One of the major efforts of the Science and Conservation Center at ZooMontana involves the humane control of wildlife populations by means of fertility control. To that end, the Science and Conservation Center was created in 1998, an independent non-profit organization that is the world’s only dedicated facility for the development of wildlife contraceptives and methods of application. This Center produces and carries out quality control for a wildlife contraceptive vaccine, distributes the vaccine and is the repository for all records and data required by the Food and Drug Administration and Environmental Protection Agency. Additionally, the Center and its staff coordinate and in some cases carry out field-based application of contraception to wildlife populations.

The Center receives many inquiries from around the world regarding wildlife contraception, an arcane subject that can be complicated and confusing. These inquiries center about many different species, diverse challenges, and a variety of settings, and those inquiring have a wide breadth of understanding about the subject - from very little to quite a lot. To complicate matters, there is a great deal of controversy regarding this subject, some based in misunderstanding of facts and some based in social, cultural, political or economic objections to this approach to wildlife management. To facilitate the educational process, The Science and Conservation Center, has published this overview, with the intent of providing a realistic picture of the state of the art of wildlife fertility control. To be sure, the complexity of the subject greatly exceeds the possibility of a comprehensive discussion here, but this publication can acquaint the reader with the basics necessary to develop a realistic picture, and the bibliography can lead the interested reader to a wealth of more detailed information.
WHY FERTILITY CONTROL?

At earlier times in history wildlife populations were controlled by two natural processes. These included mortality control and fertility control. When animal populations exceed the carrying capacity of their environment, animals die from starvation and disease as well as predation. At the same time, high densities among wildlife populations lead to a decrease in reproductive success; animals delay the age at which they will first breed, they produce fewer offspring, and juvenile mortality rates increase.

Urbanization and modern agricultural development led to the reduction of predators, and regulated hunting and trapping soon replaced predators as population control devices. Dwindling wildlife resources and loss of habitat led to the creation of reserves, parks, and special legislation that protect certain species from traditional lethal controls. Examples might include wild horses protected by the Wild Free-Roaming Horse and Burro Act or elk, or elephants living in national parks where large predators no longer exist, or even zoological gardens, where unregulated reproduction can lead to “surplus” animals and massive ethical problems associated with the disposition of these excess animals.

Humans have chosen to impose artificial human-induced mortality control on wild populations, through regulated hunting, trapping, and poisoning, and this is accepted as “normal” human activity. In many areas of the world, and with many species, traditional human-induced mortality control will continue to be the primary management tool. In recent history, however, increasing urbanization, the withdrawal of private lands from the public hunting domain, regulatory prohibitions on the use of poisons, legislation against trapping, low fur prices and, most important, changing public attitudes about lethal wildlife control methods have reduced the effectiveness of human-induced mortality control as a management tool for many species. Thus, we now face exploding populations of some adaptable or highly protected species but without adequate management tools with which to protect environment and animals alike.

The use of human-imposed fertility control however, is still often viewed as “bizarre” or “unnatural”, and the reasons for this view are not understood. It may have something to do with the simplicity or relatively lower cost of mortality control, or something as simple as a cultural mindset. Regardless of the answer to this question, we are rapidly facing a point in time when safe, humane and publicly acceptable wildlife management paradigms are beginning to replace lethal methods. The public demands it and the animals we have displaced deserve it.

