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Realities of Immunocontraception as a Management Option for White-tailed Deer in Suburban Environments

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Making decisions about deer management is challenging because of the need to bring together a wide array of values and facts.[1] The challenge is heightened because often the facts are poorly understood. The intent of this presentation is to provide a better understanding of what we know about the biology and application of immunocontraception as a technique for managing white-tailed deer (*Odocoileus virginianus*) populations in suburban environments. We will explore three questions. What is immunocontraception? How can we estimate the number of animals that must be treated to manage a population using contraceptive techniques? How do we estimate the cost of applying immunocontraception to a free-ranging population of deer?

What is immunocontraception?

Immunocontraception is not a difficult concept because we all have a common reference in human reproduction. We know that human reproduction is mediated by a system of organs and hormones. Without getting too deep into the biology, we recall that hormones produced by a part of the brain known as the hypothalamus stimulate

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1 W.F. Porter, *Ignorance, Arrogance, and the Process of Managing Overabundant Deer*, 25 WILDLIFE SOC'Y BULL. 408-412 (1997).

the pituitary gland to produce other hormones. These hormones, in turn, stimulate the ovaries to produce eggs. The eggs released by the ovaries travel through the fallopian tubes to the uterus. If the eggs encounter sperm, pregnancy can occur. This system is common to all mammals, including white-tailed deer.

A key attribute of the reproductive system is the feedback loop. Specifically, once pregnancy begins, no more eggs are produced for the duration of that pregnancy. Hormones produced by the uterus and ovary feedback to the hypothalamus, shutting down production of the series of hormones that would result in development of more eggs. Medicine has learned to take advantage of this natural feedback system with the "Pill". By introducing chemical equivalents of the natural hormones, we can simulate the effects of pregnancy during critical times in the estrous cycle (Figure 1). As a result, we can cause the ovaries to cease releasing eggs even though pregnancy has not occurred. Preventing the release of eggs precludes conception.

The Pill is not a good option for contraception in wildlife because dosage and timing of delivery is critical for this approach to work effectively. Daily dosage is not easy to accomplish in free-ranging wildlife populations. Further, synthetic hormones like the Pill can be passed along the food chain, affecting animals that consume a treated deer. Immunocontraception is a creative alternative to the Pill that circumvents both of these problems.

As the term implies, immunocontraception operates through the body's immune system.[2] Here again, we can understand the biology underlying immunocontraction by relating to human experience. We are all familiar with the basics of stimulating the immune system. For instance, many of us get tetanus shots periodically. The injection contains the tetanus organism in a form that has been altered so that it will stimulate the body to produce antibodies without causing illness. Once the antibodies are present, the body reacts quickly if it encounters the tetanus organism,

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[2] *See* L.I. Muller, et al., *Theory and Practice of Immunocontraception in Wild Animals*, 25 WILDLIFE SOC'Y BULL. 504-514 (1997).

eliminating the organism before the infection can begin. To maintain sufficiently high levels of antibodies to resist tetanus, we receive a booster shot every five to ten years.

Immunocontraception seeks to stimulate the body to produce antibodies against the proteins produced by the reproductive system. Like the tetanus shot, immunocontraception involves introducing a foreign protein into the body by injection. One protein now being used is Porcine Zona Pellucida, or PZP. The zona pellucida is a protein membrane that occurs on the outside of the egg of all mammals. Biologists obtain the protein from the eggs in the ovaries of pigs, hence the name, Porcine Zona Pellucida. When we introduce this protein membrane into the body of a deer, the immune system begins to produce antibodies specific to the zona pellucida protein. Thus, when the ovary releases an egg, the antibodies mistake the zona pellucida as a foreign protein and attack the egg, preventing conception (Figure 2).

Because the reproductive system in mammals involves many different proteins, we can use the immune system to target a variety of proteins and achieve contraception in many ways. For instance, one of the proteins that is important to the reproductive cycle is Gonadotrophin Releasing Hormone, or GNRH. We can prevent conception by stimulating the immune system to develop antibodies to GNRH. Here, the approach is to couple GNRH with a foreign protein, thus forming what is known as GNRH-A. The body naturally releases GNRH from the hypothalamus during part of the estrous cycle. When GNRH appears in the blood stream, the antibodies created against GNRH-A will deactivate the natural GNRH. Because the pituitary does not receive GNRH, it does not produce the hormones that stimulate egg production by the ovary. If no eggs are released from the ovary, pregnancy cannot occur (Figure 3).

