FERTILITY CONTROL: AN OPTION FOR NON-LETHAL CONTROL OF WILD CARNIVORES?

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Three types of fertility control, surgical sterilization, hormonal chemosterilization, and immunosterilization, are reviewed with regard to their potential for controlling problematic populations of carnivores. The fertility control agent and delivery protocol of choice may vary considerably according to: (i) the reason for control; (ii) the degree, urgency and duration of population reduction required; (iii) concerns about ethics and public opinion; and (iv) the status, population dynamics, social structure, mating system, size, behaviour and reproductive endocrinology of the target animals. Although they are often perceived and advocated as more preferable methods of population control than lethal approaches, it is important that wildlife managers as well as members of the public realize that the ethical acceptability of the various fertility control techniques may differ considerably – and that numerous questions regarding their effectiveness, humaneness and ecological safety remain unanswered.

Keywords: *animal welfare, carnivore, contraception, fertility control, population control, wildlife management*

Introduction

Fertility control versus lethal control of carnivores

The control of wild or feral carnivore populations is often attempted in order to protect humans, domestic animals or native wildlife from the nuisance or predation they cause, as well as from the diseases they carry and spread (de Almeida 1987; William & McKegg 1987; Ginsberg & Macdonald 1990; Harris & Saunders 1993). Of all mammals, carnivores are second only to rodents as a target for control (Howard 1967). In principle, populations can be controlled by increasing mortality rate (lethal control), by reducing the birth rate (fertility control), or by reducing immigration and/or increasing emigration (eg by the use of repellents or scaring devices).

Classically, attempts have been made to control carnivores by lethal means. However, where lethal methods may be ineffective, impractical or unethical, it is desirable to explore alternatives. Non-lethal techniques are often viewed more favourably by the public than lethal approaches (Andelt 1987; Loague 1993; Curtis *et al* 1995; Fitzgerald *et al* 1996; Stout *et al* 1997). Control of wildlife via fertility control is being heavily promoted on the grounds that preventing births is a more sensible, humane, and ethical management approach than allowing young to be born

and later spending resources to capture and/or kill them (Oogjes 1997). Despite this growing consensus, there are numerous unresolved questions not only concerning the impact of birth control on the welfare of animals and the health of ecosystems (Gill and Miller 1993; World Health Organization 1993; Nettles 1997), but also regarding its effectiveness. Oogjes (1997) argued that effectiveness is also an important consideration from an animal welfare perspective, because the more effective a control method is the greater the reduction in the number of animals that will suffer.

Fertility control has been used successfully for the control of some insect pests by swamping the countryside with sterile but sexually active organisms (LaChance *et al* 1967; Spradbury 1994). However, whether the fecundity of a free-ranging carnivore (or indeed mammal) can be curbed sufficiently to cause a large population to decline, and to remain at low density for a prolonged period of time, still needs to be convincingly demonstrated (Bomford 1990; Tyndale-Biscoe 1994; Warren 1995). This might seem surprising, as sterilization has been advocated as a potentially more effective method of suppressing a population than killing the same number of animals (Knipling 1959; Kilgore 1967; Sturtevant 1970; Knipling & McGuire 1972; Marsh 1988; but see Bomford 1990; Garrott 1993; 1995; Swinton *et al* 1997). Knipling and McGuire (1972) even argued that the theoretical advantage of fertility control should be greater when applied to vertebrates instead of insects. Moreover, of the 10 mammals which pose problems to human interests in the UK reviewed by Smith *et al* (1995), the three best candidates for fertility control were all carnivores: the red fox , *Vulpes vulpes*, the European badger, *Meles meles,* and the feral cat, *Felis catus*.

The functional relationship between population growth rate and animal abundance typically follows a sigmoid curve, with the rate of growth being gradually limited by density-dependent factors (food, space, pathogens) as population size increases. When lethal methods are used, the population growth rate of the survivors soon becomes maximal due to the removal of density-dependent inhibitions (Howard 1967). Therefore, unless reduced in density to the lower portion of the sigmoid population growth curve, such populations quickly recover to levels that equal or even exceed the original carrying capacity (Batcheler 1968; Rowley 1968; Marsh 1988). It has been argued (eg Marsh & Howard 1973; Gao & Short 1993) that sterilization, on the other hand, could prevent this compensatory population growth. However, the arguments used in favour of fertility control need to be carefully evaluated.

Sterilized individuals may continue to compete with fertile conspecifics for food and mates, and, ideally, to defend territories from intruders. However, if fertility control is only partial or temporary (as is almost invariably the case), one can nevertheless expect similar, compensatory, density-dependent increases in the birth rates in the remaining fertile individuals, and decreases in the mortality rates in all animals present in the population. In fact, the mortality rate of sterilized animals may even be further decreased because they save on the energetic costs associated with reproduction (Goulet & Sadlier 1974; Caro 1986; MacWhirter 1991; Smith *et al* 1995; McShea *et al* 1997). As the cub:adult ratio will be lower in a fertility-controlled population, the relative potential for compensatory increases in fecundity could be great.

In addition, if the competitiveness of sterilized individuals is altered, the full effect of fertility control will not be realized (Knipling & McGuire 1972). If sterilization reduces libido, or upsets social hierarchies or spacing behaviour, it can even become ineffective for population control (Marsh & Howard 1973; Bomford 1990). As Caughley *et al* (1992) illustrated, the effect of a female sterilant on the production of offspring in a social group strongly depends on the dominance relationships among the females and how dominance is affected by sterilization. A good knowledge of (the effects of sterilization on) the social structure and mating system of the target species is thus essential for predicting the possible outcomes of fertility control attempts.

Stenseth (1981) and Hone (1992) demonstrated that the *potential* effects of reductions in fecundity are greater for *r*-selected species – characterized by small body size, short lifespan, short gestation, short birth interval, large litters, and a rapid rate of development (Pianka 1970) – than for *K*-selected species. Indeed, the *potential rate of reproduction* (ie if there are no environmental constraints) of a *K*-strategist is much less than that of an *r*-selected species. The intrinsic growth rates of carnivores with life history characteristics of *K*-strategists are likely to exhibit the non-linear, 'large mammal' type of functional response to density. This means that density-dependent effects only begin to constrain growth at high densities close to the carrying capacity of the habitat, while at low to medium densities net growth is directly proportional to abundance (Fowler 1981). Thus, only slight reductions in population density will quickly trigger maximal compensatory growth of the remaining population. However, in general, the proportion of the population that needs to be sterilized is higher for carnivores closer to the *r*-selected end of the spectrum as the magnitude of their compensatory growth is much greater than for *K*-selected species. This probably explains why Hobbs and Kirchner's (1993) model suggests that smaller animals (often *r*-selected species) require a larger proportion of the population to be sterilized than do larger animals (often *K*-selected species). As a general rule, the greater the species' potential for rapid compensatory growth following the removal of density-dependent inhibitions, the more intense any control strategy needs to be in order to maintain a sustained reduction in population size.

