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Chapter 10

Novel Management Methods: Immunocontraception and Other Fertility Control Tools

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Impacts of overabundant ungulate populations on human activities and conservation include crop and forestry losses, collisions with vehicles, disease transmission, nuisance behaviour, damage to infrastructures, predation on livestock and native species, and reduction of biodiversity in plant and animal communities (e.g. Curtis et al., 2002; Massei et al., 2011; Reimoser and Putman, 2011; Ferroglio et al., 2011; Langbein et al., 2011).

Current trends in human population growth and landscape development indicate that human–ungulate conflicts in Europe, as well as in the United States, are likely to increase in parallel with increased expansion in numbers and range of many of these species (Rutberg and Naugle, 2008; Brainerd and Kaltenborn, 2010; Gionfriddo et al., 2011a). Many of these conflicts have been traditionally managed by lethal methods. However, current trends in distribution and numbers of wild boar, feral pigs and deer in Europe and in the United States (e.g. Sacz-Royuela and Telleria, 1986; Waithman et al., 1999; Ward, 2005; Apollonio et al., 2010) suggest that recreational hunting is not sufficient to control ungulate densities. In addition, ethical considerations regarding humane treatment of animals are increasingly shaping public attitudes about what are considered acceptable methods of mitigating human–wildlife conflicts, and lethal control is often opposed (Beringer et al., 2002; Wilson, 2003; Barfield et al., 2006; McShea, 2012).

Public antipathy towards lethal methods increasingly constrains the options available for ungulate management, particularly in urban and suburban areas and in protected areas where culling is often opposed on ethical, legal or safety grounds (Kirkpatrick et al., 2011; Boulanger et al., 2012; Rutberg et al., 2013). Consequently, interest in non-lethal methods, such as translocation or fertility control, has increased (Fagerstone et al., 2010).
Reviews of translocations of problem wildlife as a mechanism for reducing human–ungulate conflicts concluded that this method may cause significant stress, increase mortality and traffic accidents, is relatively expensive and has the potential to spread diseases and pathogens (Daszak et al., 2000; Corn and Nettles, 2001; Conover, 2002; Beringer et al., 2002; Massei et al., 2010a). Examples of translocations of pathogens and hosts include the spread of bovine brucellosis and bovine tuberculosis following the translocation of bison (Bison bison) in Canada (Nishi et al., 2006), the potential spread and dissemination of diseases such as the Aujeszky’s disease virus following the translocation of wild boar between hunting estates in Spain (Ruiz-Fons et al., 2008) and warble and nostril flies spread to conspecifics by caribou (Rangifer tarandus) after translocation of animals from Norway to Greenland (in Kock et al., 2010).

Fertility control is often advocated as a safe, humane alternative to culling for managing overabundant wildlife (Fagerstone et al., 2010; McLaughlin and Aitken, 2011; Kirkpatrick et al., 2011). Early attempts to use fertility control to manage ungulates failed for reasons that included toxicity of the drugs used, transfer of these drugs to the food chain, manufacturing costs and the fact that repeated applications of contraceptives were required to induce long-term infertility (Gray and Cameron, 2010; Kirkpatrick et al., 2011). In the last two decades, a reawakened interest in alternatives to surgical sterilisation for companion animals and livestock has led to the development of novel fertility control agents (Herbert and Trigg, 2005; Naz et al., 2005; Massei et al., 2010b). In parallel, several fertility control agents have emerged for wildlife applications.

In this chapter we provide a comprehensive, critical overview of fertility control to mitigate human–ungulate conflicts. In particular, we discuss the availability and use of fertility control agents in ungulates, we review delivery methods for these agents, we provide a synthesis of the conclusions of empirical and theoretical studies of fertility control applied to populations and we offer suggestions to guide decisions regarding the suitability of fertility control to mitigate human–ungulate conflicts.

### 10.1 Fertility inhibitors for ungulates

#### 10.1.1 Fertility control and reproduction

Chemical fertility control can be achieved through contraception or sterilisation. Contraception prevents the birth of offspring but maintains fertility, whilst sterilisation renders animals infertile (Kutzler and Wood, 2006). In mammals, the series of events that leads to ovulation and spermatogenesis begins in the brain, where gonadotropin-releasing hormone (GnRH) is produced in the hypothalamus. GnRH is transported through small blood vessels to the anterior pituitary gland, where it binds to GnRH receptors to stimulate the release of the pituitary gonadotropins, LH (luteinizing hormone) and FSH (follicle-stimulating hormone) (Figure 10.1).
These gonadotropins in turn stimulate the synthesis and secretion of sex hormones such as oestrogen, progesterone, and testosterone which are responsible for ovulation, spermatogenesis and sexual behaviour. The reproductive cycle and the production of eggs and sperm can be disrupted by administration of substances that interfere with the hypothalamic–pituitary–gonadal axis by blocking the synthesis, release or actions of hormones produced by the hypothalamus, the pituitary gland, or the testes and ovary. In females, a further target for contraception is the zona pellucida (ZP), a protein coat that surrounds the ovulated egg and allows species-specific sperm recognition and fertilization. In males, sterilisation can also be achieved by chemicals that cause testicular sclerosis and permanent sterility (Crawford et al., 2011). The following section presents a brief overview of fertility control agents commercially available or widely tested on ungulates. Taking into account field applications, the review includes only those drugs that induce infertility for at least 6–12 months following administration of a single dose.