The scientific community is also responding to this need, and thus far, six international conferences on wildlife fertility control have been held around the world, and public acceptance has followed suit.
The concept of wildlife fertility control is not new and research has been carried out for many years. Most of this work was based on the fruits of human contraceptive research and therefore mirrored human contraceptive technologies. This in turn meant that until recently, the most common approach to wildlife contraception was through the use of steroid hormones, and particularly natural and synthetic estrogens, progestins, and androgens, similar to those found or used in human contraception. Zoos really led the way, administering these compounds to captive animals, where delivery was not an issue, but their use in free-roaming wildlife was another matter. These compounds often worked in a pharmacological sense but they fell far short of the standards that permit them to be used with free-roaming wildlife. Basically, they failed because (1) they had to be given in extremely large quantities, ruling out remote delivery, (2) they had to be administered too often, (3) they caused a variety of pathologies in treated animals, (4) the cost was relatively high, (5) they often had profound effects upon social behaviors, (6) they were often unsafe to administer to pregnant animals, and (7) they passed through the food chain to predators - human and otherwise - and scavengers. Because of these shortcomings, there was little hope that they would ever be publicly acceptable for use in free-roaming wildlife by regulatory agencies. For more extensive reading on the history of wildlife contraception we suggest Kirkpatrick and Turner 1991, (referenced in the Bibliography).
CHARACTERISTICS OF THE IDEAL WILDLIFE CONTRACEPTIVE

The failure to achieve practical results with steroid hormones led to a re-examination of the problem. It became apparent by the early 1990s that research was proceeding without a “gold standard” by which to evaluate each new approach. Without such a standard evaluation of potential wildlife fertility control methods could be likened to a discussion of law without a constitution. Thus, a theoretical “standard” was created and included:

1. Contraceptive effectiveness of at least 90%.
2. The ability for remote delivery, with no 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 and any future discussions of new wildlife contraceptive agents or discussions of current agents should attend to these characteristics (see Kirkpatrick and Turner 1991).

IMMUNOCONTRACEPTION

In 1988, a new approach to wildlife contraception was launched. Immunocontraception is based on the same principles as disease prevention, through vaccination. We vaccinate ourselves and other animals against diseases by injecting dead or attenuated (weakened) disease bacteria or viruses, or with molecules that are harmless but similar to the toxins that these disease organisms produce. Our immune systems produce antibodies that attack the material we injected and any similar organism or their toxins in our systems. An immunocontraceptive vaccine works in much the same way, only it causes the production of antibodies against some essential event or structure in the reproductive process. There are a variety of immunocontraceptive vaccines under development or already registered, including vaccines against brain reproductive hormones such as gonadotropin-releasing hormone (GnRH) and vaccines against the sperm and the egg, which in turn prevent fertilization. The advantages of vaccines are that they can be delivered remotely in very small doses, and because they are primarily protein, they are readily destroyed in digestion and cannot pass through the food chain. The vaccine which thus far has had the largest application to wildlife is the Porcine Zona Pellucida, or PZP vaccine.
What is PZP and How Does It Work?: A non-cellular membrane known as the zona pellucida (ZP) surrounds all mammalian eggs. The ZP consists of several glycoproteins (proteins with some carbohydrate attached), one of which, ZP3, is thought to be the sperm receptor (the molecule which permits attachment of the sperm to the egg during the process of fertilization). The PZP vaccine is derived from the ZP protein 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 the female’s own eggs and distort their shape, thereby blocking fertilization (see Paterson and Aitkin 1990).

Thus far PZP has been a successful form of contraception in wildlife because (1) it has prevented pregnancy an average of 90% or greater of the time in treated animals, (2) it can be delivered remotely by small darts, (3) the contraceptive effects are reversible, (4) it is effective across many species, (5) there are no debilitating health side-effects even after long-term use, (6) it has almost no effects on social behaviors, (7) the vaccine cannot pass through the food chain, and (8) it is safe to give to pregnant animals (see Kirkpatrick et al. 2009).
How is the Vaccine Delivered?: The PZP vaccine must be injected into the muscle of the target animal. This can be done by hand if the animal is restrained, or by dart, for remote delivery. There are many commercial dart systems available but the thick viscosity of the vaccine requires a large needle and a quick injection. Thus far, Pneu-Dart® systems (Williamsport, PA) work the best. The Pneu-Dart® 1.0 cc barbless darts can be fired from Pneu-Dart® capture guns or from several other commercial dart guns (Dan-Inject®, for example). The darts are disposable, and after hitting the animal in the rump or hip (the only acceptable location for darting) they inject by means of a small powder charge and pop out. Because of their bright colors the darts are usually retrieved in the field. Unrecovered darts cannot be discharged by stepping on them nor by any other kind of casual contact. Over a 20 year period on Fire Island, Assateague Island, and Cape Lookout National Seashores, and more than 2,000 treatments of deer and horses, 98% of darts have been recovered.

