ECOLOGICAL CHALLENGES TO CONTROLLING WILD RABBITS IN AUSTRALIA USING VIRALLY-VECTORED IMMUNOCONTRACEPTION

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ABSTRACT: The European wild rabbit in Australia threatens the sustainability of agriculture and conservation of native flora and fauna. Improved means of reducing these impacts are sought including effort to develop virally vectored immunocontraception (VVIC). VVIC for the wild rabbit involves complex interactions between the rabbit, myxoma virus and insect vectors of the virus. Development of the method includes not only reproductive molecular biology and genetics and manipulation of virus genetics, but also many problems in reproductive biology, ecology and population dynamics of the rabbit in diverse environments. Furthermore, epidemiology of enzootic myxomatosis, and behavior and population dynamics of several vector species of mosquito and flea must be considered. Some of these ecological problems are described with a brief description of the approach to experimental analysis.

KEY WORDS: vertebrate pest control, biological control, immunocontraception, *Oryctolagus cuniculus*, myxoma virus, insect vectors, ecology, models

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INTRODUCTION

Virally vectored immunocontraception (VVIC) is a new theoretical concept that is aimed at managing the abundance of often inaccessible wild animal populations by interfering with their fertility and fecundity (Tyndale-Biscoe 1994b). Currently an attempt is being made to develop the concept for managing three introduced vertebrate pests of Australia, the European wild rabbit (*Oryctolagus cuniculus*), the European red fox (*Vulpes vulpes*), and the house mouse (*Mus domesticus*) (Tyndale-Biscoe 1994a). VVIC, as applied to the European wild rabbit in Australia, involves interactions among the rabbit, the myxoma virus that infects rabbits, and several species of insects that are vectors of myxoma virus. Some ecological problems are envisaged in attempting to develop this concept. This paper describes those challenges and the approach taken in attempting to assess their relevance and magnitude. Before discussing those problems, the author briefly describes aspects of the problem and ecology of the wild rabbit in Australia, its pathogenic myxoma virus, and the main insect vectors of myxoma virus.

THE EUROPEAN WILD RABBIT IN AUSTRALIA

The European wild rabbit was introduced successfully to Geelong near Melbourne in 1859 for sport hunting. It spread rapidly and occupied its present range, the southern two-thirds of the continent, within about 50 years (Stodart and Parer 1988). This country is vast and much of it is arid or semi-arid, sparsely settled, and remote from urban infrastructure. The rabbit occupies most environments within that range, from sub-alpine humid to sub-tropical and temperate humid to lowland arid. Habitats occupied range from woodland to grassland and sandy dune. Mediterranean climates are its stronghold, but it also abounds in arid regions of erratic unpredictable rainfall, and it has a tendency to be limited by predominant summer rainfall.

Over most of that range the rabbit can increase seasonally to very high densities which have a severe impact on the native vegetation and fauna, and cause significant losses to agricultural production and sustainability (Williams et al. 1995). Historically, the density of rabbits and their impact was extreme over most of the distribution, but the introduction of the myxoma virus in 1950 diminished the problem significantly for the more mesic coastal regions. Nevertheless, the rabbit problem remains extreme in the inland semi-arid and arid regions (Williams et al. 1995). There myxomatosis occurs irregularly and infrequently because of the inadequate and variable abundance of mosquito and flea vectors, and the long interval between episodes of rabbit breeding (Cooke 1984). In the mesic and more intensively settled areas the rabbit is managed by control programs that employ mainly poisoning, warren-ripping by tractor, and toxic fumigation of warrens (Williams and Moore 1995). In the arid and semi-arid regions little active control is undertaken. Rabbit populations undergo irregular cycles of "boom and bust" driven largely by weather and occasional myxomatosis epizootics (Williams et al. 1995). Since October 1995, rabbit calicivirus disease (RCD) has caused very high mortality of rabbits in some parts of the arid and semi-arid interior; its long-term role is not known yet (B. D. Cooke, pers. comm.).