Matters are often not as simple as this. Fertility control might be rendered inefficient even in *K*-selected species because of several other complications. Undisturbed populations of *K*-selected species are more likely to be near the carrying capacity of their habitat, in which case mortality is usually highest among juveniles, with only a small proportion being recruited to the breeding population (Eberhardt 1977;1988; MacNab 1985). For such populations, fertility control is unlikely to reduce population density as long as the birth rate is higher than the recruitment rate (Bomford & O'Brien 1990). If it is not, sterilization may simply prevent the birth of young which would have otherwise died as juveniles. *K*-selected species also have a long life expectancy and a slow population turnover rate, which means that the impact of fertility control on population size will be gradual. Such a delay may be unacceptable for certain control objectives.

Although the relative effectiveness of lethal versus fertility control may differ for each situation and population, there do not seem to be many reasons to believe that fertility control would be more effective at reducing population density than lethal control. The main arguments in favour of fertility control must, therefore, be based on other grounds, such as ethical and public acceptability. These factors, however, will also be influenced by the perceived effectiveness of the method. Fertility control could also be of great value when used in conjunction with other control methods, for example, to prevent rapid recovery of populations already reduced by other or additional means, or to target bait-shy and genetically resistant animals which survive poisoning campaigns (Marsh 1988; Bomford & O'Brien 1990; Hone 1992; Garrott 1993;1995; Tuyttens & Macdonald in press). The control of wild or feral carnivores in urban areas may not be feasible by lethal means such as shooting and poisoning. Fertility control might offer an alternative for controlling populations in these refugia (R Short personal communication 1997). In addition, fertility control may cause less disruption of the social structure of the targetted population than lethal control (Tuyttens & Macdonald in press). For example, computer simulations indicate that the possible perturbation of the spatial organization of badger clans induced by lethal control could seriously reduce the success of such a strategy to control the spread of tuberculosis from badger to cattle (Swinton *et al* 1997).

The myth of the ideal carnivore fertility control agent

The ideal wildlife fertility control agent has been given a multitude of attributes (Marsh 1988; Kirkpatrick & Turner 1991; Seal 1991; Robinson & Holland 1995). Only two of these proposed attributes seem generally relevant: the agent should be highly effective, and environmentally benign. Other characteristics – such as ease and mode of delivery, effect on health, behaviour and social structure of the target animals, species-specificity, cost, reversibility, and duration of action – should also be considered but may vary according to situation, goals, and species (Dunbar 1993; Garrott 1995). We add two more considerations to this list. Firstly, from an animal welfare viewpoint, it could be argued that the fertility control agent should target the reproductive cycle as early as possible and ideally before conception takes place or the foetus is considered sentient (J Braeckman personal communication 1995; see below). Secondly, from a practical viewpoint, the timing of administration of the fertility control agent in relation to the reproductive state of the target animal should not be critical in order to be effective.

In this paper, three different types of fertility control – surgical sterilization, hormonal chemosterilization, and immunosterilization – are reviewed in the light of the above considerations and their applicability to the control of carnivores.

Surgical sterilization

Despite their efficacy, surgical methods of fertility control (eg removal of the gonads) are not practicable for the control of large populations of wild animals. Surgery is also irreversible (which may or may not be an advantage) and costly; and it may be associated with behavioural changes, risk of infection and the hazards of anaesthetics. The main disadvantage of surgical techniques for controlling large populations of wild animals, however, is that it requires the capture of the animals, which is often expensive, time-consuming, difficult – and stressful for the animal. Surgical techniques, however, could be the best choice to prevent reproduction of a small population of carnivores that are easy to trap, or which are being trapped for other operations.

Both sexes can easily be sterilized by quick and standard procedures. In order to minimize the effects on social behaviour, it is better to sterilize males by vasectomy (cutting both vas deferens) than by removing their testicles. Females are best spayed by tying off the oviducts at both sides. Tubal ligation and vasectomy did not affect territorial and pair-bonding behaviour in captive coyotes, *Canis latrans* (Zemlicka 1993); and neutered cats appeared to maintain their dominance status (Neville & Remfry 1984). Tubal ligation of dominant vixens in free-ranging fox groups seemed to affect neither their dominance status nor the size of their home ranges (Vertebrate Biocontrol Centre 1994). However, Saunders & McIlroy (1996) recently reported that the home ranges of sterile vixens overlap a lot, while those of intact vixens are generally exclusive. This apparent sharing of space by infertile vixens may increase the fitness of reproductive females, and, hence, reduce the impact of the control operation on population density.

Hormonal chemosterilization

There are many potential chemosterilants, but only a few seem suitable for the control of large populations of wild carnivores. This non-exhaustive review mainly concentrates on hormonal chemosterilants affecting either both sexes or only females, because these show most promise for the majority of carnivores. (Readers interested in non-hormonal and male-only chemosterilants are referred to other reviews, eg Kilgore 1967; Ericsson & Baker 1970; Jackson 1973; Cooper *et al* 1974; Farnsworth & Waller 1982; Kirkpatrick & Turner 1985; Marsh 1988; Bomford 1990; Kirkpatrick & Turner 1991.)

Oestrogens

Large doses of oestrogens, which are cheap and easily available, have long been used to prevent implantation following misalliance in dogs, *Canis familiaris*, and cats (Jackson 1953). Synthetic oestrogens have also been used frequently in attempts to control populations of many pest species. Diethylstilbestrol (DES) inhibits reproduction of coyotes (Balser 1964; Brushman *et al* 1967; Linhart *et al* 1968), red and grey foxes, *Urocyon cinereoargenteus* (Linhart & Enders 1964; Oleyar & McGinnes 1974; Allen 1982), American mink, *Mustela vison* (Travis & Schaible 1962), and possibly stoats, *Mustela erminea* (C Kim personal communication 1997).