Normally, each animal is darted twice the first year, with the first injection being given up to a year before a booster, just preceding the breeding season (March for wild horses or September for deer). Thereafter, a single annual booster inoculation will maintain contraception (Kirkpatrick et al. 1991). The second inoculation of the first year requires (1) that you are able to recognize the individual animals, or (2) that you do the first inoculation with a special “marker dart” which leaves a dye mark on the animal at the same time it injects the vaccine, or (3) that animals are treated opportunistically and randomly, with the hope of eventually treating a large proportion of the total population over the course of several years.

An alternative strategy is to give only a single inoculation the first year, from which there will be little contraception, and then a single annual inoculation thereafter, from which there will be significant contraception (see McShea et al. 1997).
Wild Horses: The vaccine has been used successfully to manage the wild horse population of Assateague Island National Seashore under the authority of the National Park Service (NPS). This population has been treated since 1988 without health problems, and the population has decreased more than 30% since management-level application began in 1995. Wild horses are also being treated on Cape Lookout National Seashore for the NPS, on Carrot Island, for the Rachel Carson National Estuarine Reserve, and on Corolla Island, both in NC, the Pryor Mountain and Little Book Cliff National Wild Horse Ranges, MT and CO, respectively, the McCullough Peaks wild horse range in WY, on many areas of Nevada, Utah, Oregon for the Bureau of Land Management (BLM), on the Carson National Forest, for the National Forest Service, on several wild horse sanctuaries, and on the Navaho and Pima/Maricopa Indian Reservations in NM and AZ. In addition to controlling the horse population on Assateague Island, treatment has extended the lives and improved the health condition of older mares, by removing the stresses of pregnancy and lactation (see Kirkpatrick and Turner 2002; Kirkpatrick et al. 1990, 1991; Liu et al. 1989; Turner and Kirkpatrick 2002; 2003, 2007, 2008).

Zoo Animals: In order to prevent the production of “surplus” animals, zoo animals in more than 120 zoos have been successfully treated with PZP. Thus far PZP has shown contraceptive effects in more than 80 species. In all probability, PZP will prove to be a successful contraceptive for all ungulates (hoofed animals), but it also works in bears, pinnipeds (seals and sea lions) and elephants. We do note differences between species in the timing of the booster inoculations. Porcine Zona Pellucida vaccine is now a standard recommendation for many species by the Contraceptive Advisory Group of the Association of Zoos and Aquariums (AZA). The obvious advantage of the PZP vaccine for zoo animals is that it can be administered without the stresses of restraint (see Kirkpatrick et al. 1992b, 1995b; Deigert et al. 2003; Frank et al. 2005; Asa and Porton 2005).

Deer: The PZP vaccine was shown to block pregnancies in captive white-tailed deer as early as 1990. Since that time, numerous projects have been mounted with free-roaming deer in MD, NJ, NY, CT, WA, VA and OH. The two largest projects are on Fire Island National Seashore (FINS), NY, where approximately 215 deer are treated annually since 1993, and on the campus of the National Institute of Standards and Technology (NIST), in MD, where more than 150 deer have been treated since 1996. In both these programs the deer population has been decreased significantly. The studies and projects thus far have shown that contraception with PZP will often extend the breeding season of the female by one to two months, but that the energy cost is far less than that of getting pregnant and nursing. Although they will often follow the treated female deer, males do not carry on fights or expend additional energy beyond the normal breeding season (see McShea et al. 1997; Naugle et al. 2002; Turner et al. 1992, 1995; Rutberg and Naugle 2008).