Targeting other proteins such as GNRH is an interesting approach to contraception because it allows us to consider treating males as well as females. A common characteristic of the reproductive system in both sexes is the presence of hypothalamus and pituitary glands. As in females, GNRH produced by the hypothalamus of males stimulates the pituitary. If we inject GNRH-A into the body of males, the antibodies produced result in the deactivation of the GNRH when it is released by the hypothalamus. Without GNRH, the pituitary in males does not to release hormones that stimulate the testes to produce sperm and testosterone. Thus we achieve contraception by preventing the development of sperm.

In reality, contraception is not easily achieved through the immune system. If we think about the biology a little more in depth, we realize that we are immunizing against proteins naturally found within the body. The immune system has evolved to carefully distinguish between foreign proteins and those that occur naturally in the body, and attack only the foreign proteins. To get the immune system to attack a protein that occurs naturally in the body requires that we hyper stimulate the immune system. As with tetanus, we can increase the antibody levels with booster shots. Use of PZP requires two shots in the first year and at least one shot, annually. Further, to reach the high levels of antibodies necessary, the PZP or GNRH-A must be combined with an adjuvant.[3] An adjuvant is a protein that causes exceptional stimulation of immune system. Currently, only Freund's adjuvant is authorized by the Food and Drug Administration for experimental use with PZP in free-ranging (i.e., not captive) deer populations.

Veterinarians are uncomfortable with the use of Freund's adjuvant. First, Freund's adjuvant is such a potent stimulant that it sometimes causes localized infection in the animal. The infection is short lived, but it would be better for the animal if no infection occurred. Second, Freund's adjuvant causes treated animals to test positive for tuberculosis. Animals treated with Freund's adjuvant do not contract tuberculosis, but cross react in medical tests. Tuberculosis in wild populations poses a significant health hazard to the livestock industry, so it is important to be able to monitor effectively. The false-positive reaction of animals treated with Freunds adds uncertainty to monitoring for tuberculosis and is

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3 *See id.*

therefore detrimental. Experimentation now underway is in New York and elsewhere is exploring alternative adjuvants.

To deliver PZP or GNRH-A to deer, we create a vaccine by combining the PZP or GNRH with Freund's adjuvant and load the mixture into a dart. The dart contains a syringe which injects the vaccine. We shoot that dart from a specially-designed rifle into the large muscle mass of the hip of the deer. In captivity, these techniques are highly effective. Experimentation is now underway to determine how effective the approach will be in populations of free-ranging deer.

How many females must be treated with contraception?

To answer this question, we begin by examining the control of populations using the traditional technique of removing females. Understanding the conceptual basis for removal as an approach for managing deer populations provides a good foundation for discussions about contraception.

When we remove animals from population we generally mean removing them by hunting, or by culling (i.e., removal over bait by sharpshooters). We know that a population of adults will produce fawns and at least some of those fawns will survive to reach sexual maturity. Biologists use the term *recruitment* to characterize those fawns that survive to sexual maturity.[4] We also know that there will be some mortality each year among adults in the population. If recruitment is greater than mortality during the year, the population will grow.

Suppose our management goal is to hold the population constant. There are three basic questions that must be answered to hold a population constant: (1) How many fawns are going to be recruited into the population? (2) How many adults will be lost from the population through mortality? (3) How many additional adults we

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4 *See* D.R. MCCULLOUGH, THE GEORGE RESERVE DEER HERD (1979).

will need to remove from the population to balance recruitment and loss? Superficially, this calculation is a simple subtraction.

The calculation is actually more complicated because recruitment varies depending on the abundance and nutritional condition of the adult females in the population. Assume for a moment that there is no mortality in a population. If our population has one female and she produces two fawns (i.e., the average litter for white-tailed deer), the population can increase from one to three. However, if the population has three females, the increase will be from three to nine (three adults plus six recruits). Notice that adding females to the population accelerates the rate at which the population grows.