DES is inexpensive, fat soluble, stable under temperature extremes, orally active, and has a far stronger antifertility action than natural oestrogens. However, its use is hampered because it requires precise timing in relation to the target animal's breeding cycle, has poor bait acceptance, and carcinogenic properties. Mestranol (MES) also affects reproduction in foxes (Oleyar & McGinnes 1974) but is of doubtful value for delivery via baits due to poor bait acceptance (Marsh & Howard 1969; Bomford 1990). Compounds that have a longer effect, such as quinoestrol and BDH 10131, may be superior to other synthetic oestrogens as they allow less frequent baiting (Marsh 1988; Bomford 1990). However, field trials on rats, *Rattus norvegicus*, did not suggest any practical value for quinoestrol as a control agent (Brooks & Bowerman 1971), and gave rise to doubts as to whether BDH 10131 was acting as a sterilant or a poison (Johnson & Tait 1983; Bomford 1990)

Because of the potential of serious adverse effects (eg thrombocytopenia, leukopenia, anaemia, pyometra, cystic endometrial hyperplasia, cystic ovaries), and the low margin of safety, oestrogens are no longer recommended as abortifacients for dogs and cats (Bowen *et al* 1985; Concannon & Meyers-Wallen 1991; Jöchle 1991; Munson 1993; Olson & Johnston 1993). Adding to this list the unacceptable behavioural changes that oestrogens may induce (Bartlett 1997), we do not recommend the use of this hormone for the control of wild carnivores.

Gonadotropin-releasing hormone (GnRH) agonists and antagonists

Continuing administration of high doses of a GnRH agonist, following an initial increase in gonadotropins, results in suppression of the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) (Concannon & Meyers-Wallen 1991; Olson & Johnston 1993). The duration and efficacy of the suppressive effects of GnRH agonists on ovarian, and especially testicular, function show considerable interspecific variation (Vickery *et al* 1984b;1989). In male dogs injected once a day with 10g kg^{-1} of a potent GnRH agonist for periods up to 42 days, spermatogenesis was partially reversibly suppressed at 10 days of treatment, and completely reversibly suppressed by 38 days. A similar daily dosage also caused long-term, reversible, suppression of oestrus in bitches (McRae *et al* 1985; Vickery *et al* 1989). A single injection of a GnRH agonist effectively suppressed testosterone levels for 2 months in seals (Atkinson & Yochem 1993). This approach might be feasible for the control of seasonal breeders, and should the suppression of socio-sexual and aggressive behaviours associated with this approach prove undesirable, the inhibition of sexual behaviour in males can be restored with testosterone supplements without reversing the antispermatogenic effects of these agents (Vickery *et al* 1984a).

GnRH antagonists may be superior to GnRH agonists as short-term male or female contraceptives because they are not associated with an initial increase in gonadotropins and have an immediate onset of action (Vickery *et al* 1989). The high dose required to prevent oestrous cycles and the need for constant injections (they are not orally bioavailable to any useful extent) pose serious practical problems. Although these problems can be partially alleviated by the use of controlled-release systems (Vickery *et al* 1984b;1989), this approach has little promise for

the control of large populations of wild carnivores (Kirkpatrick & Turner 1991). A single injection, in the mid-luteal phase, of a potent GnRH antagonist effectively terminated pregnancy in bitches. Efficacy was reduced when it was administered earlier in pregnancy, although this problem could be overcome by adding prostaglandin analogues (Vickery *et al* 1989). This technique, however, is still in its early development, is not species-specific, and little is known about its side-effects (Braakman *et al* 1993).

Prostaglandins

Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) and its analogues, by stimulating luteolysis and uterine contractions, successfully terminate pregnancies in bitches and queens (Concannon & Meyers-Wallen 1991; Jöchle 1991; Romagnoli *et al* 1993; Verstegen *et al* 1993a). Uterine contractions and cervical dilation probably underlie the abortion induced by $PGF_{2\alpha}$ (Braakman *et al* 1993). However, injections of prostaglandins failed to have any destructive effects on the corpora lutea of captive coyotes (Stellflug *et al* 1978). The side-effects (eg salivation, emesis, defecation, diarrhoea, hypothermia, and lethargy) caused by these compounds, the low margin of safety, the need for their repeated, high-dosage administration, and their variable efficacy depending on the stage of pregnancy, make this an in-house procedure unsuitable for fertility control of wild animals (Jöchle 1991).

Androgens

Twice-weekly oral administration of 25–50 mg of methyl-testosterone inhibits oestrus in bitches, and daily administration of 50mg for 90 days to male dogs decreased their spermatozoa output and mean testicular length (Freshman *et al* 1990). The synthetic androgen, mibolerone, is approved and marketed in the United States (in the form of a liquid solution to be added to feed) for effective, long-term, oestrus suppression in dogs without causing the objectionable masculinization seen with testosterone (Sokolowski & Zimbelman 1976; Kirkpatrick & Turner 1991). The administration of 6mg kg^{-1} day^{-1} for between 2 and 22 months to captive female timber wolves, *Canis lupus*, resulted in complete suppression of oestrus, but aggression towards cage mates increased (Gardner *et al* 1985). Several adverse effects in bitches treated with various doses of mibolerone have been reported (Olson & Johnston 1993). This drug is not recommended in cats (and other felids – Gardner *et al* 1985) because a safe, efficacious dosage has not been established, adverse effects (eg masculinization) can be seen even at lower dosages, and mortality can be expected with misuse or overdose (Concannon & Meyers-Wallen 1991). The need for repeated deliveries also limits its use to domestic animals and small, intensively managed, populations.

Synthetic progestins

These steroids act to prevent ovulation in female mammals (presumably by their inhibitory feedback on the pituitary hormones) and inhibit testicular activity in males (Johnson & Tait 1983; Bomford 1990). These drugs are frequently used to prevent pregnancy in domestic dogs and cats in Europe. They are available as injectable depot preparations (ie crystalline suspensions), or as tablets for daily use in the bitch or once-a-week treatments in the queen. Medroxy-progesterone acetate (MPA), chlormadinone acetate (CPA), delmadinone acetate (DMA), and proligestone are used as crystalline suspensions, and MPA and megestrol acetate (MA) are given in tablets (Concannon & Meyers-Wallen 1991; Jöchle 1991; Olson & Johnston 1993).