African Elephants: In order to eliminate the need to legally kill elephants in African national parks to prevent rapid population increases, the PZP vaccine has been tested in African elephants in The Kruger National Park in South Africa. The vaccine was very successful and the results paralleled those of horse contraception. One of the most important findings was that the vaccine caused no changes in the social behaviors of family groups or harassment of cycling females by bulls. As a result of the Kruger Park studies, at least eleven game parks throughout South Africa are now using PZP to control elephant populations, rather than culling them. Growth rates have been reduced to almost zero. Demand for vaccine for elephant contraception grew so rapidly, that in 2003 the SCC trained an African team to make the vaccine in South Africa (Fayrer-Hosken et al. 2001; Delsink 2006, 2007).
Other Species: The PZP vaccine has also been used successfully in feral water buffalo inhabiting the U.S. Naval Base in Guam, feral burros in Virgin Islands National Park (Turner et al. 1996), Elk on Point Reyes National Seashore (CA) (Shideler et al. 2002), and more recently, bison on Catalina Island (CA).

Training: The SCC conducts training programs for personnel from NGOs and government agencies, for the proper use of PZP in wildlife. Examples of agencies participating in these training programs include the Bureau of Land Management, Biological Resources Division of USGA, US Fish and Wildlife Service, U.S. Navy, and the National Park Service.

REGULATORY ISSUES

One of the most poorly understood dimensions of wildlife contraception is the regulatory process. Depending upon the species in question, one or more agencies, local, state and federal may be involved, and the agencies involved have changed over time. A brief description of the process and regulations follows:

Federal Regulation. Since the mid-1990’s, all SCC projects in which the vaccine crossed state lines have been reported to the U. S. Food and Drug Administration (FDA). These projects have been carried out under the authority of two separate Investigational New Animal Drug documents (INADs) issued by the FDA to The Humane Society of the United States (HSUS). One of these INAD’s covers wild horses, the other covers deer and zoo animals. For each project, the SCC files a form with the FDA specifying how much vaccine is being shipped and what species are to be treated. The INAD also requires that a detailed research protocol be filed for each project, data from each project be gathered in a systematic way and filed, and data made available to the FDA when the need arises. These files are maintained at the Center.

In about 2005, however, FDA began to transfer authority over most applications of wildlife contraceptives (other than zoo animals, which remain with FDA) to the Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). This includes wild horses, deer, geese, and other wildlife that is “capable of doing environmental damage.” The EPA approval process follows that agency’s registration requirements for pesticides. (The language of “environmental damage” and
“pesticide” is in many ways regrettable, but is forced by the language of FIFRA.) At this writing, EPA has registered two wildlife contraceptives, OvoControl® (a nicarbazine-based oral contraceptive for geese and pigeons) and GonaCon® (a GnRH-based injectable immunocontraceptive for deer). HSUS has also applied to EPA for registration of PZP for use on wild horses.

Under EPA regulations, users of registered contraceptives must follow the directions on the label, which may include requirements for certification of applicators, target species, and methods, times, and place of application. Unlike FDA-approved drugs, which may be prescribed by physicians or veterinarians for purposes other than those described on the label, there is no such thing as “off-label use” for EPA-registered contraceptives. In addition, an EPA-registered contraceptive must generally be registered in the states in which it is being applied.

Aside from meeting FDA requirements, the Animal Care Committee of each zoo must also provide permission to treat zoo animals. The federal Animal Welfare Act also requires that experimental applications of PZP to free-ranging wildlife be reviewed and authorized by the Institutional Animal Care and Use Committee of a university or responsible agency.

**Wild Horses.** Contraceptives can only be applied with the permission of and/or under the supervision of the legal owners or managers of the horses (including government agencies such as the NPS, BLM, or USFS, or sanctuary owners). As each new project is identified, The HSUS reviews the need for the project in the context of scientific and ethical issues and, if approved, issues permission to proceed. Applications of PZP to wild horses by federal agencies also require compliance with the National Environmental Policy Act (NEPA), which generally entails preparation of an Environmental Assessment (EA).