The majority of the fertility inhibitors reported in the literature target females, although some are effective for both genders and a few have been specifically developed for males. In many ungulate species the mating system is promiscuous, thus requiring extremely high levels of male sterility for fertility control to have any effect at the population level. For instance, in feral horses (Equus caballus) breeding still occurred even when 100% of the dominant harem stallions were sterilized (Turner and Kirkpatrick, 1991; Garrott and Siniff, 1992). In addition, some contraceptives may affect secondary sexual characteristics such as antler development (see later sections) and their use is not recommended for male deer.
A fertility control agent suitable for field applications should ideally have the following characteristics (Turner and Kirkpatrick, 1991; Fagerstone et al., 2002; Massei and Miller, 2013):

1. Nil or acceptable side effects on the target animal’s physiology, behaviour and welfare, including no interference with pre-existing pregnancy or lactation
2. Effective for at least one reproductive season when delivered through a single, injectable dose or implant, or when administered in one or multiple oral doses
3. Render all or the majority of treated animals infertile
4. Inhibit female reproduction but ideally prevent reproduction in both sexes
5. Relatively inexpensive to produce and deliver
6. No effect on any food chain
7. Species specificity
8. Stability under a wide range of field conditions.

Although none of the fertility control agents currently available meet all the above features, several exhibit many of these characteristics.

10.1.2 Hormonal contraceptives
Synthetic progestins such as norgestomet, melegestrol acetate (MGA), megestrol acetate (MA) and levonorgestrel have been widely used in zoo animals, livestock and wildlife. By binding to progesterone receptors, synthetic progestins disrupt ovulation and egg implantation in females and impair spermatogenesis in males (Asa and Porton, 2005). For instance, norgestomet, administered to white-tailed and black-tailed deer, caused infertility in 92–100% of the females for at least one year (Jacobsen et al., 1995; DeNicola et al., 1997). These drugs may cause abortion, although this effect depends on progestin type, species, dose and time of administration during pregnancy (Waddell et al., 2001; Asa and Porton, 2005). MGA did not affect pregnancy in several ungulate species, but delayed or prevented parturition in treated white-tailed deer (Plotka and Seal, 1989; Asa and Porton, 2005). Progestin implants, with an estimated duration of efficacy of ≥2 years, have been widely used for suppression or synchronisation of oestrus in cattle and they have been employed as contraceptives in zoos for about 20 years. MA implants induced infertility in female mountain goats for at least 5 years, with reproduction recorded in 10% treated goats against 68% untreated controls (Hoffman and Wright, 1990).

Implants containing different concentrations of steriods such as ethinyloestradiol (EE), and progesterone (P) have been successful in preventing pregnancy in feral mares. Suppression of ovulation appeared to be inversely related to the concentration of EE used in the implant. The percentage of animals ovulating after 2 years was 12–20% for groups that had received a combination of P and EE or the highest dose of EE respectively, against 100% for control mares; pregnancy rate for the same groups was 0% for both P+EE and EE and 100% for control females. All animals that were pregnant at the time of contraceptive treatment delivered normal foals. The results demonstrated effective contraception of feral mares for up to 36 months without compromising pregnancy (Plotka et al., 1992).
Another group of hormones widely used as contraceptives are the gonadotropin-releasing hormone (GnRH) agonists: these are synthetic peptides that mimic GnRH and stimulate the production and release of FSH and LH. Chronic administration of these drugs (e.g. >4 weeks) results in a downregulation of the pituitary gland and suppression of the secretion of FSH and LH. However, immediately following administration, a ‘flare up’ effect often occurs that can stimulate oestrus in females and cause temporary enhancement of testosterone and semen production in males (Patton et al., 2007). As agonists have a higher affinity for and do not quickly dissociate from the GnRH receptors, the ‘flare up’ is followed by prolonged oestrus inhibition and infertility (Gobello, 2007) as long as the drug is present. The effectiveness of GnRH agonists depends on type of agonist, release system, dose rate and duration of treatment (Gobello, 2007; Patton et al., 2007). The side-effects are equivalent to gonad removal but are reversible; however, GnRH agonists may cause abortion and thus their application to free-living ungulates is limited to those species that have a well-defined, relatively short breeding season (Asa and Porton, 2005).