Long-term administration of MPA and MA has been practised to control feral cat populations with some success (Remfry 1978; McDonald 1980), and 25mg of MPA for 4 or 8 days during

the breeding season resulted in a significant reduction of litters produced by captive red foxes (Storm & Sanderson 1969). Silastic implants containing synthetic progestins inhibited reproduction in skunks, *Mephitis mephitis*, and solved the problem of the requirement for daily ingestion (Bickle *et al* 1991). Injectable MPA or silastic melengestrol acetate (MGA) implants caused long-term, but reversible, suppression of oestrus in captive African lions, *Panthera leo*, tigers, *Neofelis tigris*, leopards, *Panthera pardus*, jaguars, *Panthera onca*, and a variety of other carnivores (Seal *et al* 1976;1978; Tribe & Booth 1990). Similar MGA implants inserted into the neck muscles of free-ranging Etosha lionesses prevented pregnancy without altering pride (social) or individual behaviour (Orford *et al* 1988). However, the requirement for capture or for frequent oral dosing makes progestins impractical for use with most wild species (Bomford 1990). Progestins should be cautiously administered, following reports of adverse clinical signs in felids (Kollias *et al* 1984; Buergelt & Kollias 1987; Raphael *et al* 1990; Linneham & Edwards 1991) and other carnivores (Munson 1993). The more recent synthetic progestin, proligestone, is available as a canine contraceptive in Europe (Concannon & Meyers-Wallen 1991), and is replacing MPA as the injectable contraceptive of choice for many zoo carnivores such as dholes, *Cuon alpinus*, and jaguars, because of its presumed greater safety (Tribe & Booth 1990). Also worth considering for use in captive (or small populations of easy-to-trap/dart) carnivores might be the new generation progestins (desogestrel, gestodene and norgestimate), used as safer oral contraceptives for humans (Newton 1995).

Progesterone antagonists

These antagonists bind to the progesterone receptor, stabilize the receptor's structure by their high affinity, and thus prevent the progesterone from exerting its biological effect. Several hundred compounds with antiprogesterone activity have been synthesized (Van Look & von Hertzen 1995), but the most extensively studied progesterone antagonist is RU 486, also known as mifepristone (Roussel-Uclaf Laboratories, Paris, France). Mifepristone also binds to other steroid receptors, especially glucocorticosteroid (and androgen) receptors (Baulieu 1989; Van Look & von Hertzen 1995), but newer antiprogestins have been developed which are more selective for the progesterone receptor (Nie *et al* 1997). In dogs, the antiglucocorticoid effects of mifepristone are negligible at the therapeutic dose causing abortion (5mg kg^{-1}; Braakman *et al* 1993). Subjects only need to be exposed briefly to the drug when it is used for interruption of oestrous/menstrual cycle or pregnancy, and the effects are reversible. The bioavailabity of RU 486 is good (c 70%) after oral administration (Deraedt *et al* 1985), indicating a high absorbtion rate, and its half-life is of the order of 24h in humans. The efficacy of this compound for inducing abortions appears to depend on the species.

Gao and Short (1994a,b) reported that intermittent administration of RU 486 completely inhibited reproduction in wild mice, *Mus musculus*, and rats, without aversion against the oral bait being developed. Although the mechanisms are not always fully understood, mifepristone has also been shown to inhibit implantation in guinea pigs, *Cavia porcellus* (Batista *et al* 1991), ovulation in primates (Croxatto *et al* 1993), and to terminate both early and late pregnancies in humans. Its efficacy at interrupting early pregnancy in humans is influenced by the duration of pregnancy (Couzinet & Schaison 1988), and can be improved considerably by a combined therapy of RU 486 and prostaglandin analogues (Avrech *et al* 1991; Hutchinson 1993). The possible side-effects are predominantly not dangerous (but see Swahn & Bygdeman 1989).

Despite these promising results, the only carnivores which have been treated with mifepristone are the domestic dog and cat. Mifepristone has been reported as an effective abortifacient in the dog during early (Lavaud 1989) and late (Taverne *et al* 1989) pregnancy. Twice-daily oral administration of 2.5mg mifepristone kg^{-1} (for 4.5 days starting at day 32 of

pregnancy) terminated pregnancy in all five subjects within 3–4 days, without adverse side-effects (Concannon *et al* 1990). Pregnancies were also terminated after a single 8.3–40.0 mg kg^{-1} dose of RU 486 was given to bitches 26–36 days after the first mating. Abortions occurred within 2 to 11 days of treatment (Linde-Forsberg *et al* 1992). However, RU 486 does not appear to be very effective in terminating pregnancies in cats (Sankai *et al* 1991; Olson & Johnston 1993) and some other vertebrates (Nijk 1992). It has been argued that such species-specificity could be an advantageous feature of RU 486, and open to exploitation in order to reduce the problem of secondary effects following accidental ingestion by non-target species (Gao & Short 1993;1994a,b). Once-yearly administration of RU 486 during the gestation period could be sufficient to render seasonal breeders, such as badgers and foxes, infertile for a whole year. Its main advantage compared with some other abortifacients for use in wild carnivores is that precise timing of delivery relative to the stage of pregnancy does not seem to be critical; it prevents implantation, as well as early and late pregnancies.

Prolactin inhibitors

In many species, regulation of corpus luteum activity is influenced by both luteolytic (prostaglandin) and luteotrophic hormones. Both prolactin and LH can be luteotrophic but their roles in controlling the function of the corpus luteum vary among mammalian species (Rotchild 1981). LH is the principal luteotrophic factor in ruminants (Niswender *et al* 1985), pigs (Ziecik *et al* 1980) and horses (Roser & Evans 1983); whereas both LH and prolactin are necessary to maintain the corpus luteum in rats, dogs (Concannon 1980; Concannon *et al* 1987; Okkens *et al* 1985; Onclin *et al* 1993; Verstegen *et al* 1994), and cats in the second stage of gestation (Jöchle & Jöchle 1988; Verstegen *et al* 1993a,b). The prolactin inhibitor bromocriptine, administered during the second half of gestation (ie after week 6), caused abortion in 50 per cent (Wichtel *et al* 1990) to 91 per cent (Clinn *et al* 1985) of pregnant bitches. During the first half of gestation, however, the luteolytic effect of bromocriptine on prolactin was only temporary and not sufficient to interrupt gestation. Its use has also been curtailed by serious side-effects in a high percentage of cases.

The prolactin inhibitor, cabergoline (Agrimont SRL, Milan, Italy), a new ergoline derivative, is a more potent and long-lasting dopamine agonist than bromocriptine (Benedetti *et al* 1990). The main advantages of cabergoline compared with other dopamine agonists are its very simple administration schedule, high efficacy, long duration of action, wide margin of safety, and absence of severe side-effects. However, Bhatt *et al* (1991) reported that pleuropulmonary disease may occur. The high therapeutic index[1] (TI) of cabergoline (TI = 13 000) suggests that it has a low toxicity (Marks *et al* 1996).

It has been repeatedly reported during the last decade that small dosages of cabergoline reliably induce abortion in bitches and queens when administered during the later stages of gestation (Jöchle & Jöchle 1988;1993; Post *et al* 1988; Verstegen *et al* 1993b). Resorption, or expulsion, of the foetus induced by cabergoline typically takes place within 6 days of treatment, and is initiated through a stable drop of the plasma progesterone, causing luteolysis (Verstegen *et al* 1993b). Adverse side-effects, apart from occasional vomiting, have very rarely been observed (Post *et al* 1988; Jöchle *et al* 1989).

