population control will allow the problems to be solvable through these other approaches.

To be truly useful to animal shelters and for control of stray and feral populations, the ideal immunosterilant should require only one shot, be free of harmful or unpleasant side effects, and cause permanent sterility (although a multi-year, one-shot contraceptive vaccine might be somewhat helpful for controlling stray and feral populations). Ideally, such a sterilant should also mimic the behavioral and health effects of surgical sterilization, including reduced aggression in males and reduced incidence of ovarian cancer in females.

As noted above, a number of hormonal methods have been used successfully for contraception of dogs and cats (see The History of Wildlife Fertility Control). Some, including megestrol acetate (Ovaban®) and Mibolerone (a synthetic androgen, "Cheque,"), are licensed for use as oral contraceptives on dogs and/or cats. However, behavioral and health side effects are common, and of course these methods are of no use to animal shelters and for control of stray and feral populations, since effectiveness ends soon after treatments stop.

Thus, as in wildlife, immunological approaches may prove more fruitful, and research efforts in these fields have been accelerating. In an attempt to immunize dogs against their own LH, injections of human chorionic gonadotropin (hCG) were administered (Al-Kafawi et al. 1974). This experiment failed because canine LH did not cross-react with anti-hCG antibodies. An immunological approach to fertility control was also attempted in cats (Chan et al. 1981). Feline ovaries were homogenized and used to raise rabbit antibodies against the protein fractions. The antibodies, when administered to pregnant cats, caused some fetal resorption, but the results were discouraging. As in dogs, nonspecificity of the antibody appeared to be the cause for failure.

In a different immunological approach, male dogs were immunized against their own GnRH with GnRH conjugated to human serum globulin or tetanus toxoid (Hassan et al. 1985; Ladd et al. 1994). Plasma testosterone, LH, and sperm counts were all depressed; however, the effect was reversed when antibody levels dropped. A GnRH vaccine would have several important advantages. First, it should work on both sexes. Second is that it should convey the same benefits as surgical sterilization, including loss of libido and estrus, reduction of aggressive behavior, and reduced incidence of reproductive tract cancers.

Another promising approach to dog contraception/sterilization is immunization with the PZP vaccine (Mahi-Brown et al. 1985, 1988). Small and infrequent doses of the PZP vaccine appeared to cause cellular-mediated immune responses in the bitches and led to a longer-term infertility. Long-term studies were not carried out, but in the short term this cellular immune response was associated with histological alterations of the ovaries, and concerns about potential pathologies would have to be resolved before this approach could be considered safe (Mahi-Brown et al. 1988). Some of these concerns might be resolved by use of a more highly purified PZP preparation than were used in these studies. As mentioned above, careful selection of recombinant ZP peptides should allow a more targeted immune response and help resolve these concerns (Paterson et al. 1999; Prasad et al. 2000).

FROM RESEARCH TO MANAGEMENT: CULTURE, REGULATIONS, AND POLITICS

Immunocontraception faces a variety of technical, cultural, regulatory, and political obstacles before it will be used as a tool for management of free-ranging wildlife. The technical issues have already been discussed: what is needed is a safe, effective, one-shot, multi-year vaccine that can be delivered remotely to wildlife under field conditions. In some ways, however, the technical obstacles are the least significant.

In our view, the single most formidable barrier to the adoption of immunocontraception as a wildlife management tool is the entrenched culture of wildlife utilization. In the United States, this culture is most evident in the wildlife management establishment, which includes the state wildlife management agencies, much of the U.S. Fish & Wildlife Service, the hunting community, the arms and archery manufacturers, the trapping and fur industries, and the other commercial interests that profit directly or indirectly from the killing of wildlife (Hagood 1997; Gill and Miller 1997). In this paradigm, wildlife has no value or significance apart from its use. This is evident in the jargon of the culture: deer are not deer, but "the deer resource"; beavers and otters are not beavers and otters, but "fur-bearers;" wildlife is "game" or "non-game;" ending an animal's life is "harvesting."

In a culture of utilization, contraception of "game" animals is illogical. Why prevent animal births, when you can instead stimulate births and "harvest" a surplus for human use? Moreover, the choice to contracept rather than kill introduces into wildlife management a new moral dimension disconcerting to those who think in terms of exploitation: that each individual animal has a claim on the world and on us — a claim to its own life. Recognizing this claim collapses the jargon of "harvest" and "resource," and undermines the paradigm of utilization it supports.

The moral challenge that wildlife immunocontraception poses to the culture of utilization is, in our view, the only possible explanation for the extraordinary antipathy it has generated in the state wildlife agencies and the hunting community. It is certainly not the threat that the technology itself poses to hunting; immunocontraception, at least the dart-delivered kind, is not and will not be an effective management tool in the environments in which most recreational hunting occurs (Kirkpatrick and Turner 1995).