Population growth cannot accelerate forever because nutritional limitations affect reproduction. Each new individual added to the population requires nutrition to grow to adult size and to accumulate the energy reserves (fat) to reproduce. If we think of the nutrition provided by the environment as food resources, then we can understand that there is a maximum limit to the number of deer an given locale can support. A population can grow only until it reaches the point that deer are consuming all of the food produced. This limit is known as ecological carrying capacity.

However, long before the population approaches the limit, competition for food resources increases. Some individuals are less able to compete and their nutritional condition declines. When nutrition declines enough that some females can no longer accumulate sufficient fat reserves, the estrous cycle will not occur at all. If nutrition declines further, some deer begin to die of malnutrition. The consequence of reduced reproduction and increased mortality is a decline in the rate of growth in the population.[5] At ecological carrying capacity, the recruitment of young is just sufficient to offset the mortality occurring each year.

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[5] *See* L.J. Verme & D. E. Ullrey, *Physiology and Nutrition, in* ECOLOGY AND MANAGEMENT OF WHITE-TAILED DEER 91-118 (L.K. Halls, ed., 1984).

Biologists generalize the relationship between deer abundance and recruitment graphically as a parabola known as the recruitment curve (Figure 4).[6] At the extreme right of the curve is ecological carrying capacity. The importance of this parabola lies in its ability to predict the number of fawns that a population of a given size will produce. We use the parabola to determine how many adults we must expect to die or be removed from the population to equal the number of fawns being added to the population.

There are two important points to remember about this recruitment-abundance relationship. First, the recruitment curve represents the number of *females* that are recruited. Growth in the deer population is dependent on the number and nutritional condition of the females, not males. Deer are polygamous, so the number of males in the population will affect reproduction only if the sex ratio is highly skewed (less than one male for 50 females will still result in all females being bred). Second, the recruitment curve is specific to each locale as set by the food resources of that locale. Food resources are generally considered to be those that naturally occur, but supplemental feeding often occurs in suburban communities. People concerned for the welfare of deer during the winter provide corn and other foods to supplement the natural browse. The effect of supplementally feeding a deer population is to change the recruitment curve. The increased food increases the ecological carrying capacity, thus pushing the endpoint of recruitment curve to the right (to a higher abundance).

The application of curve is best illustrated by example. Suppose that we census every year and define all deer as adults on January 1. Suppose we have a recruitment curve (Figure 5) that predicts that population of 400 adult females will recruit 200 new fawn females into the population by next January 1. If we want that January 1 population to be 400, we will need to ensure that 200 females are removed to accommodate the fawns being added.

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6 *See* MCCULLOUGH, *supra* note 4.

An interesting characteristic of this parabola is that even at 600 or 200, the number of female fawns that are recruited in the population is 100. At a population of 200, recruitment is limited by the low number of females in the population; at a population of 600 females recruitment is limited by poorer nutritional condition of many of the females. This characteristic is important because it means that we can manage a deer population either at a very high level (600 deer) or a very low level (200 deer) by removing the same number of adults (100).

Our work in Irondequoit, a suburb of Rochester, New York, shows that this fictitious scenario is plausible.[7] Data collected on population abundance, nutritional condition and reproductive success of females in Irondequoit over five years provides a way of calibrating the recruitment curve. In Irondequoit, a population goal of either 250 deer or 601 requires removal 108 deer each year by sharpshooting, or hunting (Table 1).[8]

Although we can use the same conceptual approach to determine the number of deer to treat with contraception, we cannot use these same numbers. The calculations for Irondequoit show that applying contraception to a population 600 deer requires almost twice the number of females involved as contraception to hold the population constant at 250 (Table 1). Why is there such a difference?

A simple example illustrates the reason for the discrepancy in contraception versus removal. Suppose we have a deer population that we want to hold at 4. All 4 adult females survive throughout the year and recruitment adds 4 females during the year. If we use contraception, how many adult females do we have to vaccinate in order to hold the population absolutely at 4? Obviously, we need to

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7 C.K. Nielsen, et al., *An Adaptive Management Approach to Controlling Deer in Urban Environments*, 25 WILDLIFE SOC'Y BULL. 470-477 (1997).