Cabergoline is easily administered orally in an oily solution or as a powder. Important in this respect is the study (Jöchle & Jöchle 1993) of a feral cat population subjected to daily oral treatment with 5–15 mg cabergoline kg^{-1} placed as a top dressing on fresh, canned, commercial food. The cabergoline carrier, an oily solution, seemed attractive to the cats. This product

[1] The lethal dose divided by the dose which retards neonatal growth by 50 per cent.

formulation never resulted in rejection or avoidance of the drug, even after multiple exposures over several years, and no adverse clinical or behavioural effects were observed in growing or mature, male or female animals. Continued observations of five queens after they had undergone repeated cabergoline-induced abortions, revealed that the effects of the drug were completely reversible (Jöchle & Jöchle 1993; see also Verstegen *et al* 1993a,b). However, cabergoline treatment during early or mid pregnancy, even at much higher doses and for prolonged periods, fails to cause abortions in dogs or cats indicating that the activity of their corpora lutea is either autonomous or regulated on a multifactorial basis during that stage of pregnancy (Concannon 1980; Concannon *et al* 1987; Okkens *et al* 1985). The other major reproductive function of prolactin becomes apparent when cabergoline is administered during the very late stage of gestation. Jöchle and Jöchle (1993) reported that if cabergoline treatment started as late as day 48.5 of gestation, and lasted 9 or more days, premature parturition (rather than abortion) occurred in cats. The kittens were born alive but died quickly because the mothers were unable to nurse, owing to inhibition of lactation and regression of the mammary glands 36–48 h after treatment. The possibility of this occurring must be minimized if the control of wild carnivores by cabergoline treatment is to obtain the consent of animal welfare organizations.

Strong support for the feasibility of a cabergoline baiting campaign to control free-ranging carnivores comes from a recent field trial to control the fertility of urban and rural red fox populations in Australia (Marks *et al* 1996). Baits containing 170µg cabergoline and 200mg tetracycline (acting as a biomarker), buried within a 50m radius of the dens, resulted in significantly reduced cub activity. Bait uptake was high (> 88%) but some vixens did not ingest the bait and successfully raised litters. Given the high palatability of cabergoline and the lack of bait aversion in foxes (Cowley 1993), the prospects for successful retreatment appear high. However, the study did not determine: (i) whether the reduced fertility was due to the induction of abortion (the more likely option according to the authors) or the termination of lactation; (ii) the dose required to induce sterilization; and (iii) whether the reductions in fertility were sufficient to cause a sustained population decline.

It appears that cabergoline could be a very potent carnivore abortifacient which could easily be included in an oral bait. The dosage required appears to be roughly 10 times less than that of RU 486. However, prolactin inhibitors will only induce abortions in those species in which prolactin is a crucial luteotrophic hormone during pregnancy, and have to be administered during the right stage of pregnancy. If given too early, they are unlikely to have an effect. If given too late, there is an ethical problem, in that young will be born prematurely and die from starvation as their mothers are unable to lactate. Great caution is also required with the use of cabergoline baits because of the dramatic effects they could have on non-target animals. Prolactin is not only necessary for the maintenance of lactation in all mammalian species, but is also involved in more than 85 biological functions in various vertebrate species (Djiane & Kelly 1993). In practical terms, this means that the ethical acceptability of the use of cabergoline for carnivore control is problematic unless the delivery protocol is such that bait uptake by females at the wrong stage of pregnancy and by other non-target animals can be prevented.

Immunosterilization

Immunological techniques of population control consist of the development of a vaccine that immunizes the target animal against one of its own reproductive hormones or tissues, thereby producing sterility. Immunosterilization can be aimed at specific molecules in the reproductive process, including hypothalamic peptide-releasing hormones, pituitary gonadotropic hormones, or sperm or egg receptor molecules necessary for fertilization. Pre-ovulatory or pre-

spermatogenic mechanisms, or the embryo can also be targetted. Direct immunological intervention of reproductive steroids with steroid-protein ligands is not biologically sound because almost all somatic cells contain cytosol receptors for steroids, and broad biological consequences can result (Kirkpatrick & Turner 1991). Immunosterilization is still in the early stages of its development, and most information comes from studies on domestic and laboratory animals, and humans.

Immunization against gonadotropins or GnRH

Active immunization of rats and rabbits, *Oryctolagus cuniculus*, with ovine or bovine LH, or passive immunization with anti-LH antisera, results in reduced gonadal function and fertility (Stevens 1986). Dogs can also be immunized against endogenous LH by injection of bovine LH mixed with an adjuvant (ie a substance which increases the immunogenicity of antigens when administered with them). However, the adjuvants used (in particular, Freund's Complete Adjuvant) have produced abscesses and inflammatory reactions (Nettles 1997), and the duration of the effect of the immunologic contraceptive has been highly variable (Faulkner *et al* 1975).

It has been argued that GnRH is one of the most promising candidates for immunocontraception in dogs (Gonzalez *et al* 1989), and various wildlife species (Miller *et al* 1993). However, because the GnRH molecule is not very immunogenic, it cannot induce an antibody response unless it is altered in some way to allow recognition as a foreign antigen. Analogues of, or native, GnRH have therefore been conjugated to a variety of carrier proteins to raise GnRH sera (Millar *et al* 1984). Both sexes of several species have been immunized with these conjugates with variable success (Gonzalez *et al* 1989; Stelmasiak & Van Mourik 1990). Gonzalez *et al* (1989) demonstrated that immunization against GnRH, conjugated to the carrier protein, keyhole limpet haemocyanin, and using threonyl muranyl dipeptide as an adjuvant, can have a contraceptive effect in dogs. The physiological effects of antibody titres against GnRH include suppression of reproductive behaviour of males and females, suppression of synthesis and secretion of gonadotropins and steroid hormones, gonadal atrophy and the associated arrest of gametogenesis. Immunization of male dogs against their own GnRH with GnRH conjugated to human serum globulin results in depressed plasma testosterone, LH and sperm counts (Hassan *et al* 1985).

The suppression of reproductive behaviour in males and females, as well as other behavioural changes which may be associated with this technique, however, are unwanted side-effects in most cases of carnivore population control (but see Stelmasiak *et al* 1993). In males, testosterone may be added in order to maintain normal behaviour (Ladd *et al* 1988; 1989). The vaccines against these hormones are neither orally active (Bomford 1990) nor species-specific (Sutherland *et al* 1996). Immunization against GnRH and gonadotropins therefore appears to be inappropriate for the control of most wild or feral carnivores.