But the antipathy is unmistakable. Almost every attempt to get a state permit to conduct an immunocontraception field study on deer has exploded into a titanic political battle, with the state agencies often leading (or goading) the opposition. One proposed study, in Amherst, New York, was blocked by a lawsuit by Safari Club International. Another was nearly blocked by the personal intervention of several pro-hunting members of Congress. The publications of the hunting industry regularly feature articles on how immunocontraception can't work, is too cumbersome, is too expensive, is failing in this way or that, and of course, is inferior to hunting in every way. One more extreme hunting newsletter featured a letter that drew parallels between our research and that of the Nazis. In community deer meetings, angry hunters stand up one after another to denounce immunocontraception as a fraud, as a threat to wildlife management and a traditional way of life, as "playing God," and as an anti-hunting plot (see Kirkpatrick and Turner 1997). And a national bowhunting advocacy group recently began issuing action alerts notifying its members of public speaking engagements by this article's authors.

Still, in the U.S., the wildlife utilization culture is probably waning, especially in the cities and suburbs where most people now live (Kellert 1985, 1993). And the interest and support for wildlife immunocontraception in the public, the media, and in some state legislatures suggests that this obstacle will be overcome.

In much of the world, however, the culture of wildlife utilization remains dominant, and is reflected in the multi-billion dollar worldwide trade in wildlife and wildlife parts (Freese 1998). Among people struggling to support their families and maintain human life and dignity, such attitudes are understandable, if tragic. But no such "necessity defense" can be constructed for the profiteers, the entrepreneurs from wealthy nations who make fortunes trading in wild-caught birds and bear gall bladders and rhino horn. And while the international community frowns on smuggling, the entire premise of treaties such as the Convention on International Trade in Endangered Species of Fauna and Flora (CITES) is that wildlife trade is good, as long as it is "sustainable."

Again, wildlife contraception makes little sense in that context. Why contracept elephants, when you could shoot them, eat the meat, and sell the hides and tusks for great profit? The answers to that question are not simple, and ultimately rest on the morality of shooting elephants and the long-term economic, social, and spiritual advantages of treating these and other wild creatures with respect and compassion. But the question will have to be answered, and answered convincingly, before immunocontraception can be widely applied to elephants and other locally overabundant wildlife throughout the world.

The Regulatory and Practical Issues

There are several specific regulatory and practical issues that will have to be addressed and resolved before PZP or other immunocontraceptives become mainstream management tools.

Within the U.S., the most important regulatory barrier is approval by the Center for Veterinary Medicine of the Food and Drug Administration (FDA). The FDA has little experience with animal vaccines. Most animal vaccines are regulated by the U. S. Department of Agriculture (USDA), but the USDA's authorizing legislation only permits it to regulate vaccines for disease prevention. Since pregnancy is not considered a disease, regulatory authority reverts to the FDA. Unfortunately, most of the FDA regulations and standards that apply to immunocontraception are tailored to approval of drugs, which are generally more stringently regulated and require more rigorous testing than vaccines.

At this writing, research on PZP is being carried out under the authority of Investigational New Animal Drug (INAD) files established with the FDA. (In our case, the INAD is held by The HSUS.) The INAD file is the heart of a process designed to control development and testing of new animal drugs and vaccines, and guide acceptable products towards eventual FDA approval for marketing and commercial distribution. Fundamentally, the FDA asks this question when considering a product for approval: is the specific product safe and effective for its intended purpose if used as directed? The question is asked comprehensively: it extends to manufacturing, storage, packaging, means and schedule of delivery, target animals, and labeling of the vaccine or drug. These will be high hurdles for PZP or any contraceptive vaccine (especially a recombinant form) or drug to leap. But it can be done, and eventually it will be done for a safe, effective wildlife contraceptive.

Since management of wildlife in the U.S. is carried out under state authority (with some exceptions on federal land — see below), applying immunocontraceptives to free-ranging wildlife will generally permits from state wildlife agencies (Messmer et al. 1997). As implied above, many state agencies will yield such permits only slowly and grudgingly. However, as the novelty of the technique wears off, its limitations and successes are demonstrated in field studies by many research groups, a safety record is accumulated, and FDA concerns are met, the comfort level of state agencies with immunocontraception techniques will rise. Progress has already been made with state agencies, at least in their rhetoric. Whereas in the early 1990's, the response of state agencies to deer contraception was "no, not now, not ever," by the close of the decade many state agency personnel were conceding that PZP does, at least, stop deer from breeding, and began to speak of contraception as an important tool for future management efforts. Given the scope and seriousness of public concerns over deer and other wildlife, it is virtually inconceivable that state agencies could resist indefinitely the demands of the public for a humane, non-lethal tool that could help solve at least some deer conflict situations.

