

Field Test of GonaCon™ Immunocontraceptive Vaccine in Free-Ranging Female White-Tailed Deer

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ABSTRACT: Locally overabundant deer herds, particularly those inhabiting fenced or other enclosed areas in urban or suburban settings, are presenting serious problems for wildlife managers, landowners, and the general public. Traditional methods of population control, such as regulated harvest by licensed hunters, often are impractical or illegal in such settings. The development of safe and effective wildlife contraceptives is needed to control locally overabundant populations in situations where traditional management tools cannot be employed. During July 2004, we initiated a field study of GonaCon™ Immunocontraceptive Vaccine, developed by research scientists at the National Wildlife Research Center in Fort Collins, Colorado. This vaccine had previously been tested successfully as a contraceptive in captive animals including white-tailed deer, feral and domestic swine, and wild horses. The two-year field study was prompted by the need to manage an enclosed, overabundant population of white-tailed deer that had caused considerable ecological damage to a 662-acre, federally-owned, forested site in Silver Spring, Maryland. The U.S. General Services Administration, which manages the property, conducted an environmental assessment, which concluded that sharpshooting followed by immunocontraception would be the most appropriate deer management strategy. After 214 deer were removed from the site by sharpshooters, we set up and tested an automated radio telemetry system for tracking deer and monitoring their mortality. Twenty-eight does were then captured, equipped with ear tags and radio telemetry collars, and injected with GonaCon™ vaccine. Fifteen additional does were captured, marked, and released without vaccination as untreated control animals. Reproductive behavior and fawn production by the vaccinated and unvaccinated does will be monitored and compared for two years, and will be used to determine the efficacy of GonaCon™ as a wildlife contraceptive agent. Data from this study will be used to support EPA registration of GonaCon™ as a wildlife contraceptive agent.

KEY WORDS: contraception, fertility, GnRH, gonadotropin-releasing hormone, *Odocoileus virginianus*, overabundant, population control, surplus, vaccine, white-tailed deer

Proc. 22nd Vertebr. Pest Conf. (R. M. Timm and J. M. O'Brien, Eds.)
Published at Univ. of Calif., Davis. 2006. Pp. 78-81.

INTRODUCTION

An exciting new deer management tool is being field tested in Maryland by USDA National Wildlife Research Center (NWRC) scientists and their collaborators. The tool is GonaCon™, an immunocontraceptive vaccine developed by Dr. Lowell Miller and his colleagues at NWRC (Miller *et al.* 2000). Contraception offers great promise as a non-lethal means of managing deer populations that inhabit urban and other areas where hunting is prohibited.

White-tailed deer (*Odocoileus virginianus*) management is one of the more dramatic wildlife conservation success stories in North America. Although an estimated 23 to 33 million white-tailed deer inhabited North America when the first European colonists arrived (McCabe and McCabe 1984), only about 350,000 animals remained by 1900 (Trefethen 1975). Today, white-tailed deer numbers are estimated at about 25 to 30 million animals (Demarais *et al.* 2000). In some parts of the United States, deer are locally overabundant, and they cause damage to vegetation (Waller and Alverson 1997, Rooney and Waller 2003) and increased numbers of deer-vehicle collisions (Blouch 1984, Etter *et al.* 2000). Mike Conover, of the Berryman Institute at Utah State University, has estimated that deer cause at least \$750

million in damage to the timber industry each year (Conover 1997). According to a recent estimate, white-tailed deer are “ecologically excessive” (i.e., they exceed biological carrying capacity) on 73% of the species’ range in North America (Crête and Daigle 1999).

How can these overabundant deer be managed? Historically, of course, predation played a major role in controlling deer numbers, but native predators of deer are now absent from many areas where deer are overabundant. Traditionally, regulated sport hunting was used, with great success, in managing deer numbers and densities. In most parts of the country, hunting remains the most effective and efficient means of controlling deer. Unfortunately, overabundant deer now inhabit many urban and suburban areas, where hunting is prohibited because of safety issues. Other deer management strategies are needed for these areas (DeNicola *et al.* 1997), and a specialized field is emerging: deer management in urban and suburban communities (Bishop *et al.* 1999, DeNicola *et al.* 2000, Fox 2001). Among the methods used to reduce deer numbers in suburban environments are capture-and-relocate programs, and the use of sharpshooters. Both methods are very costly and fraught with problems. Survivorship of translocated deer has typically been very low, with transplanted deer being killed by

hunters and collisions with vehicles at much higher rates than those of “resident” deer at the release sites (O’Bryan and McCullough 1985, Craven *et al.* 1998). Translocated deer also tend to cause the same problems in their new environments as they did in their old ones, because they seek out residential neighborhoods where they have learned that they can find food, water, and shelter (O’Bryan and McCullough 1988). In addition, many state wildlife management agencies no longer permit translocation of deer because of concerns related to disease transmission among deer. The use of sharpshooters is very effective in reducing deer numbers, but it often produces public relations nightmares because of public opposition to lethal control of deer and perceived threats to human safety.