Immunization against gametes

Immunologic interruption of fertilization can be achieved by raising antibodies against sperm, or against the ovum protein receptors for sperm. Immunization against ovarian antigens was first proposed by Ownby and Shivers (1972), who found that rabbits exposed to hamster ovary tissue produced antisera that precipitated zona pellucida (ie the extracellular matrix surrounding growing mammalian oocytes, ovulated eggs and early embryos) preparations in vitro, and blocked fertilization. A crude antigen, prepared by mechanical separation of zona pellucida (ZP) from ova collected around the time of ovulation, produces antibodies which interfere with fertilization of immunized animals (Dunbar 1983). One of the three glycoproteins that make up the ZP is ZP3, which appears to mediate the initial binding of the sperm to the ZP. Binding of

sperm to the zona is relatively species-specific, despite a high level of conservation of zona proteins among mammals (Epifano & Dean 1994). Injection of raw ZP protein or ZP3 causes the female to raise antibodies against the sperm receptors, and renders the ovum unrecognizable and impervious to sperm cells. Alternatively, antibodies may be interfering with folliculogenesis to prevent the maturation of ova, thereby resulting in infertility. Allo-immunization with ZP glycoproteins of the same species does not elicit a significant immune response, whereas hetero-immunization with the ZP glycoproteins of a different mammal elicits a dramatic immune response, including the production of antibodies that recognize the 'self' determinants of the ZP (Maresh & Dunbar 1987; Skinner *et al* 1987). Although other components of the unfertilized egg may also be targets for immunocontraception, it appears that the zona proteins provide the best and most physiologically accessible components of the female gamete for targetting as immunocontraceptive antigens (Holland & Jackson 1994).

Brown *et al* (1996) reported that a single injection of soluble intact ZP caused long-term fertility reduction in grey seals, *Halichoerus grypus*. Immunization with antigens of pig ZP has been demonstrated to induce infertility in dogs (Gwatkin *et al* 1980; Shivers *et al* 1981; Mahi-Brown *et al* 1982; Dunbar 1983) and some zoo carnivores (Asa 1993; Kirkpatrick *et al* 1993). However, bitches immunized with the porcine preparation showed persistent increases in serum concentrations of oestrogens, and a prolonged (pro)oestrus. This is not only an undesirable side-effect (Mahi-Brown *et al* 1985) but also puts them at risk of various disorders (Olson & Johnston 1993). Not only may ZP proteins cause auto-immune inflammation of the ovary (oophoritis), but species-specific regions on the appropriate genes are also rare or not very antigenic (Skinner *et al* 1984; Rhim *et al* 1992; Naz *et al* 1995).

Although higher antibody concentrations may be needed (Muller *et al* 1997), immunological interruption of fertility can also be achieved by vaccination with an antigen causing the female and/or male to produce antibodies against sperm. One advantage of this approach is that it is feasible to develop vaccines with good target specificity, as some sperm proteins display a high degree of species- and tissue-specificity. Smith *et al* (1995) contend that sperm-specific proteins represent the best candidates as antigens for species-specific contraceptive vaccine development. Naz *et al* (1995) reason that the feasibility of this promising approach is based on two lines of evidence. Firstly, the presence of anti-sperm antibodies in the male or female has long been recognized as a cause of involuntary infertility that is difficult to treat (Holland & Jackson 1994; Robinson & Holland 1995). The second line of evidence is provided by the experimental demonstrations of the contraceptive potential of sperm antigens in male or female animals of various species. The sperm antigen PH-20 was identified in hamster sperm (Primakoff *et al* 1988), and SP-10 has been located on sperm from humans and other primates, and pigs (Herr *et al* 1990). Both antigens can be injected into the female or male, which then produce antibodies against sperm, preventing fertilization without interfering with hormones or behaviour. Other sperm antigens that have been proposed and investigated as candidates for immunocontraception have been reviewed by Bradley and Reed (1990), Holland and Jackson (1994), and Naz *et al* (1995). Although a number of red fox sperm antigens have been identified, cloned, and characterized for tissue- and species-specificity (Bradley 1994), to our knowledge, none of these sperm antigens have been tested on wild carnivores.

Immunization against implantation and gestation

Implantation or gestation are other potential stages of the female reproductive cycle that can be targetted. This could be accomplished by immunization against trophoblast- (placental) specific products, or proteins produced by the embryo which have a vital role in the establishment and maintenance of pregnancy (Anderson & Alexander 1983; Anderson *et al* 1987; Naz *et al* 1995).

The most advanced work in this area is concerned with the development of a vaccine directed against human chorionic gonatotrophin (HCG), a hormone produced by the pre-implantation embryo and essential for successful implantation and the establishment of early pregnancy (Griffin 1994). Clinical testing on a number of prototype vaccines showed no adverse side-effects, and more trials are planned to further assess the efficacy, acceptability, and potential to offer long-term (12–18 months) protection following a single injection. A vaccine against HCG prevented pregnancy in more than 80 per cent of immunized women and it has been suggested that a similar vaccine could be developed to control feral horses (Stevens 1990). Immunization in rabbits against their uterine protein, uteroglobin, is also under investigation (Taussig 1993).

Such vaccines have the potential advantage of being species-specific and of provoking a specific immune response without interfering with the endocrine system and hence social behaviour (Nie *et al* 1997). Moreover, since implantation is not completed, and pregnancy not started, anti-HCG vaccines are not considered to be abortifacients (Griffin 1994). Arguably, targetting such a relatively late stage of the reproductive cycle could be a more efficient strategy, as mothers will have invested more heavily in reproduction, and the potential for compensatory increases in their own (or other females') fecundity might be minimized. Smith *et al* (1995) reported that immunological inhibition of implantation (or gestation) is particularly promising for the control of animals with delayed implantation. However, much fundamental work is required before this approach could be applied to wild carnivores.

Delivery systems

A major difficulty for fertility control of free-ranging carnivores is the delivery of the vaccine or chemosterilant to the target animals, which often requires intramuscular injection. Kreeger (1993) reviewed the characteristics of remote delivery systems for the administration of contraceptives to wildlife. Powered guns, bows and blowpipes, for example, can be used to deliver a dart or a biobullet containing the agent. The remote delivery of pig ZP vaccine by darts fired from a capture gun has been successfully applied to control large mammals (Kirkpatrick *et al* 1990; Kirkpatrick & Turner 1991; Turner *et al* 1992). However, the need to dart each inoculated animal again with follow-up booster injections hampers its widespread use for free-ranging wildlife control. A single-dose vaccination – making use, for example, of mechanical or osmotic pumps, or diffusional or chemically controlled systems to provide a timed release of the agent (as discussed by Kreeger [1993]) – might prove effective in the future. However, the application of such a technique is less appropriate for controlling large populations of free-ranging carnivores, and particularly so for small, shy, nocturnal, species.