The next important questions are the practical ones: who will pay for wildlife contraception, and who will carry it out? As noted in this chapter's introduction, the state agencies are uniquely unsuited to pay for or conduct wildlife management through immunocontraception. To begin with, they don't have the money or the personnel (and this lack certainly aggravates agency worries over the potential spread of immunocontraception as a management tool). Second, the resources they do have are generated principally by hunters, who repeatedly and loudly voice their objections to having their license fees spent on contraception. Third, state legislatures have become accustomed to the state wildlife agencies generating their own funds and depending on the efforts and revenues of hunters to conduct management activities. Consequently, the legislatures are extremely reluctant to start diverting general revenues to these agencies. Although some immunocontraception studies have received state funding and support (notably in New York and Connecticut), the prospects for the state wildlife agencies getting any money to actually conduct immunocontraception management programs in the field are very limited.

If the state agencies do not fund and conduct these programs, who will? We believe the answers are already beginning to emerge. Generally, HSUS immunocontraception studies have been funded at least in part by the land owners, land management agencies, and communities in which they occur. The wild horse contraception projects at Assateague Island and Cape Lookout national seashores are being funded and carried out by the National Park Service, which is also involved in supporting and carrying out the deer project at Fire Island National Seashore and the tule elk project at Point Reyes National Seashore. Likewise, wild horse contraception studies on western public lands have been cooperative efforts of The HSUS, the research team, and the Bureau of Land Management; over time, the BLM is increasing its responsibility for carrying out these programs. The National Institute of Standards and Technology (NIST, part of the U. S.

Department of Commerce) is jointly undertaking a deer contraception study with The HSUS on the NIST campus in Maryland. The U.S. Navy is implementing fertility control of water buffalo on Guam. Local agencies, such as Columbus-Franklin County Metro Parks in Ohio, and Morris County Parks in New Jersey, have also taken lead roles in conducting deer immunocontraception studies on their own properties. At Fire Island and in Groton, Connecticut, funding has been provided by local communities and residents.

Deer management, especially, is increasingly being carried out at the local level. Confronted with local deer conflicts, town councils, county governments, park commissions, and other municipal bodies across the country have developed local deer management plans, and employed city police, animal control officers, "volunteer" hunters, and private contractors to carry them out. This localization has been formally recognized in Maryland, where the state deer management plan emphasizes local needs and preferences, and in New Jersey, where pending legislation establishes "Community-Based Deer Management Plans." These plans would be developed locally by county and municipal governments, submitted to the state Division of Fish, Game, and Wildlife for review and approval, and carried out by either government personnel or private contractors. While the emphasis of these plans clearly now rests on killing, fertility control is explicitly recognized in the NJ legislation as a local management alternative.

So in our crystal ball, we see this: immunocontraception projects (indeed, all urban wildlife management) will be funded locally, carried out by local government personnel or private contractors, and regulated by the states, which will establish policies, issue permits, oversee research, and certify private contractors and other practitioners.

The Ethics of Immunocontraception

Ethical questions concerning the application of immunocontraception to wildlife have been raised from a wide spectrum of viewpoints, from sport hunters to hard-line animal rights advocates. We choose to take a pragmatic approach to these questions. When immunocontraception is considered for use, it will be considered as one of several management alternatives, and so to each of the questions posed below must be added, "compared to what?" (see also Oojges 1997, Singer 1997).

Is it right to manipulate a wild animal's reproductive system, and potentially its behavior, for human purposes? All other things being equal, our ethical and esthetic preference would be simply to leave wildlife alone. We recognize the intrinsic right of all wild creatures to live out their lives unmanipulated by humans, and personally take great pleasure in being observers of and participants in the continuing and ever-surprising story of life on earth. But the lives of many wild creatures — especially those close to human habitation — are already subject to human manipulation, much of it deliberately or incidentally destructive. By our settlement patterns, by our engineering of land and water, by the discharge of the byproducts of human life into the rivers, oceans, and atmosphere, by our invasion of almost every corner of the planet, we shape the terms of animal existence.

And as a practical matter, "leaving them alone" is not always a choice we have. The public demands that action be taken when public health, safety, or subsistence are threatened by wildlife; not only is this view ethically defensible, but (more to the point) we do not see this consensus changing in our lifetimes. The action taken need not be manipulation of wildlife populations; but at very high population densities, "passive" management techniques (e.g., exclusion, traffic manipulation, etc.) may be insufficient to resolve public concerns. Consequently, the alternatives likely to be considered include some form of public hunting, sharpshooting, capture and relocation or slaughter, or others that are also lethal, cruel, or both. In comparison to those alternatives, immunocontraception appears to be a fairly gentle population manipulation.

