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IMMUNOCONTRACEPTION AS A POTENTIAL CONTROL METHOD OF WILD RODENT POPULATIONS

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Abstract. Rodents have the capacity to periodically reach very high numbers in agricultural landscapes, reducing agricultural production, and causing considerable environmental and social problems for farmers and their families. Such rodent problems occur worldwide and have a long history. Currently, mortality enhancing agents (mainly poisons) are the principal method of rodent control. This approach raises environmental, ethical and humane issues, and ignores the inherent high capacity for increase in these species. We argue that it is more appropriate to reduce reproduction than increase mortality. This paper uses house mice in Australia as a case study to explore fertility reduction as a potential alternative to conventional methods of control. In particular, the question of what level of fertility control is required to have a significant effect on population growth is discussed. A computer simulation, based on the life-history strategies of house mice, examined the effect of different levels of fertility control on mouse population dynamics. This simulation provides a reference for future studies of confined populations of mice used to test the effects of fertility control, refines the design of these experiments and identifies the type of data needed to be collected. Immunocontraception, the process of inducing the body's immune system to attack its own reproductive cells, is suggested as a method for reducing fertility in rodent populations. The advantages and disadvantages of immunocontraception over mortality-enhancing agents are discussed, as are the potential impacts of social structure on the efficacy of immunocontraception and the possible application of this control method to other rodent pest situations, particularly rodent pest problems in Africa.

Key words: Fertility reduction, rodents, immunocontraception, mouse plagues, *Mus domesticus*, computer simulation, experimental design.

INTRODUCTION

Rodents have been the scourge of human populations since before Aristotle, 350 BC (THOMPSON, 1910), and in recent times have caused considerable losses to a variety of growing crops and to stored grain in Asia (GEDDES, 1992; SINGLETON & PETCH, 1994), Africa (LEIRS *et al.*, 1997), Australia (SINGLETON & REDHEAD, 1989; CAUGHLEY *et al.*, 1994), and elsewhere (see PRAKASH, 1988; BUCKLE & SMITH, 1994). Rodents also play an important role as carriers of zoonoses such as plague, leptospirosis, hantaviruses, Lassa fever and leishmaniases (CHILDS *et al.*, 1994; GRATZ, 1994; references in this issue).

Another major concern, which has become prominent in recent years, is the impact of introduced rodents on the conservation of native wildlife, especially on islands (WACE, 1986; MOORS *et al.*, 1992; KEY *et al.*, 1994; COWAN & TYNDALE-BISCOE, 1997).

There are two principal stategies for managing rodent pest populations - increase mortality or decrease fertility. Currently, the main method for controlling rodents in agricultural landscapes relies on increasing mortality using poisons, particularly anticoagulants. There are problems associated with the use of chemicals for control. These have been discussed elsewhere (SINGLETON & REDHEAD, 1989) and are summarised as follows.

1. Residues can contaminate the growing crop, soil and any nearby water supplies.
2. Non-target deaths can occur due to primary poisoning by consumption of bait (granivorous species) and secondary poisoning from consumption of rodent carcasses (predatory or scavenging species) (see also SAUNDERS & COOPER, 1981 for examples).
3. Large areas need to be treated if re-invasion from neighbouring areas is to be minimised, making baiting an expensive option.
4. There are ethical and animal welfare issues with respect to the suffering inflicted on the animals during poisoning (see also SAINSBURY *et al.*, 1995; OOGJES 1997).

Predation is a natural mortality-enhancing factor in rodent population dynamics. The effectiveness of predators in regulating field populations of rodents has been demonstrated (*e.g.* KORPIMÄKI & NORRDAHL, 1989; SINCLAIR *et al.*, 1991; JAKSIC *et al.*, 1992). ANDERSSON & ERLINGE (1977) concluded that generalist and migrating specialist predators can stabilise rodent populations, particularly during and after the decline phase in the rodent population, but predation is not as successful in regulating populations which are increasing or already high.

Rodents display typical *r*-species attributes: they are small, highly mobile, fecund, short-lived, have a wide niche breadth, and a variable "boom and bust" population density (SOUTHWOOD, 1977). Therefore, control methods which concentrate on increasing the level of mortality need to be well targetted or highly effective if they are to be successful. Even then, the effect is generally short-lived given the life-history characteristics of rodents. A biological method of control, particularly one which reduces the high reproductive capacity of rodents, could be a more effective alternative.

