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# WAYS TO CONTROL DOG AND CAT POPULATIONS – CONTRACEPTION IN COMPANION ANIMALS

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**Summary**

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Population control in stray dog and cat population is an important tool to reduce/limit the risks for public health and environment, but also to support animal welfare. The article gives an overview about currently approved non-surgical methods as well as techniques under development, such as progestins, GnRH-agonist slow release implants, melatonin (cats) as well as immunocontraception or approaches utilizing gene therapy (gene expression or silencing). Additionally, the knowledge about antiprogestins as an effective option for prevention of nidation and induction of abortion is shortly summarised.

**Key words:** aglepristone, GnRH agonist, immunocontraception, progestin

## INTRODUCTION

The total number of stray animals in Europe is estimated to be 100 millions and these animals pose various risks for public health, such as the spread of rabies, as well as for the environment, e.g. by prey on small animals. Consequently, reproduction control in these free-roaming feral dog and cat populations is an important tool also for animal welfare. Although culling of stray animals is performed in many countries, "catch-neuter-and-release" (CNR) programs are considered the more ethical way. As, however, surgical neutering on a large-scale is time- and cost-intensive, non-surgical contraception is of major interest. Whereas the ideal contraceptive for free-roaming dogs and cats would be a cheap and effective single-shot treatment that induces life-long sterility in both, males and females without side effects, a temporary, short- to midterm-efficient, reversible contraception could be of further interest for private owners that want to avoid surgery and potentially would like to breed their animals later in life.

## PROGESTINS

The classical, also licensed option as an alternative to surgical spaying in bitches and queens is the use of progestins. Whereas they are no longer widely used in bitches, their intermittent use in breeding queens is still common. They might, espe-

cially without sufficient care, induce severe side effects, such as cystic endometrial hyperplasia-pyometra complex, mammary tumours and fibroadenomatosis (in cats) and insulin resistance causing diabetes mellitus. Their use in stray cat populations is challenging as a regular intake must be assured. Furthermore, they are not suitable to suppress fertility and libido in male dogs and cats in the therapeutic range, making them unsuitable for wide-spread reproduction control.

## GNRH AGONISTS

### *Use in dogs*

A GnRH agonist slow release implant (GnRH-SRI) is commercially available for suppression of fertility in adult male dogs. Following an initial stimulation („flare up"), gonadotropin secretion is significantly reduced resulting in a downregulation of testicular endocrine and germinative function as indicated by basal testosterone concentrations and aspermic/azoospermic ejaculates as a consequence of an early arrest of spermatogenesis. The time point when infertility is reached is variable. Clinically, infertility is associated with testicular atrophy, a significant reduction in prostatic size and a loss of testosterone-dependent behaviour. All induced effects are fully reversible within 6-24 months (rarely longer) after implant insertion (Junaidi *et al.* 2003). This makes the SRI especially interesting for pet owners or people considering a later use a breeding stud; however, the duration of efficacy of the currently available GnRH-SRIs is not long enough for stray dog populations.

Data about off-label use in bitches are limited. Whereas prepubertal application (before 5 months of age) has been shown to effectively delay puberty in bitches, an initial estrus induction following implant injection is a major problem in adult bitches. Whereas normal estrus signs are visible nearly in 100% of bitches treated in anestrus, signs are often subtle when bitches are treated in diestrus (Körber et al., 2013). However, as estradiol-17ß has been shown to be increased following implant insertion also in diestrus (Körber et al., 2013) when progesterone is elevated physiologically, the use of the GnRH-SRI should be restricted to healthy and young bitches and implantation in a location allowing for easy removal is mandatory. Side effects, such as pyometra and ovarian cysts have been reported. Data about the duration of efficacy are lacking in prepubertal bitches and are limited in adult bitches, with available data showing a large variation (5-24 months, 4.7 mg deslorelin) rendering the current GnRH-SRI not suitable for contraception in feral bitches.