MYXOMATOSIS IN AUSTRALIA

Myxoma is a South American virus that seems to be specific to Leporids (Fenner and Ratcliffe 1965). In Australia, myxoma virus spread throughout the rabbit distribution within two years of its introduction in 1950, myxomatosis killing more than 99% of the infected rabbits and decimating local populations (Fenner and Ratcliffe 1965). Within two years attenuated myxoma strains emerged and death rates declined to slightly lower levels. Attenuation of the virus enabled the rabbits to develop a degree of genetic resistance to the virus. The virus and rabbit co-evolved to an accommodation of viral virulence and host resistance whereby most virus strains in the field were assessed to be of moderate virulence and most populations of rabbits had some degree of resistance, with wide variation between regional

populations (Fenner and Ratcliffe 1965). Later work has shown that recently most field viral strains are highly virulent, but the increased resistance of the rabbits (Parer et al. 1994) results in only moderate, but nevertheless very significant, levels of mortality (Parer et al. 1985). Thus, myxomatosis still exerts a strong controlling influence on rabbits in mesic regions.

VECTORS OF MYXOMATOSIS IN AUSTRALIA

Initially the main vectors transmitting myxomatosis among rabbits were two native species of mosquito, although many other species of biting invertebrates played a minor role in its spread (Fenner and Ratcliffe 1965). The dependence of the mosquitoes on rather high rainfall limited the extent and frequency of transmission of the disease. This prompted the search for a more reliable vector and led to the subsequent introduction of the European rabbit flea in 1969 (Sobey and Conolly 1971). This vector seems to have reduced rabbit numbers significantly in mesic coastal regions but not in arid areas. The European rabbit flea cannot persist where rainfall averages less than about 200 mm per year and where dry conditions may deter rabbits from breeding for several years (Cooke 1984). This species of flea desiccates readily (Cooke 1990a) and its breeding cycle depends on that of the rabbit, specifically the female rabbit's reproductive hormones, nesting behavior and the presence of nestling rabbits for food for larval fleas (Mead-Briggs 1964).

In order to provide a vector of myxomatosis in arid regions, another flea vector of myxomatosis, the Spanish rabbit flea (*Xenopsylla cunicularis* Smit), was released in the interior in 1993. This species is adapted to arid conditions and does not depend on rabbits breeding for its own reproduction (Cooke 1990b). Drought followed its introduction, limiting the opportunity for spread of the flea with dispersing young rabbits and for transmission of myxomatosis among the susceptible young. The recent spread of RCD among rabbits in the arid region also might impede the spread of this vector. Therefore, the likely future role of the Spanish rabbit flea as a vector of myxomatosis and RCD remains to be assessed.

THE CONCEPT OF VIRALLY VECTORED IMMUNOCONTRACEPTION (VVIC)

Because the wild rabbit remains a serious pest of agriculture and continues to devastate flora, fauna and landscape, further control methods and improved strategies are sought to integrate with the biological and conventional control methods and strategies applied currently (Williams et al. 1995). Now it is being attempting to exploit further the penetration of rabbit populations by myxoma virus, and to render infertile those rabbits that survive myxomatosis.

The concept of immunological suppression of fertility arose during the 1980s in research on humans and in related clinical research (Robinson and Holland 1995). Research on animal vaccines developed several attenuated recombinant viruses that delivered reproductive antigens via inoculation or bait but did not replicate in the host species (Kerr and Jackson 1995). Also in the 1980s, other research aimed at manipulating the genetic constitution of myxoma virus in order to modify the severity of myxomatosis in the European wild rabbit.

Late in the decade the three concepts, immunological suppression of fertility, viral delivery of genetic information, and contagious spread of the genetic information through widely dispersed and inaccessible pest populations, were combined. Research in Australia began to develop virally vectored immunocontraception (VVIC) for the European wild rabbit, the European red fox and subsequently the house mouse (Tyndale-Biscoe 1994a).

The concept of VVIC involves: 1) identification of one or more reproductive proteins that are essential to the processes of fertilization, e.g., proteins on the surface of the sperm or ova, or proteins essential for embryo implantation; 2) identifying the gene that codes for the proteins and cloning them; 3) inserting the cloned genes into an appropriate intergenic site of a suitable infectious virus, together with any necessary cloned promoter genes; 4) infection of the host by the modified virus and initiation in the host of an immune (antibody) response to the virus and to the reproductive proteins (antigens) encoded in the infecting virus and produced during viral replication; and 5) attachment of the circulating antibodies to the specific reproductive proteins of the host, as well as to the reproductive proteins of viral origin, so that the normal processes of reproduction, fertilization or implantation, whichever was targeted, can no longer function. Theoretically, the infected host can no longer breed.