Sustained-release subcutaneous implants containing GnRH agonists have been tested successfully in several livestock and wildlife species. For instance, implants of the GnRH agonist deslorelin (Suprelorin®) have been used to inhibit reproduction for 1–2 years in cattle and in several other wildlife species (e.g. D’Occhio et al., 2002; Herbert and Trigg, 2005; Eymann et al., 2007). Another GnRH agonist, leuprolide, administered in biodegradable implants was found effective at preventing pregnancy for one breeding season in 100% of female elk (wapiti) and mule deer with no effects on behaviour, body condition, haematology and blood chemistry (Baker et al., 2002, 2004; Conner et al., 2007). Regardless of proven efficacy, the use of hormonal contraceptives on free-ranging ungulates is still controversial because of potential welfare effects on pregnancy, environmental impact and possible transfer to consumers through the food chain (Kirkpatrick et al., 1996; De Nicola et al., 2000).

### 10.1.3 Immunocontraceptive vaccines

Most studies of fertility control applications in free-ranging ungulates have focussed on immunocontraceptive vaccines. These vaccines stimulate the immune system to produce antibodies to proteins or hormones essential for reproduction (Miller and Killian, 2002), thus rendering animals contracepted or infertile. To achieve long-term infertility, adjuvants are used, which are chemicals, large molecules or entire cells of killed pathogens, that enhance the immune response to a vaccine (Fraker et al., 2002). Using liposome-based formulations has also been shown to increase the immune response of some immunocontraceptive vaccines (Fraker and Brown, 2011). The effectiveness, duration and side effects of immunocontraceptive vaccines can vary with species, sex, age, individual differences in immunocompetence, as well as the active component of the vaccine, its formulation, delivery system and the dose and type of adjuvant (Miller et al., 2008a, 2009; Holland et al., 2009; Kirkpatrick et al., 2011). The most studied immunocontraceptives in ungulates are zona pellucida- and GnRH-based vaccines (Table 10.1).
Table 10.1 Effectiveness of single-dose immunocontraceptive vaccines to cause infertility in ungulate species in captivity and field trials. The effectiveness is expressed as proportion of infertile females in the control (C) and treatment (T) groups in the years following administration of the vaccine.

<table>
<thead>
<tr>
<th>Species</th>
<th>Type of study</th>
<th>Vaccine type, adjuvant type and vaccine dose</th>
<th>% infertile females</th>
<th>References</th>
</tr>
</thead>
</table>
| White-tailed deer     | Captive       | GonaCon and AdjuVac various formulations   | T GonaCon-KLH = 100% 60% 50% 50% 25%  
T GonaCon-Blue = 100% 100% 80% 80% 80% | Miller et al. (2008a) |
| White-tailed deer     | Field         | GonaCon-KLH and AdjuVac                     | T = 67% 43%         
C = 8% 17%                | Gionfriddo et al. (2011a) |
| White-tailed deer     | Field         | GonaCon-KLH and AdjuVac                     | T = 88% 47%         
C = 15% 0%                | Gionfriddo et al. (2009) |
| White-tailed deer     | Field         | PZP (SpayVac) and AdjuVac                   | T = 100% 100%       
C = 22%                   | Locke et al. (2007) |
| White-tailed deer     | Field         | PZP and AdjuVac                             | T = 100%            
C = 22%                   | Hernandez et al. (2006) |
| White-tailed deer     | Captive       | PZP and SpayVac, with AdjuVac or Alum      | SpayVac-AdjuVac: 100% 100% 100% 80% 80%  
IVT-PZP-AdjuVac: 100% 80% 80% 80% 80% 80%  
SpayVac-Alum: 80%  
NWRC-PZP-AdjuVac: 80% 0%  
(200 μg)  
NWRC-PZP-AdjuVac: 100% 20% 20% 20% 0%  
(500 μg);  
C = 0%                | Miller et al. (2009) |
<table>
<thead>
<tr>
<th>Species</th>
<th>Status</th>
<th>Treatment</th>
<th>Effectiveness</th>
<th>Reference</th>
</tr>
</thead>
</table>
| Wapiti                   | Captive | GonaCon-B and AdjuVac            | T = 90% 75% 50% 25%  
C = 0% 0% 0% 14%       | Powers et al. (2011)           |
| Wapiti                   | Captive | GonaCon-KLH and AdjuVac          | GonaCon-KLH (1000 µg) = 92% 90% 100%  
GonaCon-KLH (2000 µg) = 90% 100% 100%  
C = 27% 25% 0%         | Killian et al. (2009)          |
| American Bison           | Captive | GonaCon-KLH and AdjuVac          | T = 100%      
C = 0%               | Miller et al. (2004)           |
| Wild boar                | Captive | GonaCon-KLH and AdjuVac          | T = 92% infertile for at least 4-6 years  
C = 0%             | Massei et al. (2008)           |
| Fallow deer              | Field   | PZP (SpayVac) and FCA            | T = 100% 100% 100%  
C = 4% 3% 4%         | Fraker et al. (2002)           |
| Feral horse              | Captive | GonaCon-KLH and AdjuVac          | T = 93% 64% 57% 43%  
C = 25% 25% 12% 0%     | Killian et al. (2008)          |
| Feral horse              | Field   | GonaCon-B and AdjuVac            | T = 61% 58% 69%  
C = 40% 31% 14%        | Gray et al. (2010)             |
| Feral horse              | Captive | PZP (SpayVac) and AdjuVac        | T = 100% 83% 83% 83%  
C = 25% 25% 12% 0%     | Killian et al. (2008)          |
| Feral horse              | Field   | PZP with FCA and QS-21           | T = 95% 85% 68% 54%  
C = 47% 42% 49% 48%     | Turner et al. (2007)          |
| Feral horse              | Field   | PZP and AdjuVac                  | T = 63% 50% 56%  
C = 40% 31% 14%        | Gray et al. (2010)             |
|                         |         |                                  |                | Gray et al. (2011)     |
The zona pellucida (ZP) that surrounds an ovulated egg is composed of four types of proteins, named ZP1, ZP2, ZP3 and ZP4, each with different functions in mediating structure and species-specific sperm recognition and binding. Differences in these proteins among mammals are partly responsible for the variable results obtained when using a particular ZP vaccine on different species (Kitchener et al., 2009; Gupta and Bansal, 2010). For instance, porcine ZP (PZP) immunocontraceptive vaccines, derived from ZP isolated from pig ovaries, inhibit fertilisation in many wildlife species including ungulates (Table 10.1) but not rodents, cats and wild pigs (Fagerstone et al., 2002; Kirkpatrick et al., 2009, 2011). Likewise, differences in the results of studies using ZP-based vaccines may reflect different formulations of native, purified or recombinant ZP vaccines and different methods of extraction of PZP from pig ovaries (Miller et al., 2009; Kirkpatrick et al., 2011; Bechert et al., 2013).

