ANTIFERTILITY AGENTS IN VERTEBRATE PEST CONTROL

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There is an increasing need for new means of population control from the simplest organisms up to the larger mammalian species (include man if you wish.) A number of interesting and promising leads, such as environmental manipulation, introduction of predators, diseases, parasites, etc., and particularly antifertility agents, have been proposed for some time, but research into the latter approach in mammal control is quite recent and limited. The use of toxic agents has long been the principal method of vertebrate population control, but the potential for the use of antifertility agents to suppress reproduction may provide an important advancement.

I wish I could tell you that all we have to do is to develop or discover the right antifertility agent and we have the problem solved. Unfortunately this is far from the truth.

Based on present knowledge of antifertility agents in vertebrate pest control, it appears that we will need a variety of agents and even more important, a wide variety of techniques of application plus the detailed knowledge of proper timing, dosage, and dispersal of bait for effective results. In many instances, the problems of application far outweigh the development of a suitable drug.

At present it appears that the greatest potential lies with animals that breed once a year and secondly with birds such as pigeons. When it comes to rodents, a major problem arises; a temporary antifertility agent will have to be continuously available to block reproduction throughout the year or else permanent sterility agents wi11 be needed which are apt to be so toxic they provide little advantage over a poison.

I do not wish to be pessimistic; I merely want to point out some of the problems that exist in trying to develop antifertility agents for use in animal control. At present there is only a limited amount of work being done on such compounds for use in vertebrate pest control. Dr. Wetherbee of the Bureau of Sport Fisheries and Wildlife at the University of Massachusetts is carrying on a screening program for antifertility agents in birds. As far as I know now, other investigations involving vertebrate species are at present limited to work on foxes under the National Institute of Health grant to the New York State Conservation Department and Cornell University. However, as rapidly as the opportunity arises, the Denver Wildlife Research Center plans to pursue this line of research on other species.

Another new approach we are investigating is the use of anti-metabolites. These are chemicals or drugs that interfere with or antagonize normal metabolic or physiological processes. The approach here is to determine weak points in the animals' physiology and design or locate a chemical to block or interfere with a specific metabolic function. In this manner we hope to obtain control agents that are specific for certain species.

We know so little about the application of antifertility agents to most vertebrate pest species that I am going to limit the rest of my discussion to our work with antifertility agents in coyote control. Many of the species with which we deal are those which are the most adaptable to our civilization. The coyote, for example, has increased in numbers in recent years, and has spread its range considerably over the last two decades. Its howls have been reported to have drowned out a soprano at a concert at the Hollywood Bowl. Young coyotes have been reared under the screen of a drive-in theatre and in highway culverts. These incidents indicate their adaptability, but their major negative values stem from economic losses to the livestock industry.

Predator control can be of two types: (1) elimination of individual animals causing damage, and (2) general population reduction where frequency of animals causing damage is high. Current control methods rely mainly on the use of the steel trap, coyote-getters (cyanide gun), 1080 bait stations, and strychnine drop baits along with some den hunting and aerial hunting. Most of these methods have lost much of their original effectiveness because of necessary restrictions placed on their use to maintain safety in control operations.

Our primary objective is to develop safe, selective, effective, and acceptable methods of alleviating damage by certain species of wildlife. When reduction of populations is called for, a logical first approach is to find a means of suppressing reproduction rather than attempt to increase mortality rates. Reproduction is the only force that can overcome all mortality factors operating against a species. Suppressing reproduction will cause the population to decrease as surely as increasing one or more mortality factors.

The advantages of suppressing reproduction are:

1. It may be more practical to prevent animals from being born than to reduce their numbers after they are partially or fully grown and established in a secure environment.

2. Increasing one or more mortality factors often results in a compensating increase in reproduction or survival or both. This reduces the effectiveness of any control program. By suppressing reproduction, the compensating increase in reproduction may be overcome, while survival may be increased in the remnant population.

3. Movement or ingress which occurs when animals are removed from a population may be lessened by occupation of territories by treated adult coyotes.

4. Nontoxic antifertility agents are safer to use than existing lethal agents and devices and likely would be more readily accepted by the public. This could result in more effective population control in areas where the use of lethal techniques is now restricted.

In order to test this theory and develop the means of application to nuisance mammal populations, with the coyote as our initial target species, the problem was divided into two phases: First, the search for and selection

of suitable reproductive inhibitors or antifertility agents; second, the development of successful techniques of oral application to a wild population.

There are a number of approaches to blocking reproduction. The potential points of attack are, in the female:

1. Suppression of the anterior pituitary secretion of gonadotrophins.

2. Prevention of follicle development and maturation.

3. Blocking the passage of ova in the oviduct.

4. Prevention of fertilization.

5. Prevention of implantation.

6. Interference with gestation.

And in the male:

1. Suppression or interference with secretion of gonadotrophins.

2. Inhibition of spermatogenesis at one of the five stages.

3. Interference during transport and storage of sperm.

Since each species or group of species offers special problems, the following requirements for a suitable antifertility agent in predator control were established.