Thus, the theoretical concept of VVIC seems a very attractive potential technique for reducing rabbit abundance and impact over extensive areas of Australia (Tyndale-Biscoe 1994b; Holland and Jackson 1994). It seems to have advantages over hormonal and chemical methods of manipulating fertility which currently tend to be limited and localized in effectiveness (Bomford 1990). A potential advantage might be the retention of hormonal integrity and any social behavior that suppresses reproduction of conspecifics (Bomford 1990; Tyndale-Biscoe 1994b). However, the life history and mating system of the pest species must be suitable for fertility control or undesired outcomes may result (Caughley, Pech and Grice 1992).

Several potential variations of the concept can be chosen to match the problem and reduce any risks associated with the solution. These include bait delivery of encapsulated reproductive antigens, or use of recombinant bacteria which may be non-infectious or contagious. For example, the intent for the fox has been modified to bait delivery in the first instance (Bradley 1994).

The main potential advantages of this family of concepts are: 1) humane control of pest species; reduced fecundity may result in fewer individuals to suffer control action, drought or other diseases; 2) a capability of affecting individuals remotely and over extensive inaccessible areas; 3) cheap control of highly fecund pests; 4) species specificity and no non-target impact; and 5) non-polluting methodology.

The attractiveness of these potential advantages should not eclipse our perception of the difficulties involved in

developing the concept to reality. There are many challenges in the fields of reproductive molecular biology, immunology, molecular virology, epidemiology and ecology. Questions of social and ethical concern (Tyndale-Biscoe 1995) will not be addressed here.

CONSTRAINTS ON THE FORM OF VVIC

Biological constraints in anatomy, physiology, biochemistry, and immunology of the pest species, and genetics of the viral agent will dictate what is possible in VVIC. These functional traits will influence the initiation of an immune response, and its intensity and maintenance, either to self or non-self reproductive antigens, and whether VVIC can function via males, females or both.

Social and ethical issues will impinge on what is acceptable or not in VVIC, and what the design of the infertility agent should aim for, and how it is applied. Clearly VVIC must affect only the species intended, not any non-target species. This requirement will limit the choice of antigens to those that are either specific to the pest species, or induce an immune response only in the pest species. Other species-specifying strategies include the host-range of the virus carrying the sterility agent, and the specificity of any insect vectors that deliver the virus to the host pest species. Another social-ethical issue is the humaneness of the infection caused by the chosen viral agent and the humaneness of the immune response to the reproductive antigen. The form of the VVIC agent will influence the nature and difficulty of the ecological problems that must be overcome also. The choice of myxoma virus for VVIC in the European wild rabbit in Australia clarifies some of these issues (Holland and Jackson 1994; Kerr and Jackson 1995) but many remain uncertain.

THE NATURE OF THE INFERTILITY CAUSED BY MYXOMA VECTORED IMMUNOCONTRACEPTION (MVIC)

It will not be known whether males and females or either can be rendered infertile until antigens have been selected, inserted into the myxoma virus, and shown to induce infertility successfully in wild rabbits. MVIC could focus on causing dysfunction in a number of ways, such as preventing fertilization or implantation, although fertilization is preferred on the grounds of humaneness. While MVIC targets fertilization, infertility of the female is all that is required, and this might be achieved through viral presentation of the antigens of either ovum or sperm to females. Presentation of sperm antigens to female rabbits may be advantageous if males also react to them. If we assume random mating, and the probability of a mating female being infertile is p, and the probability of infertility of a mating male is q, then the probability of a mating being fertile is: $(1 - p)(1 - q) = 1 - p - q + pq$ and the probability of a mating being infertile is: $1 - (1 - p - q + pq) = p + q - pq$. However, it is possible that the testes of rabbits may be protected immunologically (viz. Holland and Jackson 1994), either partially or wholly. If males cannot be rendered infertile and immunocontraception can be effected only through females, then $q = 0$, and the probability of an infertile mating is less, being only p. This demonstrates a potential advantage of using sperm antigens for MVIC, if possible, either alone or in addition to ovum antigens.

Individuals may vary in their susceptibility to VVIC, possibly because of variation in recognition of the reproductive antigens or epitopes, or in the intensity of the immune response induced. The variation could be as extreme as some individuals failing to react while others become completely infertile. Such variation is fertile ground for natural selection against those which react to the antigen presented. If such variation in response to the final construct is evident it may be necessary to use strategies that counter such selection before it is deployed in the field.