Wildlife contraception may provide at least a partial solution to the problem of managing overabundant deer in cities and towns. The NWRC has been active in the development and testing of wildlife contraceptives since 1992. Many types of contraceptives and their effects on many wildlife species have been investigated by NWRC scientists, but in this paper we focus on one contraceptive agent, an immunocontraceptive vaccine, GonaCon™, that has been widely tested in white-tailed deer.

GonaCon™ vaccine completely shuts down reproduction in treated animals of both sexes (Miller *et al.* 2000). It contains a GnRH peptide conjugated to a large carrier molecule (called keyhole limpet hemocyanin, or KLH) that comes from a limpet (a mollusk that inhabits intertidal zones) (Miller *et al.* 2000). The conjugate is then combined with AdjuVac™, the adjuvant developed at NWRC (Miller *et al.* 2000).

Initially formulated as a two-shot contraceptive agent, GonaCon™ has now been refined so that a single injection can produce infertility for multiple years without boosting. The single-injection formulation of the vaccine has been tested successfully in several mammalian species (Miller *et al.* 2004) including free-ranging California ground squirrels (*Spermophilus beecheyi*, Nash *et al.* 2004), captive Norway rats (*Rattus norvegicus*, Miller *et al.* 1997), domestic and feral swine (*Sus scrofa*, Miller *et al.* 2003, Killian *et al.* 2003), wild horses (*Equus caballus*, Killian *et al.* 2004), bison (*Bison bison*, Miller *et al.* 2004), and white-tailed deer (Miller *et al.* 2000). Infertility among treated female swine and white-tailed deer, for example, lasted up to 2 years without requiring a booster vaccination (Miller *et al.* 1997, 2000).

To understand how GonaCon™ works, we compare what happens in untreated versus treated animals. In the untreated mammal, stored GnRH peptide is released from secretory granules in the hypothalamus at the base of the brain. The GnRH diffuses into the surrounding capillary blood and then travels via the hypophysial portal system to the anterior pituitary, where it diffuses from the capillaries and binds to and activates the LH (luteinizing hormone) and FSH (follicle-stimulating hormone) gonadotrophs. This activation causes the release of stored LH and FSH, which diffuse back through the capillaries and into the bloodstream. These hormones then travel to and activate the gonads, resulting in steroid synthesis and normal sexual activity.

In the GonaCon™ -treated mammal, the GnRH vaccine stimulates the production and release of GnRH-specific antibody from the B-cells into the bloodstream. The antibody circulates throughout the body, and when it reaches the capillary region of the hypothalamus, it comes into contact with GnRH that has diffused into the capillaries after being produced in the hypothalamus. The GnRH and its antibody bind together, producing large immune-complexes that travel to the anterior pituitary. Because of their large size, these immune-complexes are unable to diffuse out of the bloodstream at the pituitary capillaries. Instead, they remain in the venous blood and leave the pituitary without stimulating the release of LH and FSH. Without the LH and FSH that normally stimulate the synthesis of steroids in the gonads, animals of both sexes remain in an asexual, non-reproductive state. As long as there is sufficient antibody to bind to all of the GnRH circulating in the hypothalamic/pituitary portal system, all sexual activity will be suspended and animals will remain non-reproductive (Miller *et al.* 2000).

Scientists at NWRC and at Pennsylvania State University collaborated on a series of studies of GonaCon™'s safety and efficacy using captive white-tailed deer in Pennsylvania (Miller and Killian 2001, Killian 2006). Then, during summer 2004, we began an efficacy field study of GonaCon™ vaccine in Maryland. Efficacy field studies are required by the U.S. Environmental Protection Agency (EPA) as part of the registration process for a new wildlife contraceptive agent. The deer study is being conducted on a mostly forested parcel of land managed by the U.S. General Services Administration and located in Silver Spring, Maryland, near Washington, D.C. The site, on which hunting is prohibited, is called the Federal Research Center at White Oak (White Oak), and is 662 acres (268 ha) in size. Several years ago, an environmental assessment (EA) of deer management determined that the preferred management alternative was to cull the herd and then implement a deer contraception program. The EA recognized that applying contraception to a severely overpopulated herd without first reducing deer numbers to a desired level was not an effective way to reduce population size. Accordingly, during October 2003, 214 deer were removed from White Oak by wildlife professionals from the Maryland office of USDA APHIS Wildlife Services through nighttime sharpshooting. An estimated 50 to 80 deer remained at White Oak (Kevin Sullivan, pers. observation).