8 We assume that dispersal of deer out of the town is exactly offset by dispersal of deer into the town and that all other mortality is documented. Almost all other mortality is deer killed in accidents with automobiles and by documenting the mortality carefully, we can make appropriate adjustments to the removal quota.

treat every one of the adult females because, with all adults surviving, we can afford no fawns being recruited into this population.

Now suppose that instead of contraception, we remove animals before they give birth. How many animals do we have to remove? We have to remove just two. We can then allow the remaining two to produce fawns. Thus, the number of animals involved in our management has been reduced by half because we remove them before they have a chance to produce fawns. Running these calculations for many different population sizes in Irondequoit shows that as the number of females in a population grows, the percentage of the females that must be treated increases. At high populations, we need to treat a higher percentage of the population than at low populations.

How do we estimate the cost of applying contraception?

Cost depends on the effort required to treat a single deer and the total number of deer that must be treated. Effort required to manage a free-ranging population of deer is largely unknown. Studies are now ongoing, but until the results are available, we must resort to estimates derived from hunting and sharpshooting.[9] The amount of effort that we must invest in treating each deer varies with deer abundance (Figure 6). An apt metaphor is finding needles in a haystack. If we have a haystack containing many needles, the amount of time we will spend finding those needles is relatively small. However, if there are few needles in the haystack, we will invest much more time finding them. Thus, the cost of managing the population will grow as the population declines. Our work in Irondequoit provides a preliminary estimate of the relationship between deer abundance and effort.

Research has yet to provide solid information on this relationship. As portrayed in Figure 6, the relationship is a straight line. This is the simplest hypothesis and in the absence of more

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9 Nielsen, *supra* note 7.

experience, it provides the most reasonable representation of the relationship. However, the experiments now underway in Irondequoit and elsewhere may show that the relationship is not linear. Effort could increase disproportionately as populations change. Obviously, knowing the relationship between deer abundance and treatment effort is important to estimating costs.

We can get a preliminary estimate of effort using the best information available. In Irondequoit, we estimated the number of hours it would take to do removal versus contraception if the goal was to hold the population at either 257, a low level, or 601, a high level. The effort to remove animals at 257 is about twice the effort it would to remove 108 animals at 601 (Table 2). The increased effort is a product of the three factors discussed above. The first factor is population abundance. Finding 108 deer in a population of 601 requires less time than finding 108 deer in a population of 257. The second factor is the treatment effect. Contraception requires vaccination of more females than would need to be removed. The third factor is technology. Current immunocontraception technology requires that we dart all females twice in the first year, and perhaps in all subsequent years. Removing deer requires a single encounter.

The cost of managing deer in suburban environments will be significantly different from the cost of tradition management on rural landscapes and will require detailed information about the deer population. Traditional management generates revenue for the public through license sales and excise taxes on guns and ammunition. Contraception will generate costs because professionals will need to be hired to conduct the treatment. Because all costs are scrutinized closely by town boards, there will be strong incentive to maximize the efficiency of treating a deer population. Efficiency will require detailed information about the population. We will need to know deer abundance and recruitment rates with high precision because the difference in cost of treat 100 deer versus 200 will be substantial.

The foundation for management will be the recruitment curve. We will need to calibrate the curve. It takes two points to calibrate that curve, the peak and the limit to population abundance.

Irondequoit has accomplished this calibration over a five-year span by conducting annual population counts and collecting reproductive information from females removed through the bait and shoot program. Experiments now underway are focusing on calibrating the effort relationship. Better information will require greater initial investment, but will reduce costs of management Ultimately, we will have to optimize the cost of the information gathering and management actions.

Summary

Immunocontraception may provide a cost-effective alternative to traditional forms of population management for deer. By creating antibodies to proteins on the egg of a deer, or to reproductive hormones, we can prevent conception. Clinical trials show this approach can be highly effective. Experiments with free-ranging populations are now underway, but results are not yet available. Effective application of immunocontraceptive will entail gathering information about the abundance and recruitment rates of the population. The effort required to control growth of a population will depend on the desired level of abundance and the method of control. When decisions are made about the optimal level for the deer population, cost will need to be a factor in those decisions. At present, the costs of managing deer in urban environments are uncertain.