The prospects for controlling rodents using biological methods have been reviewed by SINGLETON (1994) who concluded that it was preferable to use agents which reduced fertility rather than increasing mortality. This is viewed as an appropriate control approach for vertebrate pests generally (*e.g.* CAUGHLEY *et al.*, 1992).

The primary aim of this paper is to examine fertility reduction as a possible means of controlling rodents. An important question that needs to be addressed is what level of fertility control is necessary to produce a sustained effect in wild populations? A case study of house mice in Australia is used to examine this question. A computer simulation of two levels of sterility allowed us to examine the possible effects on population growth rate and abundance of mouse populations compared against an unsterilised control population. The simulation will be used to assist in the design of enclosure experiments in which wild mouse populations, housed under semi-natural conditions, will have a proportion of the females surgically sterilised to mimic the effects of a fertility-reducing agent.

The concept of immunocontraception as a possible way of achieving sterility is discussed and the advantages and disadvantages of this method compared with mortality enhancing methods currently available for controlling rodents. Immunocontraception is then discussed in terms of its likely effects on rodent social structure and its application to rodent pest situations other than house mice in Australia, particularly rodent pests in Africa.

CASE STUDY

The house mouse, *Mus domesticus* (Schwarz & Schwarz, 1943) causes considerable economic and social stress to rural communities due to its ability to form plagues at irregular intervals in the grain-growing regions of eastern and southern Australia (SINGLETON & REDHEAD, 1989; CAUGHLEY *et al.*, 1994). It would be unrealistic to expect that mice could be completely eliminated from these areas. Rather, the aim should be to decrease mouse populations so that the degree of damage inflicted is at or below the level that causes economic hardship to growers.

Results from studies of mouse populations in Australia's cereal-growing regions indicate that average litter size is greater in the 12-18 months prior to a plague than at other times (SINGLETON & REDHEAD, 1990). In the mallee wheatlands, the length of the breeding season is longest 12 months prior to a plague (SINGLETON, 1989). Previous modelling of mouse population dynamics suggests that if these occasional seasons of high mouse productivity were prevented, mouse plagues may not occur (REDHEAD, 1987).

HONE[1] produced an empirical estimate of the level of fertility control required for reduction in population growth from the intrinsic rate (r) to zero in 13 mammalian pests, including mice. The estimate for mice was determined indirectly using rates of increase and a generation interval obtained from field data (REDHEAD, 1982). HONE predicted that the proportion of females that needed to be sterilised was 0.60. Two points arise from this. One is that immigration would increase this estimate. The other, is that for much of the time the rates of increase of populations of mice are likely to be less than r and it is probably not necessary to reduce the rate of population increase to zero, depending on the timeframe and damage thresholds.

Computer simulation

To simulate the effects of sterility, we constructed a simple demographic model of a mouse population with three age classes (juvenile, 0-5 weeks; sub-adult, 5-6 weeks; and adult, >6 weeks) and three reproductive classes (male, intact female and sterilised female). Only sub-adults and adults were in the trappable population (SINGLETON, 1987). The assumptions and parameters used in this model are summarised in Tables 1 and 2.

[1]HONE, J. (199-) – How much fertility control of vertebrate pests is enough? *J. Anim. Ecol.* (submitted).

Software to implement the model was written in-house in the Pascal programming language.

TABLE 1

Assumptions underlying demographic modelling of the predicted effect of surgical sterilisation on enclosed, wild mouse populations

Assumption	*Justification*
Breeding synchronous within and across enclosures	Based on previous experiments using wild mice in the enclosures (see BARKER *et al.*, 1991) and the Whitten effect (WHITTEN, 1966).
Survivorship equal across sexes and age cohorts	Based on BARKER *et al.* (1991)
No compensation in birth or death rates with density or treatment	Compensation detectable by comparing actual data to predictions from model
Sex ratio of progeny is 1:1	
All females bred that were capable of breeding	Resources in excess