It is also possible that infertility may be incomplete within individuals. The number of litters per year or the number of young per litter may simply reduce. In that case, individual variation is likely and natural selection may apply here also. The consequences for population control may differ if individual productivity declined instead of ceasing.

A variation on the theme of incomplete infertility is the possibility of a limited duration of infertility, temporary infertility. Immunity to myxomatosis persists for the lifetime of the recovered individual (Fenner et al. 1953), but it is not known if the response to the reproductive antigen would persist similarly. The persistence of immunity to myxomatosis suggests that there would be little chance that further inoculations of virus by insect vectors would reactivate or boost the infertility. Experimental inoculation of laboratory rabbits supports this inference (Kerr and Jackson 1995).

THE EUROPEAN WILD RABBIT AS A CANDIDATE FOR VVIC

The form of VVIC chosen will depend also on aspects of the biology of the rabbit. Even for a species as intensively studied as the wild rabbit, some aspects of rabbit biology that are crucial for VVIC are not known and will need to be investigated. It is also very pertinent that a widespread species, like the wild rabbit in Australia, varies markedly in population dynamics over the various regions and habitats (Gilbert et al. 1987). Undoubtedly, biology will vary in concert with the population dynamics.

One of the most important issues for MVIC for the wild rabbit is whether the dynamics of rabbit populations would compensate for the failure of some rabbits to breed, or would compensate for the intended decreased density of rabbits. Such compensation could nullify the intended benefits of MVIC or determine that greater reductions in fertility must be achieved for population reduction. Several aspects to this general question of compensation are considered below.

The Mating System of the Rabbit

The social aspects of mating will influence whether rabbit populations may compensate for infertility and affect the required level of penetration of the sterility agent into rabbit populations. Also, knowledge of the mating system of the wild rabbit is essential for conceptual or mathematical models of proposed systems of MVIC. The probability that a male rabbit mating with

a female at oestrus is sterile depends on the male having been infected with the sterilizing virus. That probability increases with age; young males would be more likely to be fertile. Domestic rabbits are induced ovulators; the act of mating initiates ovulation in about 10 hours (Asdell 1965). However, this may not be so for wild rabbits (viz. Myers and Poole 1962). The question of induced ovulation is pertinent to MVIC because it may determine whether only one or several males may fertilize ova at a female's oestrus, and thereby affect the probability that the mating is sterile. It is not known how many males mate with a female rabbit at oestrus, nor whether only one or more of these males fertilize the ova shed in one ovulation. Also, it is not known whether older males leave more progeny than younger ones, or whether any social dominance dissociated from age determines procreative success (viz. Daly 1981).

The Responses of Rabbit Populations to Infertility

It is not known how female rabbits respond to the presence of females that do not breed. The responses may vary, depending on the social status of the fertile and infertile females. The issue is whether the fertile females leave more or fewer progeny because of the presence of the infertile females. Such fecundity responses could result from variation in the proportion of the fertile females that breed, the number of litters they produce in a season, and the number of young in the litters. It is also possible that the fertile females might respond in this way, not for social reasons, but because of reproductive reaction to the altered population density of rabbits and the consequences for available resources such as quality or abundance of food and warren space.

Similarly, the progeny born to the fertile females may survive differently because of the altered population density of adults and young rabbits, and the different levels of available resources of food and warren space. Any such effects are likely to flow on to differences in growth rates, time to maturity, proportion surviving to maturity and the age at which they breed. Earlier maturity may mean that, in extended growing seasons, some young might breed in the season of their birth, with profound implications for population growth rates. These responses of females and progeny to infertility in rabbit populations are not known but are needed to predict the outcome of VVIC.