Acknowledgments

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Appendix

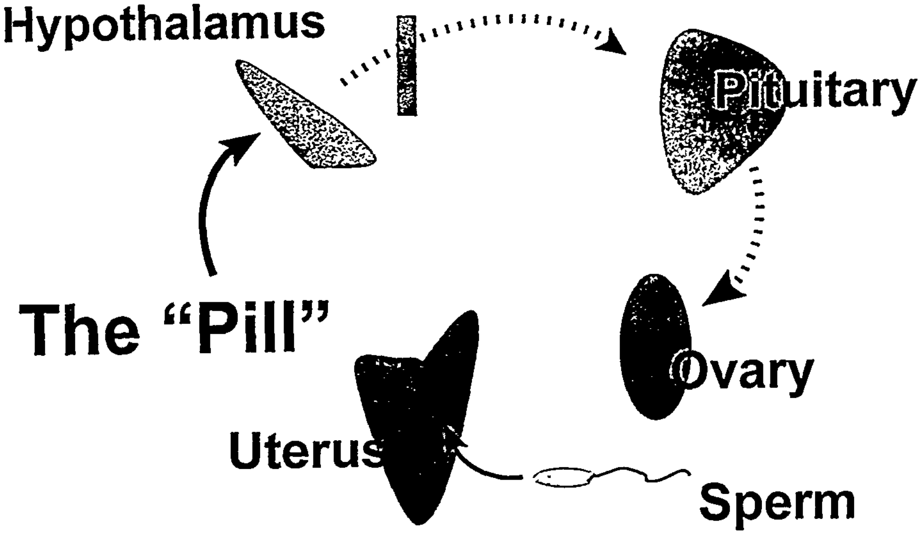

Figure 1. Organs and hormone cascade of the mammalian reproductive system. In humans, the "Pill" introduces hormones that simulate pregnancy, signaling the hypothalamus to stop production of Gonadotrophin releasing hormone. As a consequence, the pituitary gland does not release hormones that cause the release of eggs from the ovary. Conception is prevented because no eggs reach the uterus.

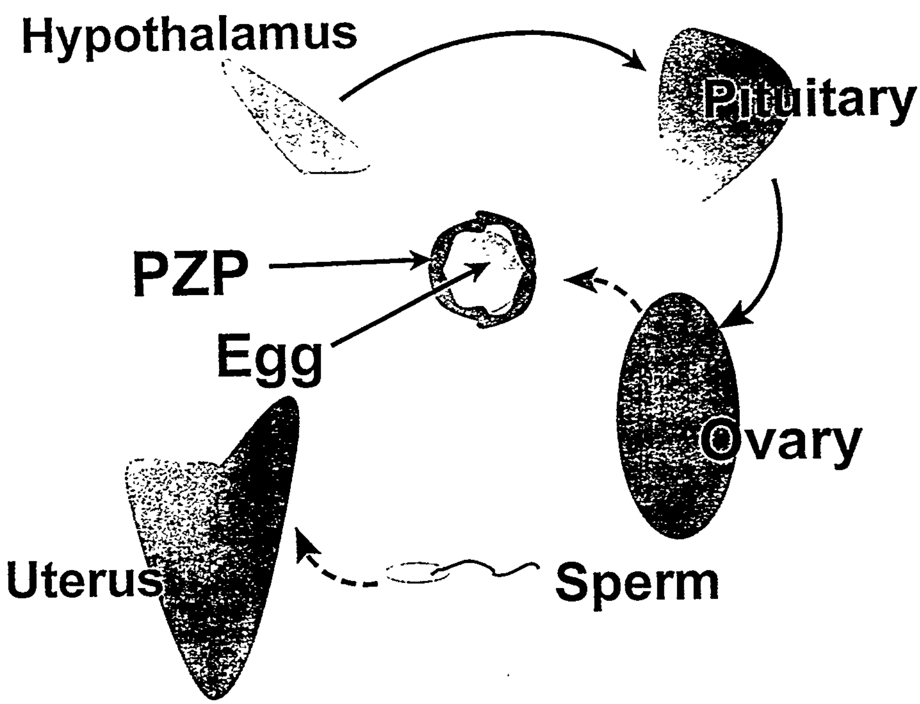

Figure 2. Action of antibodies to Porcine Zona Pellucida (PZP) causes the immune system to attack eggs as soon as they are released from the ovary. Conception is prevented because a viable egg does not reach the uterus.

