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Pursuing Alternative Strategies for Healthier Medical Contraception in Dogs

Rita Payan-Carreira , Paulo Borges and
Alain Fontbonne

Additional information is available at the end of the chapter

Abstract

Although extensively used in the control of the reproductive cycles in either the domestic or feral dogs as well as in wild carnivores, medical progestin-based contraception still raises concerns to the veterinary practitioner and owners on its safety and efficiency. These concerns endorsed, in last decades, the research in the development of new alternatives for effective, reversible, and safe contraceptive methods for carnivores, mainly pursuing a larger-scale control of canine reproduction and the development of products with few side effects. Nowadays, the medical contraceptives often intend to master, in a reversible way, the reproductive cycle in genetically valuable dogs, which presumes that they would be active for short periods of time and ought to safeguard the animal fertility. However, hormonal contraceptives are also used worldwide to control the reproductive activity in either domestic or feral cats, for long-term treatments, because of a pretended short-term economic interest. Progestogens are the most frequently used hormonal contraceptive in carnivores. They are rather easy to obtain across the globe and relatively cheap; they have diverse drug presentations, allowing their use independently of the veterinary assistance, and are effective in preventing pregnancy. Still a significant number of undesirable health side effects are attributed to progestins when employed with some chronicity, when applied in older animals or even when misused. In the past two decades, several new approaches to managing dog reproduction were proposed to avoid progestins. However, their efficiency and cost are still to be proven as a viable alternative around the world. This chapter aims to review the medical methods available as alternative to the progestins in canine contraception, addressing particularly the future perspectives, opportunities, and limitations linked to currently available substitutes, based on our practice. This information can be of utmost interest to students, clinicians or colonies' technicians.

Keywords: medical contraception, estrus suppression, GnRH antagonists, GnRH agonist, immunocontraception, dogs

1. Introduction

The control of the reproductive activity in dogs is a main issue in today's societies. Overpopulation of stray and feral dogs is an universal problem and raises public health concerns related to the increased risk of zoonotic diseases and compromise of the environmental health that may foster the permanence of diseases in other species or the degradation of ecosystems [1], as well as to the social and urban problems associated with animal-human conflicts.

At the start of this chapter, the authors would also strengthen that the best measure for a safe and definitive measure for the suppression of reproductive cycles in animals not intended for future breeding is ovariectomy (in prepubertal or young postpubertal female dogs) or ovariohysterectomy [2–4]. These procedures also have a protective effect on the incidence of uterine and mammary diseases, if performed early in the animal life. However, spaying of young animals, whether male or female dogs, is not an universal option; in some countries, it is described as an unnecessary surgical insult to the dog, and therefore must be performed only under medical indication. In other, the surgery is rejected for economic reasons, and medical contraception is regarded as a more economical alternative to surgery. The therapeutic options for mastering the companion animal reproduction substantially improved in recent decades. Also, the nonsurgical contraceptive treatments drew the attention of the industry and researchers, allowing the recent introduction of new methods in the clinical practice targeting safer long- and short-term suspension of gonadal activity in dogs. The information on the available methods alternative to progestins needs to be discussed and their advantages and disadvantages have been reviewed to disseminate basic information of their use and ease the introduction of safer products in canine medicine [5].

The suppression of canine reproductive activity includes: (1) the sterilization of both male and female, as a form to control either the ownerless or free-roaming or community-owned dogs as well as privately owned, confined or roaming dogs; and (2) the canine contraception for the periodic suspension of ovarian activity, which can also be applied on the male counterpart. This chapter focuses on the medical contraception in dogs. Moreover, as the manipulation of the ovarian activity in dogs, even if directed to its suspension, presumes the basic knowledge of the normal endocrinology of the estrous cycle of bitch, it will be reviewed, before discussing the nonsurgical contraceptive treatments available in dogs.
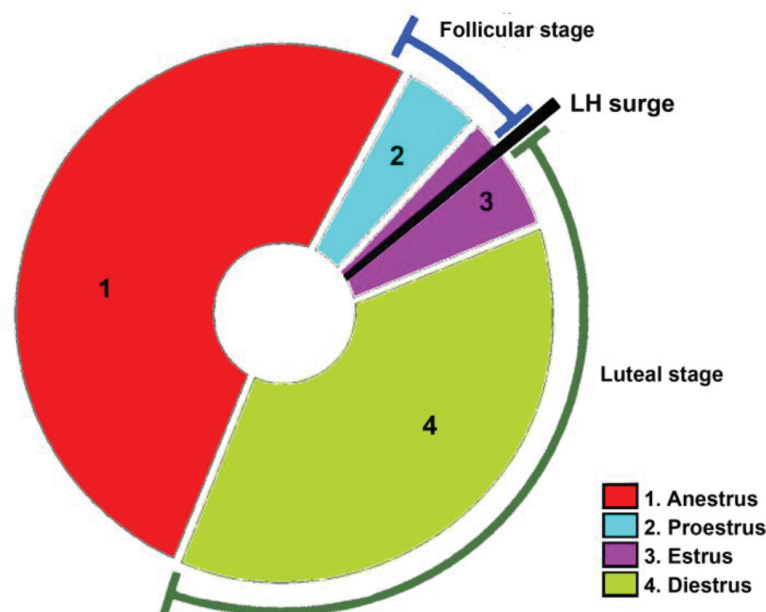
2. The canine estrous cycle