Immediately adjacent to White Oak is a U.S. Army property known as the Adelphi Laboratory Center (Adelphi). This site also is fully fenced, but it is smaller than White Oak, encompassing 202 acres (82 ha). The habitat is very similar to that at White Oak, and hunting is prohibited. No cull was conducted at Adelphi, where an estimated 50 deer occur. Does at Adelphi are used as untreated control animals in the field study, which began at White Oak and Adelphi in July 2004.

Major habitat types at White Oak and Adelphi are deciduous forest, open grasslands, grassy areas along roads, and ornamental landscaping near buildings. An automated, fixed-station radio telemetry system was set

up at White Oak. The two telemetry antennae systems were installed to pick up radio signals from deer anywhere on White Oak or Adelphi. The primary function of the telemetry systems is to enable monitoring of mortality among the study animals. When a mortality signal is received by the system, a phone call is automatically made to a cell phone that is monitored by one of the Maryland-based, USDA Wildlife Services biologists. The biologist then immediately goes to the study site and recovers the deer carcass for necropsy. The analysis of blood chemistry and hematology is an important part of the evaluation of GonaCon™, so it is critical that we recover carcasses of study animals soon after death.

Examples of deer damage to vegetation at White Oak and Adelphi include the almost complete removal of forest understory vegetation, as well as extensive damage to ornamental tree and shrub plantings near buildings on both sites. Deer can be seen crossing paved roads on both sites at any time of day or night, creating a hazard to traffic.

METHODS

Fieldwork began in July 2004, when deer were captured with tranquilizer darts containing a cocktail of Telazol™ and Xylazine™, fired from a pickup truck that traveled slowly along the network of roads that traverse both study sites. Each captured doe was fitted with two types of ear tags plus a radio telemetry collar. Vital signs were monitored as deer were processed. Eye ointment was used to prevent desiccation of the eyes. Blood was collected at time of capture and will be collected again from each study animal at the end of the 2-year field study. An IV injection of Tolazine™ was given to each doe to reverse anesthesia and hasten recovery. Twenty-eight does were captured at White Oak and injected with GonaCon™ vaccine. Fifteen does were captured, marked, and released at Adelphi without injections (as control animals).

The efficacy of GonaCon™ will be determined by comparing, over a 2-year period, the proportion of treated does that produce at least 1 fawn to the proportion of untreated does that produce at least 1 fawn. During summer 2005, we observed deer at our two study sites to collect the first year's data for these comparisons. We had hoped to be able to determine how many fawns each doe produced, but definitive observations of fawns with their mothers (such as a fawn seen nursing on a doe) proved to be very difficult to obtain (we only saw one such nursing event). Therefore, although we had dozens of observations of fawns and does together in various numbers, we were unable to tell which fawns belonged to which does (except in the one case). We were able, however, to determine which does had given birth this year through observations of udder condition, although we could not tell if one or two fawns had been born, and we could not determine survivorship of the fawns.

RESULTS

We made definitive observations for 13 of the 15 untreated control does at Adelphi. Eleven of the 13 does (85%) produced at least 1 fawn during 2005. At White

Oak, we obtained definitive observations for 25 of the 29 does that had been injected with GonaCon™ vaccine. (Three of the remaining 4 does had died during the previous year.) Only 3 of 25 does (12%) had produced 1 or more fawns during 2005. We concluded that GonaCon™ vaccine reduced fawning rates by 86% when the reproductive success of untreated does at Adelphi is used as a baseline.

Additional insight into the efficacy and safety of GonaCon™ will come from analyses of blood and tissues collected at the end of the 2-year field study, when all study animals will be recaptured for blood sampling, and 10 treated and 10 untreated does will be necropsied.

DISCUSSION

Data from this efficacy study will be submitted to the EPA as part of the registration process for a new wildlife contraceptive agent. We are confident that GonaCon™ vaccine will become a valuable addition to the tools used by wildlife professionals to manage populations of overabundant wild animals in settings where other methods such as regulated sport hunting cannot be applied. It must be emphasized that wildlife contraception using GonaCon™ vaccine and other infertility agents will not replace sport hunting as a wildlife population management tool. Wildlife contraception will be applied only in special situations where traditional management methods cannot be used.

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