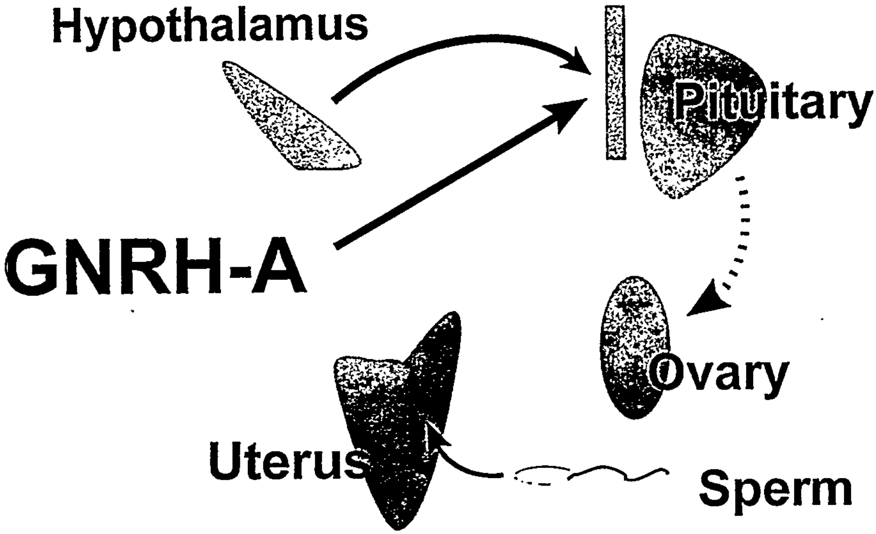

Figure 3. Action of antibodies to Gonadotrophin Releasing Hormone (GNRH-A). The development of antibodies to GNRH-A prevents the hypothalamus from stimulating the pituitary gland. Pregnancy is prevented because the estrous cycle is halted. Vaccination of males with GNRH-A has the same effect on the pituitary and prevents production of sperm and testosterone.

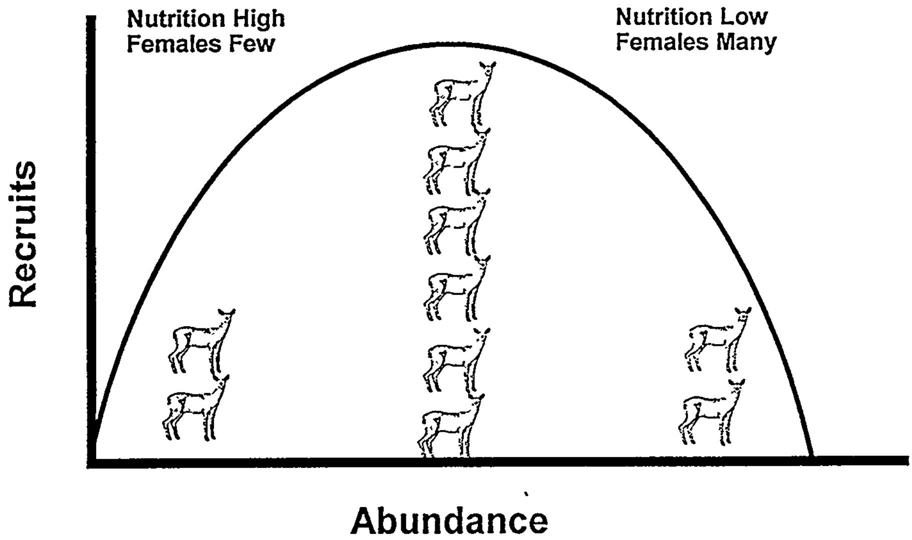

Figure 4. The recruitment curve for deer depicting the relationship between number of young added to the population each year and the abundance of sexually mature females in the population. Numbers of young added to the population are limited at low abundance by low numbers of mature females. Numbers of young added to the population are limited at high abundance because nutritional condition of females is low. The point at the extreme right on the curve is an approximation of ecological carrying capacity.