Early immunocontraceptive vaccines had to be delivered as a primer injection followed by a booster, which made field applications impractical (Putman, 1997). Initial vaccine formulations also used Freund’s complete adjuvant (FCA). Some constituents of this adjuvant, namely mycobacteria (Mycobacterium tuberculosis) and mineral oil, were found responsible for granulomas (thickened tissue filled with fluid) at injection sites, for false-positive results in TB skin tests in deer treated with these vaccines and for potential carcinogenicity to consumers of treated animals (Kirkpatrick et al., 2011). Significant progress has been made through the development of a novel adjuvant (AdjuVac™, National Wildlife Research Center, United States), containing inactivated Mycobacterium avium and based on a modified version of the Johne’s disease vaccine.

Injectable ZP-based immunocontraceptives have been employed extensively to reduce fertility in zoo ungulates, in free-living deer, feral horses and elephants (Table 10.1). In particular, the combination of AdjuVac and PZP-vaccine made ungulates infertile for several years after a single dose (Table 10.1). In some species, such as white-tailed deer, some ZP vaccines may cause pathologies such as inflammation of the ovary (Curtis et al., 2007) but in others, such as wild horses, no ovarian damage was observed after 3 years of treatment (Patton et al., 2007). Following injection of ZP-based immunocontraceptives, injection site reactions such as granulomas are common, whilst the occurrence of draining abscesses is around 1% in various species (Gray et al., 2010; Kirkpatrick et al., 2009). As ZP-based immunocontraceptives inhibit fertilisation but not ovulation, animals treated with these vaccines tend to have multiple infertile oestrous cycles which may lead to extended breeding seasons, increased movements and potential late births (Miller et al., 2000; Curtis et al., 2007; Nuñez et al., 2009, 2010; reviewed in Kirkpatrick et al., 2009, 2011). Multiple infertile oestrous cycles following treatment with PZP vaccine were observed in white-tailed deer, wapiti and horses (Heilmann et al., 1998; Killian and Miller, 2001; Curtis et al., 2002; Ransom et al., 2013). Other studies suggested that treatment with ZP vaccines did not affect behaviour and body condition of mares (Ransom et al., 2010; Kirkpatrick et al., 2011), white-tailed deer (Hernandez et al., 2006) and wapiti (Heilmann et al., 1998). However, an
extension of the breeding season in deer treated with PZP vaccine resulted in increased energy expenditure by males (Curtis et al., 2002). PZP vaccines were found safe to administer to pregnant or lactating females (Kirkpatrick and Turner, 2002; Patton et al., 2007) and had no long-term effect on health of white tailed deer (Miller et al., 2001). In 2012, an injectable PZP-based vaccine, ZonaStat-H, was registered by the US Humane Society and approved by the US Environment Protection Agency (EPA) as a contraceptive for population control of wild and feral horses and feral donkeys.