TABLE 2

Life history and population parameters included in demographic modelling of the predicted effect of surgical sterilisation on enclosed, wild mouse populations. a.b. = after birth

Parameter	*Estimate*	*Reference / Justification*
Litter size	5.25 (SD = 1)	From wild mouse colonies used to derive founder mice
➥ Gestation period	➥ 19 days	
➥ Juvenile period (includes weaning period	➥ In nest 21 days; on surface 14 days (0 - 5 weeks a.b.)	Wild mouse colonies and
➥ Age at sexual maturity	➥ 42 days (6 weeks a.b.)	WHITTINGHAM & WOOD (1983)
Sub-adult period (trappable but not sexually mature)	7 days (5 - 6 weeks a.b.)	SINGLETON, 1987
Minimum period between litters	Includes lactational diapause 23 days	WHITTINGHAM & WOOD (1983)
Survivorship	97% per 7 days (99.5% per day)	Based on BARKER *et al.* (1991)

Each simulation began on day zero with 12 adult females and 8 adult males in each population and ran for 140 days with a daily time step. A founding population of 20 was chosen as this was likely to be the initial population per replicate in future studies of confined populations of mice used to test the effects of fertility control. There were three treatments: all founder females intact, 67% of founder females sterilised, and 75% of founder females sterilised.

Because the initial number of mice was small, we used integer arithmetic to represent the number of mice in each state. A daily mortality rate of 0.005 was assumed for all age-sex classes and binomial samples were removed daily from each class to simulate natural mortality. We assumed that intact females had ready access to males and so became pregnant on day one of the experiment and gave birth 19 days later. To allow for the fact that a small number of female mice have a lactational diapause which delays the onset of parturition (WHITTINGHAM & WOOD, 1983), the gestation length was set to 23 days rather than 19 days, as shown in Table 2.

To sustain the level of sterility imposed on each treatment population, the females from the first litter produced by the founders ($F1_1$ litter) were sterilised at the same level as the founder females.

As it is likely that the experimental enclosures will provide mice with ample space for nest sites and unlimited access to food (assuming social influences are not important for inhibiting access), the model assumed no density dependence in mortality rates and that all intact females produced litters. Litter size was taken as a normally distributed random variable with mean 5.25 and standard deviation 1.0 rounded to the nearest integer (see Table 2 for justification of this litter size). A binomial sample from each litter was assigned to each sex class (male/female) such that the expected sex ratio was 1:1.

Because the model is stochastic, the mean of ten runs was used to predict trappable population during the course of the experiment (Fig. 1). This was done for populations with 0%, 67% and 75% sterility of females. The control population (0% sterility) was higher than the sterilised populations and there was a difference between the 67% and 75% level of sterility.

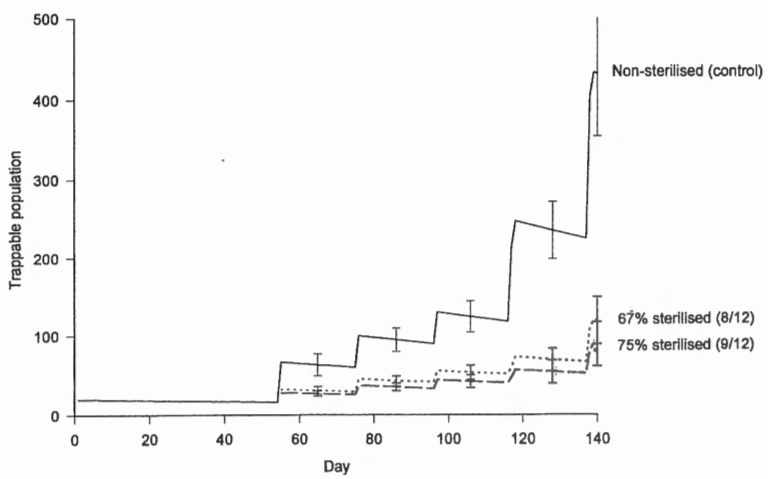

Fig. 1. – Predicted trappable population of wild mice housed in outdoor enclosures where a proportion of the females (0%, 67% and 75%) have been sterilised. Each plot is the mean of 10 runs of a demographic model with the variance shown (±S.D.) at each step of the plot. $F1_1$ to $F1_4$ indicates when F1 generation litters (those produced by the founding population of mice) will enter the trappable population (5 weeks of age – see Table 2). $F2_1$ indicates when the first litter of the F2 generation (produced by the first F1 generation litter – $F1_1$) enters the trappable population.