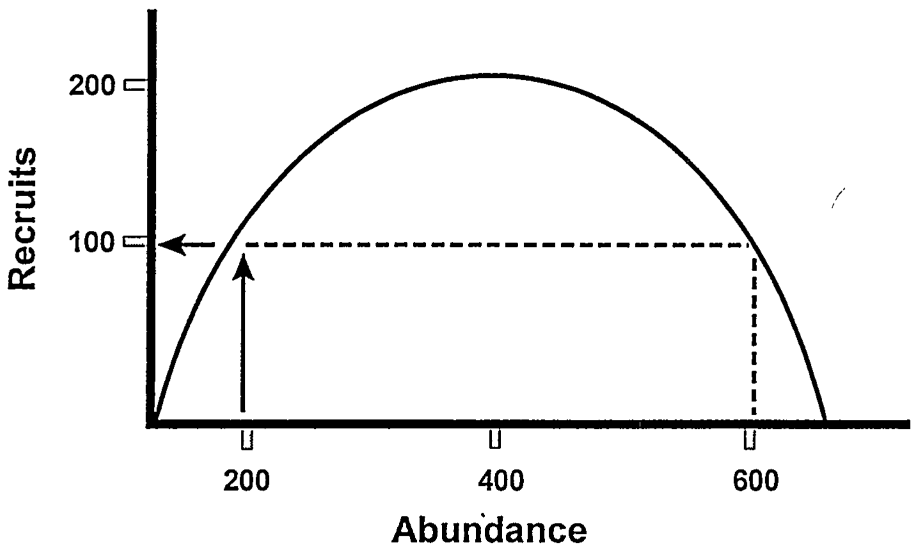

Figure 5. Recruitment curve showing that numbers of young recruited (added to the population) is the same for two levels across the parabola.

Numbers of Deer to Manage

Pop'n Goal	Remove	Contracept
257	108	136
601	108	234

Table 1. Comparison of the numbers of deer in a population that must be removed versus treated with contraceptive vaccine each year to maintain a constant population of 257 or 601. Numbers are derived from studies in Irondequoit, New York.[10]

10 Nielsen *supra* note 7.

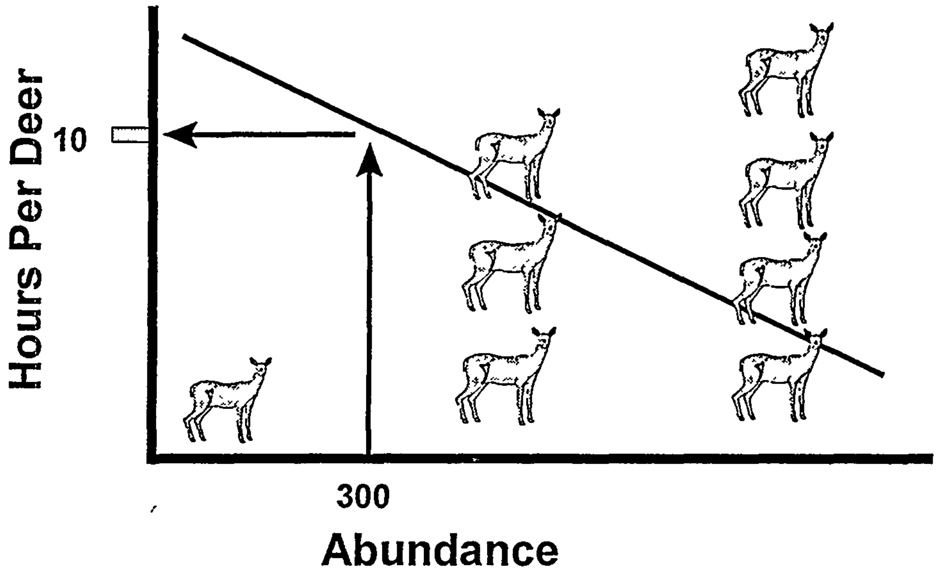

Figure 6. Relationship between effort expended to remove or treat each deer and abundance of deer in the population. As the abundance declines, effort per deer increases.

Hours Per Year to Manage

Pop'n Goal	Remove	Contracept
257	1,064	2,253
601	545	2,697

Table 2. Comparison of effort (hours per deer) to maintain a deer population at constant level of abundance using removal (by sharpshooting) versus treatment with contraceptive vaccine. Numbers are derived from studies in Irondequoit, New York, and elsewhere.[11]

11 Nielsen *supra* note 7.