Isn't immunocontraception unnatural? Many sport hunters feel that they fill the ecological niche vacated by the natural predators that have been eliminated from the landscape, and that hunting is therefore a natural activity. (Some take this further, asserting that humans are hunters by nature, and that hunting fulfills some biological imperative.) To this role they contrast immunocontraception, which they dub "unnatural" and "playing God."

Again, the question must be answered with, compared to what? A strong case can be made that sport hunting is not natural: the use of all-terrain vehicles, laser sights, GPS units, and other late 20th-century gadgets and gizmos is not natural. Nor are the pervasive population, behavioral, and (maybe) genetic effects of American sport hunting: the focus on taking trophy animals, the likely disruption of normal social organization, the distortion of normal population age and sex structures. Nor are sport hunter (predator) populations regulated by game (prey) populations, as they would be in nature. Although the population, behavioral, and genetic effects of immunocontraception are not yet fully known, they are unlikely ever to achieve the broad and profound impacts of sport hunting.

Is it right to kill pigs (to make PZP) to save deer and horses? No. PZP is produced from the ovaries of pigs purchased from slaughterhouses. If we believed that more pigs were dying because we were making PZP, we would stop. But over 100 million pigs are killed in slaughterhouses each year, and we cannot believe that PZP research has any impact on that total. Nevertheless, this consideration adds urgency to the search for a synthetic form of the vaccine, especially if a form of ZP should ever prove applicable to companion animals. In that case, the commercial production of millions of doses per year might actually affect the market for dead pigs, and extraction of PZP from pigs on that scale would be ethically unacceptable to us.

Would it ever be appropriate to use oral contraceptives or transmissable contraceptives on free-ranging wildlife? Oral contraceptives for wildlife, packaged in attractive baits, would certainly make vaccine delivery easier and cheaper. Consequently, they would broaden the range of potential applications. This could be good or bad. Again, we would consider it desirable if contraceptives could replace noxious lethal controls with minimal behavioral and ecological effects. Like poison baits and pesticides, however, oral contraceptives offer many opportunities for abuse. Rather than the careful and limited application that dart delivery forces on our current use of immunocontraceptives, oral contraceptives could be scattered incautiously and indiscriminately, leading to unpredictable biological effects on a large scale. These risks are amplified if the immunocontraceptives are not species-specific.

Transmissable contraceptives up the ante yet again. In his 1985 novel, *Galapagos*, Kurt Vonnegut describes a world in which the human population is driven nearly to extinction by a virus that sweeps across the planet rendering its human hosts infertile (except for a small group isolated on the Galapagos Islands, where the plot then unfolds). This is the deepest fear that transmissable contraceptives raise — once released, such an agent could not be controlled, and its unanticipated effects could be catastrophic for the target species, non-target species, and even our own species. We believe that there would be absolutely no support in the United States for release of such an agent: no wildlife overabundance problem with which we are presently coping could justify even considering assuming that level of risk.

Australia, where much of this research is being conducted, is following a different story line. The introduction and phenomenal prosperity of European rabbits, red foxes, domestic cats, and house mice has devastated dozens of native marsupial species in a true ecological catastrophe. Australia's response has been to kill these (once-welcomed) invaders by the millions, with poison, traps, guns, blasting, gas, disease, and every other cruel destructive device imaginable. That humane catastrophe, in conjunction with the ecological catastrophe, has led animal protection groups in Australia to support (with conditions) the ongoing research into transmissable immunocontraceptives (Oojges 1997). But because the risks of releasing such an agent would extend beyond Australia, a clash between Australians and the rest of the world might be anticipated, even among animal protectionists.

CONCLUSION

In spite of the frustrations and obstacles, personal, political, and bureaucratic, we remain optimists about the future of wildlife contraception. Maybe that's just who we are. But our optimism draws support from our experience. One of us (JFK) has been working on wildlife fertility control for almost thirty years; the other (ATR), for just under a decade; and we have seen progress. Operationally, we've gone in thirty years from capture, field surgery, and implantation with gobs of physiologically and environmentally suspect steroids, to darting animals in the field at 25-50 yards with one-fifth of a teaspoon of biodegradable vaccine. In the public perception, wildlife contraception has gone from a joke ("how're ya gonna get them condoms on the studs/bucks? yuck, yuck") to a pretty darned good idea, "if you can make it work." And even in the deer meetings we've survived to describe (Kirkpatrick and Turner 1997; Rutberg 1997), after all the shouting and blustering and posing and accusing is over, in the back of the room, there's usually someone who takes us aside, someone quiet, who says, "You know, these animals really are a problem, but it's not right to kill them, so if you could find another way to control them it would make people really, really, happy."

For the animals — the old mares on Assateague, the old does on Fire Island, and the rest — and for those people in the back of the room, we should all be working.

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