Although a variety of automated delivery systems have been suggested (Stelmasiak & Van Mourik 1990), the delivery of an orally active (and preferably species-specific) agent by bait has been argued as a feasible (Ruprecht 1993) or the best (Smith *et al* 1995) option for fertility control of free-ranging carnivores. Baits of various types have been used to deliver toxicants, vaccines or chemosterilants to wild carnivores (Linhart 1993), and techniques for the distribution of these agents by hand or aircraft have been reviewed (Johnston *et al* 1993; Ruprecht 1993). The control of rabies in foxes in Europe (and North America) by oral bait vaccination has provided much expertise (Boyle 1994). The requirements of vaccines and bait-delivery systems for the control of rabies (Perry 1989) are largely similar to those for immunosterilization (Smith *et al* 1995).

Adjuvants such as liposomes (Michalek *et al* 1992) and cholera toxin β-subunit (Black *et al* 1987) have been shown to enhance the immunogenicity of oral vaccines. Other delivery systems enhancing the immune response have been reviewed by Alexander and Bialy (1994) and Smith *et al* (1995). To date, immunizations with single hormone or gamete antigens have resulted in

about a 70 per cent response level, while it has been suggested that the use of several antigens together (or sequentially) may improve this figure significantly (Alexander 1994).

With the recent developments in reproductive immunology and molecular virology, the use of micro-organisms, expressing species-specific gamete antigens which spread through the target population by sexual transmission, by contagion, or by arthropod vector, is now theoretically possible. Infected animals would be rendered sterile and a large proportion of the population would be reached without interfering with the steroidal functions of the gonads in the animal (Tyndale-Biscoe 1994). The latter aspect is believed to be particularly important for species, such as many carnivores, with a highly structured social system, in which levels of sex hormones can influence rank order in the social hierarchy and where this is closely linked to reproductive success. There are many essential – and desirable – characteristics required of the bacterial or viral vector for immunosterilization (Shellam 1994). For example, the vector must be species-specific, naturally infect target species, and be capable of carrying DNA encoding for the reproductive immunogen as well as promoters to express the foreign gene and cytokines to enhance its effectiveness (Tyndale-Biscoe 1994).

The myxoma virus has been claimed as a suitable vector for immunosterilization in rabbits as it has been circulating exclusively in rabbit populations for more than 40 years (in Australia) and as it can carry additional DNA (Tyndale-Biscoe & Jackson 1990; Tyndale-Biscoe 1991;1994). The ideal is to construct a recombinant myxoma virus containing a gene encoding a gamete antigen which is essential for reproduction. This virus will then be transmitted throughout the rabbit population by its host vectors, and rabbits infected by this means will raise antibodies against the gamete antigens, thus rendering them infertile. Potential constraints of this method include the requirement that the virus is readily transmitted between individuals and that the virus only infects the target population. Such a virus, once released into the environment, could not be recalled, could be exported to countries where rabbits are not considered pest species, and could have an uncertain outcome. Tyndale-Biscoe (1994) concluded that such a high risk/low cost fertility control strategy would not be suitable if the target species is a desirable animal, rather than a pest species. Such judgements, however, can vary radically from place to place. Given the poor knowledge of their impact and consequences, the use of recombinant viral vectors expressing antigens that are directly (ie via an arthropod) or sexually transmitted through the target population must therefore be viewed with extreme caution.

One alternative that may carry fewer risks, might be to use recombinant viral or bacterial vectors containing genes encoding gamete antigens, which cannot be transmitted through the population but are delivered to the target animals in a bait. This approach has been evaluated for use in red fox control in Australia (Bradley 1994). Recombinant vaccinia viral vectors and attenuated strains of *Salmonella* bacterial vectors are being assessed as possible vaccine delivery systems for inclusion in a bait. However, neither these vectors, nor the antigen are fox-specific. It is, nevertheless, worthy of further investigation as the immunization persistence within the target species is an important advantage of live subunit vaccines (Connell *et al* 1992; Smith *et al* 1995).

Conclusions

All three types of fertility control – surgical, chemo- and immunosterilization – have been shown to be able to suppress fertility in at least some species of carnivores, but no single method has yet demonstrated its potential to cause the sustained decline of a large natural population. There is no single fertility control agent that is ideal for all carnivores or every situation. The choice of fertility control agent and delivery system is interrelated, and depends on the objectives and

urgency of the control operation, the abundance, size, population dynamics, social structure, mating system, endocrinology and behaviour of the target animals, ethical considerations and public opinion. Although these variables may vary considerably for each population of carnivores that needs to be controlled, a few generalizations can nevertheless be made.

For the control of captive or small populations, where it is feasible to trap or capture a sufficient proportion of the animals, surgical sterilization, hormonal implants, or intramuscular injection of the sterilant could be used. If the population consists of a small number of large, diurnal carnivores, remote delivery of a vaccine by darts fired from a gun might also be possible. Of course, in these cases the fertility control agent does not have to be species-specific or orally active, and the dose administered can be controlled. If the demographic status of the target species is such that its reproductive and genetic integrity should be preserved (eg an endangered species), surgical sterilization is not recommended, but, instead, a control agent should be used that is reversible and has a controllable duration of action. Costs can be argued to be a secondary concern.

For larger populations, or for carnivores which are difficult to capture or dart, the widespread distribution of the fertility control agent is a major problem. The use of recombinant viral vectors containing gamete antigens that spread through the target population via sexual transmission, contagion, or an arthropod vector has been suggested as a very low-cost delivery system to control undesirable pest species (Tyndale-Biscoe 1994). However, because of the high risk and uncertain outcome associated with the release of such a micro-organism into the environment, we recommend extreme caution in considering this approach for wild carnivores.