Each step in the plots indicates the entry of a new cohort of mice into the trappable population. The first three litters ($F1_1$ to $F1_3$) are litters produced from the founding population and are the first generation. The fourth F1 litter becomes trappable at the same time as the first litter of the second generation ($F2_1$). The experiment would need to cease at or just after day 120 when the $F2_1$ litter enters the trappable population and before the females from this group produce a litter. This means that all mice recruited into the trappable population have come from cohorts with the appropriate level of sterility.

Regular sampling times during the experiment can be located using Fig. 1. It would be best to sample the population just after each new cohort has entered the trappable population – around days 60, 80, 100, and 120. This will allow changes to population size to be monitored as they occur.

We plan to test the results from the simulation by conducting studies of confined populations of wild house mice surgically sterilised to mimic a fertility reducing agent. Deviations from the model may allow the importance of compensation in treated populations to be determined. The effects of compensation were not included in our simulation but they have been found to be important in similar experiments examining fertility control for rabbits (WILLIAMS & TWIGG, 1996). The simulation has already assisted in determining the types of data that need to be collected (Table 3) and will assist further by refining the design of these enclosure experiments (*e.g.* how often and when should population sampling occur).

TABLE 3

Parameters to be measured for enclosure populations of wild mice surgically sterilised to simulate immunocontraception (based on modelling exercise)

Parameter	*Justification*
Population size (trappable)	To compare with output from model
Proportion of females breeding	Tests the assumption of synchronous breeding and success of fertile females breeding (*i.e.* pregnant and/or lactating)
Survivorship of adults and trappable juveniles	Compare with level imposed in model
Litter size at autopsy at the completion of the experiment	Compare with values used in model
Recruitment	Measure of survival of neonates

DISCUSSION

The simulation of house mouse abundance over time, under the proposed conditions of an enclosure experiment using wild mice, indicated that by sterilising two-thirds of the females in the population, it was possible to have a substantial effect on population abundance and growth rate. The simulation was used also to refine the design of an enclosure experiment to examine the effect of sterility on the dynamics of wild, semi-natural mouse populations. From the graph of the predicted trappable populations over time for the various sterility scenarios (Fig. 1), key sampling points were identified, as was a suitable termination point.

One method for reducing fertility in wild pest populations such as rodents, is the relatively new concept of immunocontraception. This method has attracted much attention internationally (TYNDALE-BISCOE, 1997) and research is in progress on the use of immunocontraception for the control of mouse populations in Australia (SHELLAM, 1994).

Immunocontraception

Immunocontraception is the process of inducing the body's immune system to attack its own reproductive cells (TYNDALE-BISCOE, 1994). The feasibility of this method for controlling feral mammals in general was first discussed in 1987 and presented at a conference on fertility control in wildlife held in 1990 (TYNDALE-BISCOE, 1991). It was identified that a biological control method which reduces fecundity, and is environmentally benign and humane, would satisfy many of the ethical, environmental and ecological criteria now required of a control method for vertebrates (BOMFORD, 1990).

The proposed approach for the mouse is to use a mouse-specific virus, murine cytomegalovirus (MCMV), as a carrier for a fertility-associated protein which will induce the body's immune system to block fertilisation. This approach is termed viral-vectored immunocontraception (VVIC) and has been identified as the most promising long-term control strategy for house mice in Australia (SINGLETON, 1994).

The fertility-associated protein used to promote an immune response could be from the egg, the sperm or other parts of the reproductive tract. At present, the best prospect appears to be a peptide from the mouse zona pellucida gene, ZP-3, which has been shown to cause long-lasting contraception in mice (MILLAR *et al.*, 1989).