Vaccines based on gonadotropin-releasing hormone (GnRH) generate antibodies towards GnRH, thus preventing the hormonal cascade that leads to ovulation and sperm production. Several multi-dose GnRH-based immunocontraceptive vaccines, developed for use in livestock are unsuitable for wildlife due to the difficulty of recapturing individuals to administer booster doses and to their relatively short-term (a few months) effectiveness (reviewed in Naz et al., 2005; McLaughlin and Aitken, 2010). Single-dose injectable GnRH-based vaccines, specifically formulated for wildlife applications, offer better prospects for managing ungulates. Among these vaccines, the most studied is Gonacon™, currently registered in the United States by the EPA as an immunocontraceptive for white-tailed deer, feral horses and feral donkeys. Gonacon™ consists of a synthetic GnRH coupled to a mollusc protein (Miller et al., 2008b).

Formulated as an injectable, single-dose immunocontraceptive, Gonacon™ caused infertility for several years in males and females of several ungulates (e.g. Miller et al., 2000; Killian et al., 2008; Massei et al., 2008; Gray et al., 2010; Massei et al., 2012) (Table 10.1). As Gonacon™ interferes with steroid production, treated females do not exhibit oestrous behaviour. Male deer treated with GonaCon™ also showed a complete lack of sexual activity and reduced testicle size, but they also exhibited abnormal antler development (Miller et al., 2000, 2009; Fagerstone et al., 2008). The lack of sexual activity, in species where this behaviour might increase human–wildlife conflicts such as deer collisions with vehicles during the rut, could be advantageous, although the effect on antler development suggests GonaCon™ should not be used on male deer. Similar to ZP-based contraceptives, antibodies to GnRH decrease with time and fertility may be restored in the years after treatment unless animals are administered booster vaccinations (Miller et al., 2008b; Massei et al., 2012).

The main side effect of Gonacon™ is the formation of a granuloma or a sterile abscess at the injection site; the severity and incidence of injection site reactions vary with species. In white-tailed deer, injection-site granulomas and sterile abscesses occurred in the deep hind-limb musculature of >85% of treated animals, although no evidence of limping or impaired mobility was observed in these deer during a 2-year study (Gionfriddo et al., 2011b). These reactions are typical responses to injection of adjuvanted vaccines formulated as water-in-oil emulsions (Miller et al., 2009). On the other hand, GonaCon™ had no adverse effects on major organs, body condition, fat deposits or blood chemistry in wild boar, white-tailed deer and wapiti (Massei et al., 2008, 2012; Gionfriddo et al., 2009, 2011b).
When given to pregnant bison and elk, GonaCon™ did not affect pregnancy (Miller et al., 2004; Powers et al., 2011). Other studies found that GonaCon™ did not induce infertility and did not prevent sexual development when administered to 3–4-month-old white-tailed deer (Miller et al., 2008a; Gionfriddo et al., 2011a). Like ZP-based vaccines, GnRH vaccines are broken down if ingested, thus they do not pose risks to predators or human consumers.

10.2 Delivery methods

Although a fertility control agent should be ideally species specific, this is rarely the case and specificity must be achieved through the delivery method. At present, fertility control agents that induce at least 1 year of infertility are administered by direct injection following capture, by implant or are delivered remotely through biobullets and syringe-darts (see below). Subcutaneous implants that release contraceptive agents into the body over a sustained period of time have been successfully employed to induce infertility for 1–5 years in a variety of wildlife species (e.g. Plotka and Seal, 1989; Nave et al., 2002; Coulson et al., 2008; Lohr et al., 2009). However, steroid implants have the potential for transferring active ingredients to predators and scavengers.

Biobullets are biodegradable projectiles used for remote administration of veterinary products (DeNicola et al., 2000). Syringe-darts, routinely employed to anaesthetise wild animals, have also been used to administer contraceptives to large ungulates at ranges of ≤40 m (Rudolph et al., 2000; Aune et al., 2002; Delsink et al., 2006). The advantages of remote administration of contraceptives to ungulates are that delivery can be targeted to specific individuals (unlike oral delivery), and that this method minimises the welfare and economic costs of trapping (Kreeger, 1997). Potential disadvantages of these delivery systems include the inability to identify successfully vaccinated animals, cost, dose regulation and incomplete intra-muscular injection (De Nicola et al., 1997; Kreeger, 1997; Aune et al., 2002). The inability to identify previously vaccinated animals is important because these animals can receive multiple doses: whilst this is not expected to have welfare costs, it certainly reduces the efficiency of any fertility control programme. Another approach to a single-dose, multiple-year immunocontraceptive is to mimic the effects of booster injections by incorporating the vaccine into controlled-released polymers formulated as injectable pellets. This approach was successfully tested with wild horses by using simultaneous intramuscular injection of 1-, 3- and 12-month pellets to provide in vivo delivery of booster doses of the PZP vaccine (Turner et al., 2007; Rutberg et al., 2013).