MYXOMATOSIS AS A VEHICLE FOR VVIC OF WILD RABBITS IN AUSTRALIA

Myxomatosis kills a proportion of the susceptible rabbits that become infected, the proportion depending on the virulence of the strain of myxoma and other factors inherent in the rabbits such as genetic resistance and the sire effect (Sobey and Conolly 1986; Williams and Moore 1991; Parer et al. 1995). The intent for MVIC is that those rabbits that survive the infection will remain infertile (Tyndale-Biscoe 1994b). Therefore, the choice of strain would influence the proportion of rabbits that the infection kills or renders infertile. Humaneness indicates that highly attenuated strains are preferred, whereas the impact of rabbits indicates that highly virulent strains should be chosen. However, other factors impinge on the choice of myxoma strain. The recombinant MVIC virus may incur a competitive disadvantage relative to the myxoma strains present in the field. Therefore, the transmissibility of the MVIC virus may need to be maximized as far as possible, perhaps specifically for the particular region and its population of rabbits. Transmissibility depends on the rate of viral replication in the skin of the rabbit, and this varies with viral virulence (Fenner and Ratcliffe 1965). The European rabbit flea transmits the more virulent strains faster than attenuated ones (Mead-Briggs and Vaughan 1975), but we do not know the relative rates for other modes of transmission. Nevertheless, it is unlikely that highly attenuated myxoma strains would be a viable option for MVIC. At present there seems to be no alternative to experimental comparison of strains, at least initially, to derive information on which to choose suitable strains for MVIC.

Another element of uncertainty in the use of MVIC results from the very recent entry of RCD into wild rabbit populations in Australia. Myxomatosis appears to be co-existing with RCD in field populations (B. D. Cooke, pers. comm.). Nevertheless, if RCD persists in field populations, as it has in Spain (Blanco and Villafuerte 1994, cited in Cooke 1995), we can expect some realignment of the epidemiology of myxomatosis with the altered dynamics of the rabbit populations and perhaps also the vector flea populations. The implications for MVIC will be complex.

INSECT VECTORS OF MYXOMATOSIS AS TRANSMITTERS OF MVIC AMONG WILD RABBITS IN AUSTRALIA

Mosquitoes are erratic vectors of myxomatosis, whereas fleas are more regular in abundance and proximity to rabbits. Consequently, fleas are more likely to be targeted as the vectors for MVIC. Transmission of myxomatosis by mosquitoes tends to be fast and short-lived, whereas flea-borne epizootics tend to trickle through rabbit populations. Mosquitoes, being irruptive, may dominate the transmission of myxomatosis in some years, probably wetter years, and perhaps in regions rich in water bodies suitable for breeding of the appropriate species of mosquitoes. While mosquitoes and fleas probably differ in their transmission characteristics, different strains of myxoma may be favored according to the relative proportions of myxoma transmission by these vector species. Thereby different strains may be favored in different times and places, and in some years the MVIC may be favored or disadvantaged depending on the transmission characteristics of the chosen strains. It may prove advantageous to use several different strains of myxoma for MVIC that are transmitted best by the different types of vector.

The dependence of the reproduction of the European rabbit flea on the breeding cycle of the rabbit poses the question of whether fleas would remain abundant enough to transmit the MVIC. That is, would a prevalence of infertile females cause flea numbers to decline to some equilibrium level too low for adequate transmission of myxoma virus? The density of European rabbit fleas needed to sustain an epizootic of myxomatosis is not know; however, it can be anticipated that the minimum required density would vary with a multitude of field

conditions. Experimentation and measurement are needed. While the breeding of the Spanish flea does not depend similarly on rabbit reproduction, the role of this vector in transmitting myxomatosis in Australian wild rabbit populations remains to be determined. The role of the Spanish flea in viral transmission is a very important factor, for mortality caused by myxomatosis and RCD in the arid and semi-arid interior where the problem of rabbit impact is severe and in urgent need of solution, and for its potential role in transmitting MVIC. This role will not be elucidated for some time because the Spanish flea is still establishing there in the adverse conditions of low rabbit numbers caused by prolonged drought and the initial impact of RCD.

THE NEED FOR EXPERIMENTATION AND MATHEMATICAL MODELING

While so many factors might impinge on the effect of VVIC, and the interactions within them are so complex, mathematical modeling must be relied upon to synthesize likely outcomes and assess the relative importance of the various factors and interactions (e.g., Caughley et al. 1992; Barlow 1994). However, it is important that real interactions are recognized and that realistic values be used in such mathematical models. Primary observation through experimentation is needed to recognize or test those interactions and to obtain those realistic values.