1. Preferably the agent should be effective in a single oral dose on either or both sexes at one or more of several vulnerable stages of reproduction.

2. There should be a wide margin of safety between the effective and lethal dose to preclude the chance of any animal picking up a lethal dose.

3. It should be relatively stable, inexpensive, and effective in doses under 500 mg for practical field application.

4. It should be relatively tasteless, odorless, or capable of being masked so it will not cause aversion to baits. Acceptance without side effects, such as nausea, is important for the same reason.

5. The sterility effect should be temporary, for one breeding season or one year, depending on the animal's breeding habits. Suppression of reproduction can then be applied or withdrawn at will without permanently affecting either the target species or other species that may be exposed.

A review of antifertility compounds under current investigation and the meager information available on reproductive physiology of the coyote indicate that the best approach was to upset the hormone balance in the female by oral administration of a synthetic estrogen, diethylstilbestrol. This drug comes closest to meeting the requirements previously stated.

It was our desire to suppress reproduction by blocking ovulation. Penned experiments were set up with wild-caught coyotes dosed at various stages and attempts were made to breed them. We have been unsuccessful in breeding wild coyotes (either drugged or control animals) in captivity, but have had them ovulate after drug administration. Due to the difficulty of breeding coyotes in captivity, future penned animal experiments will be run with dogs.

With captured, bred coyotes, pregnancy was terminated through the first half of gestation with a single 100 mg oral dose. This indicated that stilbestrol may be most effective during or just after mating.

Several features of coyote reproduction are in our favor. First, the coyote is monoestrus, breeding only once a year. Second, both males and females are fertile only during a period extending from February through April. Successful treatment during this period will block the entire year's population increase.

One limiting factor is that reproduction in the wild is spread over a sufficient period of time among individuals that application of an agent effective at short, critical periods such as ovum transport, fertilization, implantation, etc., means that only a small proportion of females would be affected at any one time. Therefore, the periods of follicle development and gestation offer the widest opportunity to obtain the greatest coverage of the breeding population.

Concerning the effect of diethylstilbestrol on males, a single oral dose did not block spermatogenesis. However, the literature indicates that repeated oral doses will. Many of the new human antifertility agents effective in repeated dosages would also likely work, but the application problems make them impractical at this time, hence the requirement for a single dose.

Recent developments in England indicate that certain alkylating agents such as isopropyl methane sulphonate may be effective in causing male sterility for a sufficient period of time when given in a single oral dose. We plan to start penned tests on these new agents this fall, while continuing field trials with stilbestrol during the breeding season.

After it was found that pregnancy was blocked or terminated by a single 100 mg oral dose in penned animals, a field trials was initiated in the spring of 1963 to determine the problems in application and to obtain a greater quantity of information than was possible in penned experiments.

A 20-township area in New Mexico was selected for treatment with a reference area 25 miles distant. Five thousand one-half ounce tallow drop baits, each containing 100 mg of stilbestrol, were placed wherever coyote sign was found. The time of baiting was immediately after the estimated peak of breeding, March 5 to 15. A check of bait stations on travel ways indicated moderate acceptance, but obliteration of sign by sandstorms prevented accurate readings. A spot check of bait stations near major waterholes indicated coyotes cleaned up nearly all the baits.

After a delay of 3 weeks to allow the drug to take effect, recovery of specimens was started. Of 142 coyotes taken during April and May on the

treated area, 74 animals were saved to determine effect of the treatment on reproduction. Of these 74 specimens, 37 were females. Only 4 adults of 20 in breeding status had viable embryos. The remaining 16 adult females were either in various stages of resorbtion, had pseudodecidual casts, or showed no embryos, yet had corpora lutea indicating ovulation had occurred. Of 21 females taken from the reference area, 13 out of 13 females in breeding condition had either viable embryos or had whelped, while I was in estrus and 7 were barren. The results are illustrated in the following table.

TABLE 1. Reproductive success of female specimens.

	Treated area	Reference area
No. female specimens	37	21
No. nonbreeding	17*	7*
No. females breeding condition	20	
	13	
No. females in estrus	0	
1		
Successful breeding females	4	13
Unsuccessful breeding females	16	0
Percent of breeding females that were Successful	20	100

*Predominantly juvenile females that had not reached sexual maturity.

A subsequent check of the treated area in the fall revealed that pup sign or tracks were missing from all but 5 of 22 watering sites on the treated area. A check of watering sites off the treated area resulted in finding pup sign at all sites but one which was on the border of the treated area.

The field trial conducted last spring indicated that failure of reproduction was associated with the treatment.

More extensive field trials are now underway. In the past month we have initiated one field test in Idaho and four in New Mexico, totaling approximately 190 townships.

We also plan to confirm the results on other species. At this time, there is every indication from literature on foxes, mink, rabbits, mice, and cattle that these species can be affected. Selectivity is accomplished by type of bait carrier, dosage, timing of application, and location of baits rather than by the drug.

We are only in the preliminary phases of this work on one species, the coyote. While we are encouraged by initial results, it is still too early to determine whether it can be used as an effective control methods agent.