Injectable forms of fertility control vaccines have been shown to effectively block fertility in a number of species. However, to be of further practical use in wildlife management, more efficient means of delivery are required. There is great interest in the development of mucosal (e.g. oral or intranasal) vaccines in human pharmaceuticals (reviewed in Woodrow et al., 2012) and this will aid in efforts towards wildlife applications where some research has already
been conducted (Cui et al., 2010). Once developed, oral fertility control agents are likely to be less expensive to administer than injectable forms, in part, because capture and handling of animals will not be necessary for the delivery of these contraceptives. However, unlike injectable vaccines, oral fertility control agents will likely require repeated applications to cause infertility (Cross et al., 2011). As oral forms of fertility control might also affect non-target animals, species specificity could be achieved through targeted delivery methods. One example is the BOS (Boar-Operated System) developed as a specific delivery system for wild boar and feral pigs (Massei et al., 2010c; Long et al., 2010; Campbell et al., 2011) (Figure 10.2).

Immunocontraceptive vaccines delivered through genetically modified, self-sustaining infectious vectors have been developed in Australia. Criticism of this approach involved concerns regarding irreversibility, the difficulty of controlling the vectors once released, possible mutations of the vectors that could affect non-target species and possible development of resistance (Barlow, 2000; Williams,

![Figure 10.2](image)

**Figure 10.2** Free-living wild boar feeding on maize-based baits from a Boar-Operated System (BOS). The metal cone slides along the pole and fully encloses the base onto which the baits are placed. Several studies found that free-living wild boar and wild pigs fed regularly from the BOS and that the device successfully prevented bait uptake by non-target species. The BOS can be used to deliver vaccines, contraceptives or other pharmaceuticals employed to manage overabundant populations of wild suids.
2002). In New Zealand genetically modified transmissible organisms, such as species-specific nematode parasites, have been explored to deliver contraceptives, although no data are available for ungulates (McDowell et al., 2006; Cowan et al., 2008; Cross et al., 2011).

10.3 Fertility control and population responses

Most recent field studies on fertility control have used immunocontraceptives, whilst modelling studies have focussed on generic contraceptives of different levels and duration of induced infertility (Table 10.2). Comparing the relative merits of fertility and lethal control to manage overabundant populations, recent research suggests that large, long-lived species are easier to manage with fertility control than smaller, shorter-lived ones because a lower proportion of the population must be targeted each year (Hone, 1999), particularly if lifelong contraceptives are employed (Hobbs et al., 2000).

Modelling the impact of fertility control versus culling for a geographically closed population of white-tailed deer, Merrill et al. (2003) concluded that, for instance, to achieve a 60% reduction over 4 years, culling should remove 40% of available fertile females each year. To maintain this level of reduction, only 13% of the available females should be sterilised every year. Based on this model, the authors suggest that an effective management strategy to control overabundant urban deer populations would require two steps. The first step will reduce the population to a given level: to achieve this, culling would be more efficient than sterilisation. The second step will maintain the population at a set level and sterilisation will become more efficient as the number of sterilised females increases (Hobbs et al., 2000). However, in long-lived species and in populations characterised by slow turnover, the benefits of using fertility control to decrease population size will only accrue in the long term (Twigg et al., 2000; Kirkpatrick and Turner, 2008; Cowan and Massei, 2008).

The effects of fertility control on population dynamics also depend on species-specific social and reproductive behaviours, on the type of contraceptive used and on its mode of action, as well as on whether a population is isolated or open. There is general consensus that fertility control is most effective for managing relatively small (50–200 animals) isolated populations of ungulates (Rudolph et al., 2000; Kirkpatrick and Turner, 2008). Avoiding disruption of behaviour is crucial, as fertility-control-induced changes in immigration and emigration might prevent fertility control achieving the required reduction in population growth (e.g. Davis and Pech, 2002; Merrill et al., 2006).

On the other hand, using fertility control methods that inhibit normal sexual behaviour can potentially reduce disease transmission by decreasing contact rates between individuals (Caley and Ramsey, 2001; Ramsey, 2007). For instance, a reduction of reproductive behaviour would result in decreased transmission of venereal diseases such as pseudorabies and brucellosis (Miller et al., 2004; Killian et al., 2006). In this context, methods that prevent ovulation are
likely to be more successful at decreasing disease transmission than those that only block fertilisation. When only fertilisation is blocked, females of many ungulate species will continue to ovulate, thus attracting males (Putman, 1997; Miller et al., 2000; Curtis et al., 2007; Núñez et al., 2009, 2010). This may have significant effects on prolonging the duration of the rut, enhancing and extending the period of male–male competition (and thus increasing risk of injury or male exhaustion).