Field studies examining both the distribution (SMITH *et al.*, 1993) and the prevalence of MCMV (SINGLETON *et al.*, 1993), and laboratory studies of the virus itself and its infection characteristics (see SHELLAM, 1994 for review), suggest that MCMV has excellent credentials to be a carrier of an immunocontraceptive for mice. One of this virus's most important features is that, being a cytomegalovirus, it is likely to be species-specific. The virus is widespread in wild mouse populations and has a high seroprevalence (>90%). Up to four strains have been isolated from individual mice and laboratory studies show that infection of laboratory mice with multiple strains can be achieved (BOOTH *et al.*, 1993). This is important if we hope to infect wild mice with a recombinant strain of MCMV in the presence of field strains of the virus.

A disseminating virus rather than a non-disseminating agent is preferred for delivery of an immunocontraceptive antigen because:

1. It has the potential to induce stronger immune responses and greater immunological memory.
2. It has the potential to spread a contraceptive protein rapidly through a mouse population.
3. It is much cheaper than using baits as a delivery agent because it can be «released and forgotten».
4. A species-specific carrier ensures that only the target species is affected.
5. The dynamics of a naturally disseminating virus is more likely to match the short generation time of mice.

The advantages of VVIC compared to methods of control which increase mortality are summarised in Table 4. VVIC has a more appropriate demographic target (fecundity rather than mortality); is species-specific by nature of the reproductive protein, carrier virus and method of transmission (ideally sexually transmitted); and because the vector is a self-disseminating virus, allows large areas to be treated at low cost.

There are potential risks associated with the use of VVIC. These are summarised in Table 4 and discussed in detail in TYNDALE-BISCOE (1994, 1995) and WILLIAMS (1997). Almost all of them relate to the issue of species-specificity and public acceptability. Hence there will need to be rigorous testing of related (and some non-related species) before any VVIC agent is released into the environment. However, it is important to view these risks in the context of the environmental and social acceptability of current management methods, and to weigh the benefits from these methods against those provided by VVIC.

TABLE 4

Advantages of viral-vectored immunocontraception (VVIC) for mouse control in Australia compared with agents which enhance mortality, and the risks and concerns associated with VVIC

Advantages of VVIC over current mortality agents of rodents	*Risks and concerns of VVIC*
Targets reproduction	Irretrievable once released
Self-disseminating, «release and forget» strategy	Public acceptance of genetically engineered organism being released
Species specific	Risk of recombinant virus losing species-specificity with time
Humane	Virus may infect laboratory colonies of mice
Large areas can be treated at minimal cost	International concerns re sterilisation of «desirable» *Mus spp.* (*e.g.* native to that country)
Environmentally benign	

Social structure

The importance of maintenance of social status amongst reproductive females in populations subjected to some level of sterilisation needs to be addressed (COWAN & TYNDALE-BISCOE,1997). Moreover, CAUGHLEY *et al.* (1992) identified types of social organisation and mating systems of target species that will not respond to immunocontraception. These findings have important consequences for the type of reproductive protein used in a VVIC agent (*i.e.* contraceptive versus castrative) and whether or not dominant females are targetted for fertility control.

Although it is difficult to examine the social structure of wild populations of mice, enclosure studies (*e.g.* CROWCROFT, 1966; SINGLETON & HAY, 1983) suggest that reproductive females have a social hierarchy which may determine whether or not a female will acquire mates. In female mice, the mainenance of a high social status is likely to be hormonally controlled. If so, an immunocontraceptive which leaves immunised females hormonally intact, allowing them to maintain their social position in the population and continue to suppress reproduction in subordinate females, would be preferred.

If dominant females contribute disproportionately to the number of offspring produced in a population, then the contraceptive agent should target these females but not compromise their social status. The breeding performance of socially subordinate females which remain fertile needs to be maintained at a low level, otherwise these animals may compensate for the reduction in population growth (COWAN & TYNDALE-BISCOE, 1997).

In rodents, the relevance of social status to fertility control through immunocontraception could be examined experimentally by comparing populations where females have been surgically sterilised using ovariectomy and tubal ligation. Ovariectomy results in females being hormonally compromised, possibly disrupting the social ranking of the female. Tubal ligation leaves the hormonal system intact, retaining any social order that is hormonally controlled.