For some species of carnivores that live, nest, or sleep underground, aerosol administration of a vaccine into the setts or holes may be feasible and worthy of further investigation (Hughes & Roger 1994). However, oral delivery of the chemosterilant or the (live subunit) vaccine by bait appears to be the preferred, if not the only, option to control the fertility of large populations of the majority of wild carnivores. The bait-delivery protocol will have to be optimized, so that bait uptake is maximized for target animals and minimized for non-target animals. The prerequisites of the fertility control agent to be included in the bait are more stringent. It should be orally active and not induce aversion even after long-term use. Its therapeutic dose should not only have a wide range, but should also be much smaller than its lethal dose, so that if more than one bait is consumed the animal will still be effectively sterilized without suffering from any adverse side-effects. Finally, if the delivery protocol cannot exclude bait uptake by non-target animals, the fertility control agent should be species-specific. In these cases in particular, immunosterilization might be the preferred approach as some antigens (sperm antigens in particular) have a high degree of both tissue- and species-specificity when compared with hormonal chemosterilants. The relatively simple digestive tracts of carnivores are believed to facilitate oral delivery of antigens (Smith *et al* 1995). However, if control is urgent, there may not be enough time (or money) to develop the appropriate technology, and using the existing hormonal chemosterilants might be the only option.

The choice of fertility control system and the timing of its application also depends on the social structure, mating system and endocrinology of the target species (and sometimes even of non-target species). In strictly monogamous or polygynous species, sterilizing males could be a successful strategy. However, in most carnivore species a single male cannot monopolize matings. Sterilizing a proportion of the male population will not have a big impact on the fecundity of the females when only a small number of fertile males can successfully impregnate many females. Females (or both sexes) should be sterilized instead. If it is known that reproduction is restricted to a minority of dominant females or males, it might be sufficient to selectively sterilize only these dominant individuals. This will only be feasible for small, well-

known populations. This approach will also be ineffective if the sterilized animals lose their dominant position within the group, and can no longer suppress reproduction by conspecifics.

Compensatory natality by non-sterilized individuals can be minimized, by targetting a later stage of the reproductive cycle than that at which female-female competition or other density-dependent factors have had their main suppressive effect on reproduction. Arguments in favour of blocking the reproductive cycle as late as possible, in order to minimize compensatory natality, may come into conflict with the (pathocentric) ethical viewpoint that abortifacients should destroy a foetus before it is believed to be sentient being (see below). Such ethical considerations are important in the formation of the public opinion.

If density-dependent factors exert their inhibitory effect mainly after parturition (ie on juvenile survival), fertility control may not have much impact on the number of offspring produced that reach sexual maturity. In this respect, lethal control could be more efficient (as it allows the targetting of later stages of the reproductive cycle than is possible with fertility control). Indeed the most efficient strategy in such situations would be to kill offspring just before they reach sexual maturity. Such offspring are not only more valuable because they have survived all other threats so far, but will also have continued to compete with other conspecifics for food and space. In addition, their mothers, having invested heavily in lactating for and rearing their offspring-to-be-killed, may have foregone their chances of producing another litter in the near future.

The optimal timing of fertility control depends on many other factors which should be carefully considered for each species and situation separately. For example, targetting pregnancy is a particularly promising strategy for species where the target carnivore delays implantation so that the females become pregnant only once a year during a short and well-defined season. If this season is not in synchrony with the gestation period of any other non-target animal that might consume the bait, the orally delivered abortifacient may even not have to be species-specific.

The efficacy of the fertility control agent, the characteristics of the delivery system, control objectives, bait acceptance and population dynamics (eg population turnover rate, dispersal rate, and so on) will determine the intensity and scale of the control operation. The consequences of sterilization for the target species, and its ecosystem will have to be evaluated. Computer models could be useful in helping to determine the proportion of animals that should be sterilized (given that reliable demographic parameters are available). Regular monitoring of the population should be an integral part of any control strategy. Resistance against sterilization can be expected to evolve in the long term, and its consequences should not be underestimated (Sherwin 1990). The carnivores for which control can most fully be justified are generally also the most robust and flexible ones.

Animal welfare implications

Moral justification for controlling wildlife can be sought in arguments concerning both ecosystem conservation and individual welfare. The well-being of ecological communities predominates, for example, in calls to control the introduced red fox in Australia where it contributes to the extinction and decline of native species. Concern for individuals has been invoked to justify, for example, the control of skunks and racoons, *Procyon lotor,* in North America where they are important reservoirs of the rabies virus, posing a threat to human and animal health. Although complaints against carnivores often are exaggerated, many attempts have been made to reduce their abundance, usually by lethal control methods (Ginsberg & Macdonald 1990). Non-lethal methods such as fertility control are often perceived and promoted as ethically preferable to lethal methods. However, such labelling can be misleading; the ethical

acceptability of each method should be evaluated individually and then compared with alternative techniques.

We suggest the use of the same two moral considerations to help determine the ethically preferred method of population control. On the one hand, control should aspire to have minimal risks of disturbing valuable ecosystems, and on the other hand it should inflict as little suffering as possible. The debate over the release of genetically modified organisms for pest management illustrates how concerned the public and scientific community is, and should be, about safeguarding the interests of non-target animals and ecological communities (World Health Organization 1993; Sutherland *et al* 1996; Williams 1997). The animal welfare argument is most often used in favour of fertility control. However, fertility control methods may differ significantly in this respect too.

As a crude rule, the earlier fertility control is accomplished, relative to the female's reproductive stage, the better from an animal welfare viewpoint. Thus, contraceptives are preferable to abortifacients, and abortifacients interrupting pregnancies at an early stage should be preferred to late-acting abortifacients. In fact, there are no 'pathocentric' moral issues involved up to the stage where the foetus is believed to be a 'sentient' being (ie capable of experiencing pain and pleasure). At the other extreme, targetting young before they reach sexual maturity is also seen by some as a fertility control method (Sutherland *et al* 1996), and ethical justification is sometimes sought in the high rate of natural juvenile mortality. Here, we consider targetting young animals as lethal control but, however it may be defined, we have misgivings about the justification of human interventions on the basis that they parallel what occurs in nature. Human interventions require ethical justification, whereas what happens naturally does not. Too often the health problems at the level of both the individual and the population, and the long-term consequences associated with the administration of a sterilant, are inadequately known. Nettles (1997), for example, expressed concern that as animals with poor immune responses would be affected less than animals with good immune responses, immunosterilization could artificially select for immunocompromised animals which are more susceptible to diseases. Oogjes (1997) emphasized that relative effectiveness is also a crucial criterion for ethical acceptance of a certain control method; if it is effective in reducing the target population it will lead to a reduction in the total number of animals suffering.

To conclude, the ethics of using a specific method of population control will depend on its humaneness, environmental safety and its effectiveness as compared with the other methods available; and on the consequences of doing nothing. Despite there being ethical grounds for favouring fertility control (Singer 1997), anthropocentric considerations may complicate the judgement, particularly if the target species has commercial value. The controversial trials of fertility control among African elephants, *Loxodonta africana*, in the Kruger National Park are the focus of criticism from supporters of sustainable culling which provides income through the sale of elephant products and hunting licences (Koch 1996).

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