ANALYSIS OF ECOLOGICAL PROBLEMS IN MVIC FOR THE EUROPEAN WILD RABBIT

Rabbit

The mating system of wild rabbits is being examined in a group of rabbits held in large enclosures. The progression of breeding is being examined closely and litters are checked for maternity by behavior, pregnancy and lactation, and for paternity by analysis of DNA. Preliminary results indicate that the males which are socially dominant in the enclosures may sire the majority of the litters, but by no means all. Most litters are sired by one male; the frequency of multiple paternity within litters is less than 10% (L. A. Hinds, pers comm.). These preliminary results are seen as consistent with effective MVIC.

The responses of wild rabbit populations to infertility are being examined in two very large field experiments on either side of Australia in two different climatic regions. In these experiments female rabbits are sterilized at random by surgical ligation of fallopian tubules in proportions of 0% or 40% or 60% or 80% of all females. The dynamics of the 24 separate rabbit populations are monitored and recruits are sterilized annually. Progressive effects are expected over the three years of the trials, but some patterns are evident in the first year's results (Williams and Twigg in press).

The fertile female rabbits did not seem to respond to the presence of infertile rabbits; young rabbits were produced in proportion to the level of sterility imposed on the populations. Consequently, in the first year, no social responses influenced reproductive productivity, and any ecological consequences of the presence of fewer progeny did not affect the breeding of the fertile females. In the first year the numbers and survival in the adult stratum of the population did not respond to the presence of fewer young rabbits, although flow-on effects are possible in later years. However, survival of the progeny varied with the level of sterility in the population and its productivity. Survival was greater where fewer young were produced because of imposed sterility. That is, the survival of the young partially compensated for sterility. Under the experimental conditions compensatory survival seemed to nullify the effects of sterility to levels between 60% and 80% of females. Although sterility may have more effect in later years when the numbers of adults might decline, these preliminary results suggest that the wild rabbit has some resilience to MVIC because of its production of more young than the resources of the habitat can support in most years (Williams and Twigg in press).

Myxoma Virus as a Carrier

These field studies examine also the prevalence of myxomatosis in the rabbit populations by measuring serum antibodies to myxoma virus. Active cases of the disease are sampled for analysis of the genetic type (strain) of virus by assessing restriction fragment length polymorphisms (RFLPs) of DNA (P. J. Kerr, pers. comm.). Seven such strains of myxoma virus have been identified from the study sites. Two of these appear to persist in the area while others apparently arrive and do not persist.

Very high proportions of the rabbit populations are exposed each year to myxomatosis, and most rabbits are immune by mid-autumn. This suggests that the myxoma virus has the potential to transmit immunocontraceptive antigens to most rabbits in these regions. However, these observations also indicate that it may be a very difficult task for the genetically modified myxoma virus to compete with the field strains already present.

The possibility of introducing an identifiable strain of myxoma virus into wild rabbit populations in competition with the naturally occurring field strains is being tested in another field trial (A. J. Robinson and J. C. Merchant, pers. comm.). One of the seven identified field strains has been introduced actively by inoculating trapped rabbits in four areas where this strain has not been found. The rabbit populations are being monitored very closely, and rabbits observed to be infected with myxomatosis are caught and the virus is sampled and identified.

This trial is still in progress, but current results suggest that the introduced identifiable field strain has spread locally on sites where other field strains have infected rabbits. There is no clear outcome on competition because there have been few cases of the introduced strain and a field strain infecting rabbits simultaneously in the same warren. The observations on transmission of the introduced strains and field strains will be applied to spatial competitive models of MVIC. Studies already planned might identify strains with greater transmissibility than this introduced strain, but it will be necessary for the MVIC virus to contain additional genetic material, and the transmissibility of the genetically modified virus will need to be assessed in containment.

European Rabbit Flea as a Vector

The field studies of the responses of rabbit populations to sterility imposed by surgery include

analysis of the abundance of the European rabbit flea. Practiced calibrated observers count or visually assess the numbers of fleas on each trapped rabbit without knowledge of the sterility treatment assigned to the sites. The effects of the sterility treatments of the female rabbits on the vector flea populations will be analyzed only after the field assessments have ceased.