### *Use in cats*

A single injection of a GnRH agonist can induce ovulation in an estrus queen and thereby a pseudopregnant cycle resulting in a prolonged interval to the next estrus.

GnRH-SRI offer an alternative for long-term contraception of female and male cats without injection site issues. In male cats, basal testosterone concentrations are reached within 3-11 weeks after implant insertion with some individuals responding even more delayed. Animals become infertile due to azoospermia; however, different to the dog, histological appearance of the testis is more variable (Goericke-Pesch *et al.*, 2011, 2014). The duration of efficacy (4.7 mg deslorelin) described ranges between 18±3 months (Goericke-Pesch *et al.*, 2014) and 24.6± 6.5 months (Gültiken *et al.*, 2017), in one case the duration of efficacy was 4 years.

Similarly as in the dog, all induced effects are fully reversible and reestablishment of fertility has been proven (Goericke-Pesch *et al.*, 2014).

In queens, GnRH-SRI may induce estrus when given in postestrus and induce ovulation when given in estrus (Goericke-Pesch *et al.* 2013). The induced estrus can be fertile why mating should be avoided. Concomitant oral administration of progestins does not prevent estrus induction, therefore making it not recommendable. Treatment in early pregnancy resulted in normal pregnancy and oarturition, but complete absence of maternal behaviour and lack of milk production. The reported duration of efficacy (4.7 mg deslorelin SRI) ranges between 16.1 and >36 months (mean: 22.7±2.1 months, Goericke-Pesch *et al.*, 2013). All induced effects on estrus cycle, behaviour and fertility are fully reversible. When given prepubertally (50% adult body weight)/postnatally puberty can be significantly delayed with the risk of an initial estrus induction being avoided/reduced. As in a matrix model taking the average life span of free-roaming cats into consideration, a contraceptive intervention of three years was close to the success of surgery, and considered to be delivered with less cost and administrative burden, GnRH-SRI might be an option. Limitations are the initial estrus induction and the large individual variation. The question remains to be answered if application of a higher dose and an SRI releasing over a longer period could overcome the limitations.

## MELATONIN

The successful use of melatonin for temporary short-term suppression of the feline estrus cycle has been described with the duration of efficacy (melatonin SRI) varying between 61.1±6.8 days when administered in estrus and 113.3±6.1 days when given in interestrus in one study and 63±5 days in another study. Tom cats did not become infertile, consequently, they are not an option for feral cats

## OTHER METHODS

Vaginal stimulation(s) in an estrus queen, e.g. with a glasrod, can induce ovulation and similarly to an injection of a GnRH agonist or humane Choriongonadotropine (hCG) prolong the interval to the next estrus.

## IMMUNOCONTRACEPTION AND MORE

Classical immunocontraception targets either zona pellucida proteins or GnRH and a few products are approved in some countries. Whereas long-term studies using GnRH vaccines in bitches and male dogs are widely missing, consequently not allowing for a final conclusion, GnRH-immunocontraception showed some successes in achieving long-term contraception in queens, but not tom cats. New studies focus on novel antigens, novel delivery of antigens providing a "self-boost" or novel ways of augmenting the immune response. New promising approaches include also targeted delivery of cytotoxins and gene silencing/gene therapy.

## AFTER MATING – ANTIPROGESTINS

Once mating occured, antiprogestins can be administered in bitches (10 mg/kg) and queens (10–15 mg/kg) for prevention of nidation and induction of abortion, respectively. Two consecutive injections within 24 hours are required and an additional ultrasound examination to confirm termination of pregnancy in case of application from day 25 onwards is recommended.

Efficacy rates in dogs range from 99-100 % (until day 22) to 95% (until day 35) and in cats between 100% (day 5), 87-88.5% (day 20-38) and 66.7% (day 45) with a high safety profile (Georgiev & Wehrend, 2010; Georgiev *et al.*, 2006; Goericke-Pesch *et al.*, 2010).

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