Immunocontraception and its potential application to other rodent pests

The use of this approach in other rodent pests and the type of vector used will depend on the status of the target. There are three possible approaches for two types of targets:

(1) For totally undesirable, exotic species, with no closely related native species present, then a naturally disseminating virus could be used as the vector.

(2) For native species that reach undesirably high population densities in specific areas, then it would be preferable to use a bait containing the immunocontraceptive protein for strategic, localised control. In this situation, it also may be necessary to have the option to reverse the effects if required (TYNDALE-BISCOE, 1991). The short generation time for rodents may necessitate frequent baiting, depending on the persistence of infertility and the level of bait uptake. An immunocontraceptive baiting program could therefore be costly.

(3) An alternative approach to (2) for native pest species is the use of a fertility agent which is not persistent but is disseminated widely by a viral vector. If an animal develops immunity after infection and then subsequently recovers fertility, then the effect is to dampen the population peaks.

The success of any of the above will depend on the ability of the population to compensate through increased survival or breeding performance. Rodent species with a high intrinsic rate of increase, r, are likely to compensate for the level of immunocontraception but will be less likely to undergo large fluctuations in population density (see SINCLAIR, 1997). In Africa, many of the rodent pest species typically have large fluctuations in population density and generally only cause economic problems in agricultural systems when they are at high densities (see LEIRS *et al.*, 1997). Fertility control via immunocontraception therefore could be an effective, humane and environmentally benign method for rodent management in Africa.

In contrast to the situation with house mice in Australia, most of the rodent pests in Africa are not exotic species - their numbers need to be managed in agricultural and urban situations but the goal is not to eliminate them. Moreover, the average area occupied by each farm is at least two orders of magnitude smaller than that of Australian grain-growers. The logistics and costs associated with distributing a sterility bait over a couple of

thousand hectares and on a number of occasions during the breeding season of the rodent pest, are less tractable than for families in Africa who farm 0.5 to 5 hectares.

For these reasons, the baiting option (option 2) is likely to be more appropriate to the African situation. The success of a baiting program will depend on the life-history characterisitics of each species (their ability to compensate via improved survival, high emigration or increased breeding performance of those which remain fertile) as well as the cost to conduct multiple baiting. If VVIC is socially acceptable and is the only economically viable option of those available for immunocontraception, then option 3 may be appropriate. However, the use of VVIC is a long term option which requires much research effort and a detailed and thorough process of public consultation and of close scrutiny by regulatory authorities (see WILLIAMS, 1997).

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REFERENCES

ANDERSON, M., & S. ERLINGE (1977) – Influence of predation on rodent populations. *Oikos*, **29**: 591-597.

BARKER, S.C., G.R. SINGLETON, & D.M. SPRATT (1991) – Can the nematode *Capillaria hepatica* regulate abundance in wild house mice? Results of enclosure experiments in southeastern Australia. *Parasit.*, **103**: 439-449.

BOMFORD, M. (1990) – A role for fertility control in wildlife management? *Bureau of Rural Resoures Bulletin,* **7**: 1-50.

BOOTH, T.W.M., A.A. SCALZO, C. CARELLO, P.A. LYONS, H.E. FARRELL, G.R. SINGLETON, G.R. SHELLAM (1993) – Molecular and biological characterisation of new strains of murine cytomegalovirus isolated from wild mice. *Arch. Virol.*, **132**: 209-220.

BUCKLE, A.P., & R.H. SMITH (1994) –Eds *Rodent Pests and Their Control.* CAB International, UK, 405 pp.

CAUGHLEY, G., R. PECH, & D. GRICE (1992) – Effect of fertility control on a population's productivity. *Wildl. Res.*, **19**: 623-627.

CAUGHLEY, J., V. MONAMY, & K. HEIDEN (1994) – *Impact of the 1993 mouse plague.* GRDC Occasional Paper Series No. 7., Grains Research and Development Corporation and Bureau of Resource Sciences, Canberra, 73 pp.

CHILDS, J.E., T.G. KSIAZEK, P.E. ROLLIN, J.W. KREBS, S. ZAKI, S.T. NICHOL, C.J. PETERS & G.E. GLASS (1994) – Hantaviruses and their rodent reservoirs in the United States. *Proc. 16th Vertebr. Pest Conf.* (Eds. W.S.Halverson & A.C.Crabb), Univ. of Calif., Davis, 188-191.