**Deer.** The first step in deer contraception is for the affected landowners and local legal authority (city, township, county, park board or some combination thereof) to agree to carry out a deer project. The second step is a review by The HSUS, to determine the scientific and ethical dimensions of the project (do these deer really need more management?). The third step is the preparation of a proposal to the state fish and wildlife agency, regardless of whether the deer in question reside on public or private property. The principal exception to state authority is wildlife residing on federal lands, which are not subject to state authority. However, federal managers generally try to be responsive to the concerns of state wildlife agencies.

If the contraceptive is already registered with the EPA and the state, no further permissions are needed. If not, the project should be carried out under an FDA INAD or under an EPA experimental use permit. Like the INAD, the EPA’s experimental use permit is granted for use at specific sites under specific conditions.

An Assateague mare being targeted for a PZP inoculation. Effective ranges are up to 50 meters.
In addition to the regulations regarding the vaccine, the use of delivery equipment such as capture guns often requires additional state and local authorization and/or training. For example, the use of capture gun equipment within an NPS unit, even to deliver contraceptive drugs, requires special NPS certification. This includes documentation of prior experience with the delivery equipment, a certificate of completion of an NPS sponsored wildlife immobilization course or its equivalent, current CPR certification, passage of a qualifying test on the range, and a letter of certification from a superintendent of an NPS unit. Those contemplating projects with deer should also be sensitive to state laws and local ordinances regarding the discharge of firearms, which may apply to delivery equipment in some jurisdictions.

**HOW MANY ANIMALS HAVE TO BE TREATED?**

This is a very important and often-asked question, but usually it is asked without much understanding. The number of animals or percent of an animal population that needs to be treated is dependent upon many factors and there is no simple answer. For example, what is the goal? Is it the absence of all animals (impossible with contraception), or a 20% reduction or a 50% slowing of the growth rate or zero population growth? Even after the goal has been identified, data required to answer this question include at very least the reproductive rate, sex ratio, mortality rate, and immigration and emigration rate of the population. Equally important, these data on reproduction and mortality must be site-specific to the particular herd in question and not generalized data or data derived from other locations and populations. One of the most serious deficiencies noted at discussions of new projects is the lack of sound biological data and vague or no goals (Kirkpatrick and Turner 2008; Ballou et al. 2008).

Another consideration is the length of time necessary to achieve population goals. Contraception is not a good way to reduce population numbers rapidly. It takes time for animals to die off and, as seen earlier, one of the results of wildlife contraception may be increased longevity among treated animals. Wildlife contraception must be viewed as a long-term commitment. Also, humans should consider that most wildlife overpopulation problems were created over many years and that quick solutions are not the result of rational thought or fair to the wildlife.

A dart with a cut-away needle showing the small pellets containing PZP. This approach can deliver a year’s worth of contraception with a single inoculation.
Several areas of active research are underway by the PZP Wildlife Contraceptive Group, and these areas of research reflect current shortcomings of the PZP vaccine. These current research endeavors include the following:

**A One-Inoculation Vaccine:** Because of the need to inoculate animals twice the first year, and the difficulty of doing this with wild species, research is proceeding toward a “one-inoculation” vaccine. Such a vaccine would permit a single darting to cause one or more years of contraception. The approach under study incorporates the PZP into a non-toxic, biodegradable material, which can be formed into small pellets. The pellets can be designed to release the vaccine at predetermined times after injection (at one, three and nine months currently) much the way time-release cold pills work. Trials thus far have been encouraging and continued trials are underway (Turner et al. 2001, 2008). Additional research is being conducted with a biodegradable polymer gel, in collaboration with the U. of Tennessee.

**Pellet-delivery Darts:** There is a need for darts that can deliver the long-acting pellets remotely. Current collaborative research with at least two proprietary companies are directed at developing a reliable dart for remote pellet delivery.

**A Genetically Engineered or A Synthetic ZP Vaccine:** The ability to produce large quantities of the PZP vaccine at low cost will permit the increased use of this vaccine in wildlife. Currently collaborative work with the Indian National Institute of Immunology is testing a recombinant form of PZP that might be useful as a booster inoculation. Native PZP will remain the only useful “primer” inoculation.