Modeling MVIC

Mathematical models that will comprise the MVIC model are being developed. These will be modified as field studies progress and realistic data become available. A spatial model of spread of competing strains of myxoma virus (R. Pech and G. Hood, pers comm.) indicates that sterilizing strains of myxoma virus seem to be at a competitive disadvantage to equivalent non-sterilizing strains and eventually die out. The sterilizing virus reduces the rate of recruitment of young rabbits susceptible to myxomatosis, and thereby it deletes opportunities for transmission and persistence. However, the probability of persistence of the sterilizing strain increases with increasing distance of transmission between rabbit hosts. The probabilities of persistence of the sterilizing and non-sterilizing virus strains tend to equalize when the average distance of transmission of virus equals the average dispersal distance of the rabbits. This outcome suggests that an MVIC may persist longer and affect more rabbits if transmitted by potentially long-distance vectors such as mosquitoes. Transmission by fleas may enable MVIC to be used tactically in localized situations. Myxoma strains with differing transmission characteristics may be needed for areas that differ in prevalences of mosquito or flea transmission of myxomatosis. Thus, the mathematical models under development generate useful questions about how MVIC might function.

CONCLUSION

Virally vectored immunocontraception of the European wild rabbit in Australia, using myxoma virus to carry the sterilizing agent, involves very complex ecological interactions of virus, flea and rabbit. Experimental modeling of MVIC in field populations of rabbits, aided by mathematical modeling, seems to be progressing successfully in assessing the feasibility of developing the concept as an additional tool for managing the abundance and impact of this profoundly destructive pest.

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LITERATURE CITED

ASDELL, S. A. 1965. Pages 195-199 *in* Patterns of Mammalian Reproduction. Second edition. Constable, London.

BARLOW, N. D. 1994. Predicting the effect of a novel vertebrate biocontrol agent: a model for viral-vectored immunocontraception of New Zealand possums. Journal of Applied Ecology 31, pp. 454-462.

BLANCO, J. C., and VILLAFUERTE, R. 1994. Factores ecologicos que influyen sobre las poblaciones de conejos. Incidencia de la enfermedad hemorragica. 137 pp. Empressa de Transformacion Agraria, SA, Seville.

BOMFORD, M. 1990. Role of fertility control in wildlife management? Bureau of Rural Resources Bulletin No. 7, 1-50. (Canberra, Australia).

BRADLEY, M. P. 1994. Experimental strategies for the development of an immunocontraceptive vaccine for the European red fox, *Vulpes vulpes*. Reproduction, Fertility and Development 6, pp. 307-317.

CAUGHLEY, G., R. PECH, and D. GRICE. 1992. Effect of fertility control on a population's productivity. Wildlife Research 19, pp. 623-627.

COOKE, B .D. 1984. Factors limiting the distribution of the European rabbit flea, *Spilopsyllus cuniculi* (Dale) (Siphonaptera), in inland South Australia. Australian Journal of Zoology 32, pp. 493-506.

COOKE, B. D. 1990a. Rabbit burrows as environments for European rabbit fleas, *Spilopsyllus cuniculi* (Dale) in arid South Australia. Australian Journal of Zoology 38, pp. 317-325.

COOKE, B. D. 1990b. Notes on the comparative reproductive biology and the laboratory breeding of the rabbit flea, *Xenopsylla cunicularis* Smit (Siphonaptera: Pulicidae). Australian Journal of Zoology 38, pp. 527-534.

COOKE, B. D. 1995. How would rabbit calicivirus disease affect Australian rabbit populations. Unpublished report. pp. 381-383. 10th Australian Vertebrate Pest Control Conference, Hobart, Tasmania, May 1995.

DALY, J. C. 1981. Effects of social organisation and environmental diversity on determining the genetic structure of a population of the wild rabbit *Oryctolagus cuniculus*. Evolution 35, pp. 689-706.

FENNER, F., and F. N. RATCLIFFE. 1965. Myxomatosis. Cambridge University Press, London.

FENNER, F., I. D. MARSHALL, and G. M. WOODROOFE. 1953. Studies in the epidemiology of infectious myxomatosis in rabbits. I. Recovery of Australian wild rabbits (*Oryctolagus cuniculus*) from myxomatosis under field conditions. Journal of Hygiene, Cambridge 51, pp. 225-244.

GILBERT, N., K. MYERS, B. D. COOKE, J. D. DUNSMORE, P. J. FULLAGAR, J. A. GIBB, D. R. KING, I. PARER, S. H. WHEELER, and D. H. WOOD. 1987. Comparative dynamics of Australasian rabbit populations. Australian Wildlife Research 14, pp. 491-503.