COWAN, P.E., & C.H. TYNDALE-BISCOE (1997) – Australian and New Zealand mammal species considered to be pests or problems. *Reprod. Fertil. Dev.*, **9**: 27-36.

CROWCROFT, P. (1966) – *Mice all over.* G.T.Foulis and Co., London, 121 pp.

GEDDES, A.M.W. (1992) – *The relative importance of pre-harvest crop pests in Indonesia.* Chatham, UK., Natural Resources Institute Bulletin 47, 70 pp.

GRATZ, N.G. (1994) – Rodents as carriers of disease. In: *Rodent pests and their control.* (Eds A.P. BUCKLE & R.H. SMITH), CAB International, UK, 85-108.

JAKSIC, F.M., J.E. JIMÈNEZ, S.A. CASTRO & P. FEINSINGER (1992) – Numerical and functional response of predators to a long-term decline in mammalian prey at a semi-arid Neotropical site. *Oecologia*, **89**: 90-101.

KEY, G., E. WILSON, & J. CONNOR (1994) – Present status of *Rattus norvegicus* on Santa Cruz Island, Galapagos, Ecuador. *Proc. 16th Vertebr. Pest Conf.* (Eds. W.S. HALVERSON & A.C. CRABB), Univ. of Calif., Davis, 118-123.

KORPIMÄKI, E. & K. NORRDAHL (1989) – Predation of Tengmalm's owls: numerical responses, functional responses and dampening impact on population fluctuations of microtines. *Oikos*, **54**: 154-164.

LEIRS, H., R. VERHAGEN, C.A. SABUNI, P.M. WANJABE & W.N. VERHEYEN (1997) – Spatial dynamics of *Mastomys natalensis* in a field-fallow mosaic in Tanzania. *Belg. J. Zool.*, **127** (sup. 1): 29-38.

MILLAR, S.E., S.M. CHAMOW, A.W. BAUR, C. OLIVER, F. ROBEY, & J. DEAN (1989) – Vaccination with a synthetic zona pellucida peptide produces long-term contraception in female mice. *Science*, **246**: 935-938.

MOORS, P.J., A.E. ATKINSON & G.H. SHERLEY (1992) – Reducing the rat threat to island birds. *Bird Conserv. Internat.* **2**: 93-114.

OOGJES, G. (1997) – Ethical aspects and dilemmas of fertility control of unwanted wildlife: An animal welfarist's perspective. *Reprod. Fertil. Dev.*, **9**: 163-167.

PRAKASH, I. (1988) – *Rodent Pest Management*, CRC Press, Inc., Boca Raton, USA, 480 pp.

REDHEAD, T.D. (1982) – Reproduction, growth and population dynamics of house mice in irrigated and non-irrigated cereal farms in New South Wales. *Ph.D. thesis*. Department of Zoology, Australian National University, Canberra.

REDHEAD, T.D. (1987) – The role of a biological agent for tactical prevention of losses caused by mouse plagues.In: *Capillaria hepatica (Nematoda) as a potential control agent of house mice.* (Ed. G.R.Singleton). CSIRO, Division of Wildlife & Rangelands Research, Tech. Mem. No. 28., CSIRO, 6-11.

SAINSBURY, A.W., P.M.BENNETT, & J.K.KIRKWOOD (1995) – The welfare of free-living wild animals in Europe: harm caused by human activities. *Anim. Welfare*, **4**: 183-206.

SAUNDERS, G. & K. COOPER (1981) – Pesticide contamination of birds in association with a mouse plague. *Emu*, **82**: 227-229.

SHELLAM, G.R. (1994) – The potential of murine cytomegalovirus as a viral vector for immunocontraception. *Reprod. Fertil. Dev.*, **6**: 401-409.

SINCLAIR, A.R.E. (1997) – Fertility control of mammal pests and the conservation of endangered marsupials. *Reprod. Fertil. Dev.*, **9**: 1-16.

SINCLAIR, A.R.E., P.D. OLSEN, & T.D. EDHEAD (1991) – Can predators regulate small mammal populations? Evidence from house mouse outbreaks in Australia. *Oikos*, **59**: 382-392.