The factors affecting emigration and immigration in ungulate populations managed through fertility control have received little attention. For instance, a reduction in population density due to fertility control might increase immigration rate, thus negating the benefits of using non-lethal population management. On the other hand, fertility control might also encourage emigration, particularly of males looking for mating opportunities outside their normal home range. As female white-tailed deer in urban and suburban areas have relatively small home range size and high site fidelity (Grund et al., 2002), it is possible to hypothesise that fertility control will not affect the movements of these animals. Other studies found that ZP-based immunocontraceptives did not affect spatial behaviour in white-tailed deer and feral horses (Hernandez et al., 2006; Ransom et al., 2010).

Density-dependent regulation of population should also be taken into account: Merrill et al. (2003) suggested that if density-dependence was occurring, it would increase the effectiveness of sterilisation as the reproductive removal (but not the physical removal) of part of the population would intensify density-dependent feedback. Clearly, this is an area where more field studies are warranted to assess the effects of fertility control on emigration, immigration, recruitment and mortality in ungulate populations with different life-history traits.

Fertility control has been associated with increased survival and improved health condition, probably due to the reduced expenditure of energy normally required for reproduction. For example, sterilisation-induced increases in survival and total food consumption in feral Soay rams caused an increase in both animal density and impact on the plant community (Jewell, 1986). Similarly, as immunocontraceptives can significantly extend lifespan and improve body condition (Turner and Kirkpatrick, 2002; Kirkpatrick and Turner, 2007; Gionfriddo et al., 2011b), the impact of increased survival on population dynamics must be taken into account when using fertility control to manage ungulate populations.

Fertility control in ungulates has been used to decrease population size or growth, reduce vertical or horizontal transmission of diseases or reduce impacts of local populations on human activities (Table 10.2). The relative merits of fertility control and culling have been much debated, with advocates of the two methods often holding opposite, irreconcilable positions (Kirkpatrick, 2007; Curtis et al., 2008; Fagerstone et al., 2010). Modelling studies concluded that in several instances the outcome of the two methods in reducing population size or disease transmission depends on the definition of ‘efficiency’. If efficiency is defined in terms of the time taken to achieve the desired effect, then culling is
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always the most efficient solution (Bradford and Hobbs, 2008). Conversely, if efficiency is defined as the proportion of the population to be targeted, fertility control can be regarded as potentially more efficient than culling (Hobbs et al., 2000; Merrill et al., 2003). By defining efficiency as the proportion of the population that must be treated, the time and costs required are deliberately ignored (Merrill et al., 2003). In this scenario, modelling suggests that fertility control agents that render animals infertile for many years are likely to be more efficient than culling, provided that the fertility status of the treated animals is known, for instance, through ear-tags that identify animals previously treated with contraceptives.

Other advantages of fertility control over culling include:

1. Compared to fertility control, culling is more likely to cause social perturbation, increased contact rates and hence increased likelihood of disease transmission (e.g. Ramsey et al., 2006; Carter et al., 2007)
2. Animals in improved body condition, following treatment with contraceptives, might be less susceptible to disease and also mount a better immune response to disease vaccines
3. Infertile animals remain in the population, thus maintaining density-dependent feedback to recruitment and survival (Zhang, 2000)
4. A growing recognition that fertility control in conjunction with disease vaccination can be as effective as culling to manage disease transmission (Smith and Cheeseman, 2002).

As animals vaccinated against a disease reproduce, new susceptible individuals enter the population and dilute the level of herd immunity provided by disease vaccination; combining disease vaccination and fertility control, to prevent the recruitment of new susceptibles can thus reduce the effort required to eliminate the disease (Smith and Wilkinson, 2003; Carroll et al., 2010).

In some instances, fertility control might be required to reduce or halt population growth rather than to decrease population size. Exploring options to manage a small, isolated population of African elephants, Druce et al. (2011) suggested that using reversible immunocontraceptives on an individual rotational basis would increase inter-calving intervals, stabilise population structure and lower population growth to a predetermined rate.

Some authors have hypothesised that the use of immunocontraceptive vaccines to manage wildlife could result in the evolution of resistance, through selection for individuals that remain fertile because of low or no response to vaccination (e.g. Gross, 2000; Magiafoğlu et al., 2003; Cooper and Larsen, 2006; Holland et al., 2009). These authors argue that when females only are treated with immunocontraceptives, resistance might evolve if the response to the vaccine is specific for this gender and could be inherited through the maternal line. No studies have so far demonstrated such effects although unresponsiveness to immunocontraceptive vaccines was found to have a genetic component in brushtail possums (Holland et al., 2009).
10.4 Can fertility control mitigate human–ungulate conflicts?

Human–ungulate conflicts often demand immediate solutions. Stakeholders have a significant impact on management options but often hold opposite opinions. For instance, animal welfare groups tend to advocate fertility control to manage these conflicts (Curtis et al., 2008), whilst many hunting groups oppose the use of fertility control because of concerns that this method will replace sport hunting (Kirkpatrick, 2007; Fagerstone et al., 2010).