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![Population Density of Deer on Fire Island National Seashore, NY, 1995-2005](image)

*The decline in deer population on Fire Island National Seashore brought about by PZP contraception over several years.*
Oral Contraceptives: It is intuitive that the ability to deliver contraceptives to wildlife 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 contraceptives must be species-specific (that is, it must work in only one species for which it was intended). This will be very difficult with the PZP vaccine because of its protein nature.

Biologically Modified-Vectored Contraceptives: Researchers working with the Australian government have sought to engineer the genes for PZP and similar contraceptive molecules into non-pathogenic viruses. These viruses could then be transmitted from animal to animal in wild populations. While there are some attractive features to this approach, the safety, environmental, and ethical issues associated with this technology has raised strong objections from the public and regulatory agencies in the U.S. and abroad, and it probably will never be used here.

Abortifacients: Research into compounds which will cause abortion in the recipient animals has largely been abandoned. This has already been shown to be feasible in deer, but most researchers are not pursuing this approach because of the social objections that attend this method of wildlife control.

ETHICAL AND SOCIAL ISSUES

The entire subject of wildlife contraception is attended by a variety of strongly held attitudes both favoring and objecting to this approach. Public discussions are seldom rational. For example, despite the obvious limitations to the available technology some advocates will make loud and unrealistic claims that wildlife contraception can one day completely replace public hunting. On the other side, and despite evidence to the contrary, opponents will express fears of harm after eating treated animals, or will object on the basis of high cost, or will insist that a problem that took 20 years to develop be solved in one year. Anyone seriously considering involving themselves or their community in wildlife contraception should first read Kirkpatrick and Turner 1995, 1997. At very least, do not expect unemotional and dispassionate discussions to occur when this topic is broached.

The most serious ethical considerations are when to manage and why, and the nature of the alternatives. Should wildlife populations be reduced by any method because they inconvenience humans? Should contraception be applied to seals because they are suspected of harming the economy of a fishing village? Should contraception be applied to wolves because they are eating caribou that sport hunters spend large amounts of money to shoot? Should contraception be applied to an endangered species? If contraception is not used, what will be the alternative management strategy? Who makes the decisions, and on what basis? These are serious questions involving the ethics of both science and wildlife management and they must be considered before application of this technology is applied to our wildlife resources (Kirkpatrick 2007).
WHO IS THE PZP CONTRACEPTIVE RESEARCH TEAM?

The entire PZP contraceptive effort involves many people, several institutions, and numerous funding agencies. At last count there were at least 12 individuals on this team, representing the Science and Conservation Center, the University of California - Davis, the Toledo University Medical College, University of Iowa, and The Humane Society of the U.S., as well as others. This team works together, bringing many disparate disciplines and talents together to solve the problems at hand.

WHO FUNDS PZP CONTRACEPTIVE RESEARCH AND APPLICATIONS?

Funding for applications of the vaccine to wildlife has been provided by many individual communities, agencies, and organizations, including but not limited to: The Humane Society of the U.S., Park Foundation, ASPCA, the Elinor Patterson Baker Trust, THAW Charitable Trust, Burket-Plack Foundation, the Bernice Barbour Foundation, Delta-Sonics, the PNC Corporation, the U. S. Navy, the National Park Service, the Bureau of Land Management, the Rachel Carson National Estuarine Reserve, the National Forest Service, the U. S. Department of Commerce, the National Institutes of Health, the Fire Island Community Association, >100 different zoos in North America, Europe and Australia, the South African National Parks Board, several Indian tribes, and several anonymous donors. This list is not all-inclusive but provides a picture of the breadth of support for this approach to wildlife management.

HOW IS THE PZP VACCINE OBTAINED?

Once all necessary authorizations and approvals have been obtained for the use of the vaccine, it is ordered from The Science and Conservation Center, 2100 South Shiloh Road, Billings, MT 59106; phone 406-652-9718; fax 406-652-9733; e-mail Kim Frank at sccpzp@hotmail.com. The vaccine is not commercially available and it is provided at 60% of the cost of production, or about $24/dose.
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