SINGLETON, G.R. (1987) - A comparison of the effectiveness of pitfall and Longworth live-trapping techniques in population studies of house mice. *Acta Theriol.*, **32**: 245-59.

SINGLETON, G.R. (1989) - Population dynamics of an outbreak of house mice (*Mus domesticus*) in the mallee wheatlands of Australia – hypothesis of plague formation. *J. Zool. (Lond)*, **219**: 495-515

SINGLETON, G.R. (1994) – The prospects and associated challenges for the biological control of rodents. *Proc. 16th Vertebr. Pest Conf.* (Eds. W.S. HALVERSON & A.C. CRABB), Univ. of Calif., Davis, 301-307.

SINGLETON, G.R. & HAY, D.A. (1983) - The effect of social organisation on reproductive success and gene flow in colonies of wild house mice, *Mus musculus. Behav. Ecol. Sociobiol.*, **12**: 49-56.

SINGLETON, G.R. & D.A. PETCH (1994) – *A Review of the Biology and Management of Rodent Pests in Southeast Asia.* ACIAR Technical Reports No. 30, ACIAR, Canberra, 65 pp.

SINGLETON, G.R. & T.D. REDHEAD (1989) – House mouse plagues. In: *Mediterranean Landscapes in Australia* (Eds. J.C.Noble & R.A.Bradstock), CSIRO, Australia, 418-433.

SINGLETON, G.R. & T.D. REDHEAD (1990) – Structure and biology of house mouse populations that plague irregularly; an evolutionary perspective. *Biol. J. Linn. Soc.*, **41**: 285-300.

SINGLETON, G.R., A.L. SMITH, G.R. SHELLAM, N. FITZGERALD, & W.J. MÜLLER (1993) – Prevalence of viral antibodies and helminths in field populations of house mice (*Mus domesticus*) in south-eastern Australia. *Epid. & Infect.*, **110**: 399-417.

SMITH, A.L., G.R. SINGLETON, G.M. HANSEN, & G. SHELLAM (1993) – A serological survey for viruses and *Mycoplasma pulmonis* among wild house mice (*Mus domestius*) in southeastern Australia. *J. Wildl. Dis.*, **29**: 219-229.

SOUTHWOOD, T.R.E. (1977) – Habitat, the templet for ecological strategies? *J. Anim. Ecol.*, **46**: 337-365.

THOMPSON, D.A.W. (transl. by 1910) – *The Works of Aristotle.* Vol 4. Historia Animalium, Oxford.

TYNDALE-BISCOE, C.H. (1991) – Fertility control in wildlife. *Reprod. Fertil. Dev.*, **3**: 339-343.

TYNDALE-BISCOE, C.H. (1994) – Virus-vectored immunocontraception of feral mammals. *Reprod. Fertil. Dev.*, **6**: 281-287.

TYNDALE-BISCOE, C.H. (1995) – Vermin and viruses. Risks and benefits of viral-vectored immuno-sterilisation. *Search*, **26**: 239-244.

TYNDALE-BISCOE, C.H. (1997) – Summing up the conference. *Reprod. Fertil. Dev.*, **9**: 183-186.

WACE, N.M. (1986) – The rat problem on oceanic islands – research is needed. *Oryx* **20**: 79-86.

WHITTEN, W.K. (1966) – Pheromones and mammalian reproduction. *Adv. Reprod. Physiol.*, **1**: 155-177.

WHITTINGHAM, D.G. & M.J. WOOD (1983) – Reproductive physiology. In: *The Mouse in Biomedical Research Volume III – Normative Biology, Immunology, and Husbandry* (Eds. H.L.Foster, J.D.Small, & J.G.Fox), Academic Press, New York, 137-164.

WILLIAMS, C.K. (1997) – Development and use of virus-vectored immunocontraception. *Reprod. Fert. Dev.*, **9**: 169-178.

WILLIAMS, C.K. & L.E. TWIGG (1996) – Responses of wild rabbit populations to imposed sterility. In: *Frontiers of Population Ecology* (Eds. R.B. FLOYD, A.W. SHEPPARD & P.J. DEBARRO), CSIRO Publishing, Melbourne, 547-560.