The studies carried out so far indicate that if fertility control is the sole method employed to manage overabundant populations, a substantial initial effort is required (Rudolph et al., 2000; Walter et al., 2002; Merrill et al., 2003, 2006). In addition, changes in survival and immigration can reduce population-level efficacy of fertility control (Ransom et al., 2013). However, as the proportion of infertile females increases, this effort will decline and remain constant once the desired density has been achieved. Successful examples are the marked reduction in suburban white-tailed deer obtained over a 10-year timescale (Rutberg and Naugle, 2004, 2008), the zero-population growth of an isolated population of elephants achieved within 2 years (Delsink et al., 2006) and of an island population of wild horses obtained within 2 years (Kirkpatrick and Turner, 2008). For closed populations, Merrill et al. (2006) suggested that, at least in white-tailed deer, contraception of 30–45% of the animals would decrease population size after 2–3 years and that a population reduction of 60% would be achieved in 10 years.

Depending on how urgent the resolution of the conflict is, fertility control can be used alone or once the population size has been reduced through other methods (Barlow, 1997; Hobbs et al., 2000). When fertility control is chosen to mitigate human–ungulate conflicts, a number of issues should be considered before field applications are implemented. These issues cover humaneness, efficacy, feasibility, cost, timeframe and sustainability as well as alternative methods for population control. As humaneness is one of the primary public concerns regarding any type of wildlife management, defining this term is crucial to obtaining and maintaining public support in relation to specific, well-defined objectives. For instance, humaneness can be defined as (i) the level of stress experienced by treated animals, (ii) the severity and type of side effects, (iii) the proportion of animals likely to experience negative side effects following treatment with a contraceptive, (iv) the proportion of animals that will suffer from capture, handling and anaesthesia associated with administering the contraceptives, or (v) a combination of all these definitions.

When lethal control is illegal, unacceptable or unfeasible, fertility control might be the only option available for managing overabundant populations of ungulates. In these instances, key issues to be discussed at the planning stage include assessing the overall proportion of the population that must be rendered infertile to mitigate the conflict, estimating the relative effort and time required to achieve the target population size and evaluating the feasibility of field application of contraceptives.
(Hobbs et al., 2000; Bradford and Hobbs, 2008). This feasibility in turn is likely to depend on factors such as animal density, approachability of individual animals, access to private and public land, and efficacy of the contraceptive treatment (Rudolph et al., 2000; Walter et al., 2002; Rutberg and Naugle, 2008; Boulanger et al., 2012). In the early planning stages, modelling the impact of fertility control on population dynamics can assist determining whether the application of this method will meet specific management goals (e.g. Jacob et al., 2008).

The economic cost of reducing ungulate population growth through fertility control agents that require capture and handling of the animals is expected to be high. For instance, Rutberg (2005) estimated that the cost of rendering infertile a medium-to-large size individual mammal varied between US$25 and US$500. Delsink et al. (2007) calculated that in 2005 the average cost of managing elephants through aerial vaccination with immunocontraceptives was US$98–110 per animal, inclusive of darts, vaccine, helicopter and veterinary assistance. Walter et al. (2002) reported that the cost of trapping and injecting 30 white-tailed deer with immunocontraceptives for 2 years (with a spring capture and vaccination followed by two boosters in autumn of year 1 and year 2) was US$1128/deer. Labour accounted for 64% of the total cost and equipment, supplies, lodging and travel accounted for the remaining 36% of the total cost. However, after the initial year, the cost per deer dropped to US$270 (Walter et al., 2002). Boulanger et al. (2012) found that the cost of capture, handling and administering contraceptives to white-tailed deer in various studies was about US$1,000 but that 75% of this cost was due to drugs, including anaesthetics, and a veterinarian’s time. It is conceivable that costs would drop significantly if immunocontraceptives were delivered by trained staff (i.e. by wildlife managers instead of veterinarians) and ungulate capture was organised with the assistance of volunteers donating their time and skills to the project. Hobbs et al. (2000) suggested that fertility control of deer will only be cost-effective, compared to culling, where professionals are employed to cull deer instead of recreational hunters.

Identifying who should bear the costs of population management might raise awareness of the economics of available options amongst stakeholders and add a different perspective to ungulate management. This awareness would be further enhanced if the full costs, including negative environmental and welfare consequences, associated with each option are included.

In addition to the practical challenges of using fertility control on ungulate populations, regulatory and legal requirements for field applications of contraceptives must be met. For products that have not been registered in a country, trials can often be carried out under experimental permits and on a case-by-case basis (Humphrys and Lapidge, 2008).

In summary, this review highlighted that safe, effective contraceptives are now available allowing field applications aimed at reducing population growth in ungulates. Although many challenges still exist, we believe the next decade will witness a large number of field studies carried out to manage ungulate populations through fertility control. We recommend that, for each context, the use of fertility control,
alone or in conjunction with other methods, is evaluated and compared with alternative options for population control. Only then can the costs and benefits of different methods be fully established and the optimum options selected to mitigate the conflicts between human interests and ungulate populations.

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