HOLLAND, M. K., and R. J. JACKSON. 1994. Virus vectored immunocontraception for control of wild rabbits: identification of target antigens and construction of recombinant viruses, Reproduction, Fertility and Development 6, pp. 631-642.

KERR, P. J., and R. J. JACKSON. 1995. Myxoma virus as a vaccine vector for rabbits: antibody levels to influenza virus haemagglutinin presented by a recombinant myxoma virus.

MEAD-BRIGGS, A. R. 1964. The reproductive biology of the rabbit flea *Spilopsyllus cuniculi* (Dale) and the dependence of this species on the breeding of its host. Journal of Experimental Biology 41, pp. 371-402.

MEAD-BRIGGS, A. R., and J. A. VAUGHAN. 1975. The differential transmissibility of myxoma virus strains of differing virulence by the rabbit flea *Spilopsyllus cuniculi* (Dale). Journal of Hygiene Cambridge 75, pp. 237-247.

PARER, I., D. CONOLLY, and W. R. SOBEY. 1985. Myxomatosis: the effects of annual introduction of an immunizing strain and highly virulent strain of myxoma virus into rabbit populations at Urana, N. S. W. Australian Wildlife Research 12, pp. 407-23.

MYERS, K., and W. E. POOLE. 1962. A study of the biology of the wild rabbit, *Oryctolagus cuniculus* (L.) in confined populations. III. Reproduction. Australian Journal of Zoology 10, pp. 225-267.

PARER, I., W. R. SOBEY, D. CONOLLY, and R. MORTON. 1994. Virulence of strains of myxoma virus and the resistance of wild rabbits, *Oryctolagus cuniculus* (L.), from different locations in Australasia. Australian Journal of Zoology 42, pp. 347-362.

PARER, I., W. R. SOBEY, D. CONOLLY, and R. MORTON. 1995. Sire transmission of acquired resistance to myxomatosis. Australian Journal of Zoology 43, pp. 459-465.

ROBINSON, A. J., and M. K. HOLLAND. 1995. Testing the concept of virally vectored immunosterilisation for the control of wild rabbit and fox populations in Australia. Australian Veterinary Journal 72, pp. 65-68.

STODART, E., and I. PARER. 1988. Colonisation of Australia by the rabbit. CSIRO Division of Wildlife and Ecology Project Report No. 6.

SOBEY, W. R., and D. CONOLLY. 1971. Myxomatosis: the introduction of the European rabbit flea, *Spilopsyllus cuniculi* (Dale), into wild rabbit populations in Australia. Journal of Hygiene Cambridge 69, pp. 331-346.

SOBEY, W. R., and D. CONOLLY. 1986. Myxomatosis: non-genetic aspects of resistance to myxomatosis in rabbits, *Oryctolagus cuniculus*. Australian Wildlife Research 13, pp. 177-187.

TYNDALE-BISCOE, C. H. 1994a. The CRC for Biological Control of Vertebrate Pest Populations: fertility control of wildlife for conservation. Pacific Conservation Biology 1, pp. 163-168.

TYNDALE-BISCOE, C. H. 1994b. Virus-vectored immunocontraception of feral mammals. Reproduction, Fertility, and Development 6, pp. 281-287.

TYNDALE-BISCOE, C. H. 1995. Vermin and viruses: risks and benefits of viral-vectored immunosterilisation. Search 26, pp. 239-244.

WILLIAMS, C. K., and R. J. MOORE. 1991. Inheritance of acquired immunity to myxomatosis. Australian Journal of Zoology 39, pp. 307-311.

WILLIAMS, C. K., and R. J. MOORE. 1995. Effectiveness and cost-efficiency of control of the wild rabbit, *Oryctolagus cuniculus* (L.), by combinations of poisoning, ripping , fumigation and maintenance fumigation. Wildlife Research 22, pp. 253-269.

WILLIAMS, C. K., I. PARER, B. J. COMAN, J. BURLEY, and M. L. BRAYSHER. 1995. Managing vertebrate pests: Rabbits. Bureau of Resource Sciences/CSIRO Division of Wildlife and Ecology, Australian Government Publishing Service, Canberra.

WILLIAMS, C. K., and L. E. TWIGG. In press. Responses of wild rabbit populations to imposed sterility. *In* Frontiers and Applications of Population Ecology, R. B. Floyd and A. W. Sheppard, eds., CSIRO, Melbourne.