Dogs are spontaneous ovulators, monoestrous, and nonseasonal species [6, 7], despite that there are some reports on an increased incidence of estrus during winter and late spring [8]. However, the photoperiodic control of estrus has only been clearly shown in the Basenji [9].

In dogs, each cycle is separated from the following by an obligatory anestrus stage of variable duration [6]. The period between two consecutive proestruses is often named as interestrous interval. The number of cycles per year varies greatly among bitches, accounting the high vari-

ability recorded for the interestrous interval among this species. However, this variation is independent of the animal size. Although the pattern and regularity of the estrus activity may vary between breeds or even genetic lines, it is regular for each female. Some females show only one cycle per year, such as the Basenji and the Tibetan Mastiff, others show two to three cycles yearly. Thus, the physiological interestrous interval may vary between 4 and 12 months [6, 10]. For example, some lines of Rottweilers, German Sheepdogs, and Bernese Mountain dogs may show a 4-month interestrous interval, while some lines of Collies, Labradors or Teckels may present an interval of 7–8 months. Usually, the reported average is 6–7 months [6, 7]. Therefore, it is important to collect the information on the regularity of the estrous cycle in a particular bitch when designing a contraceptive medical protocol, as this may require the adjustment of the administration schedule.

Age at puberty in dogs is mostly affected by size, although nutritional or social cues may also modulate it. In female dogs, puberty occurs when the animal reaches 70–80% of its mature body weight [11].

Classically, the canine estrous cycle is divided into four stages (**Figure 1**) that recur at regular intervals [6–8]. The length of each stage of the canine estrous cycle varies individually, with exception of the diestrus that is fairly constant whether pregnancy occurs or not.

Figure 1. Schematic representation of the standard canine estrous cycle. Adapted with permission from [12].

Proestrus represents the first signs of reproductive activity; following the rapid follicular development of follicles in the ovary, which determines a rapid increase in the suprabasal estrogen levels, the female presents the external clinical signs associated with heat, such as swollen vulva, serous-hemorrhagic vulvar discharge, and increased restlessness and attraction of male [6–8]. The average length of proestrus is 9 days, but in fact it may range between 3 and 21 days [7]. The transition from proestrus to estrus is feebly detected on the basis of external

or behavioral features, and so the two stages are usually grouped under the designation of "heat". Estrus is a transitional stage. Owing to the preovulatory luteinization of the granulosa cells in the growing follicles (progesterone levels increase above 2 ng/mL from LH peak onwards), early in this stage occurs a shift in the steroid environment, which changes from peaking estrogens to the progesterone dominance that will be maintained throughout diestrus. These changes induce a decrease in the amount of vaginal discharge, which also becomes more mucous and less hemorrhagic. In this stage, the female search more actively and the contact with the male and allows mating. Estrus lasts in average 9 days, but individual variations account for a range of 3–21 days. The LH surge occurs usually 24 h after the onset of estrus, but ovulation will take another 1.5–2.5 days to occur. The ovulation product is an immature oocyte that needs an additional period of 2–3 days for tubal maturation before fertilization [6].

Diestrus represents a prolonged luteal stage, similar in length whether or not pregnancy occurs. The decrease of progesterone levels below 1–2 ng/mL is often used to delimit the end of diestrus, as externally no clinical signs allow establishing the limits between diestrus and anestrus. Still, some bitches may present a residual mucous vaginal discharge or mammary development during diestrus that are absent in anestrus. The mean length of nongestational diestrus is 60 ± 15 days, while the gestational diestrus lasts for 63 ± 1 days. The levels of progesterone are already high at the diestrus onset; the peak is maintained for almost half the stage and gradually decreases by the end of this stage; the progesterone decline is more abrupt in gestational cycles than in nonpregnant ones [6, 8].

In anestrus, the sex steroids are maintained in basal values, except in the last third of the stage, when the initial development of a wave of follicles in the ovaries occurs, thereby inducing a small increase in estrogens [13, 14]. Although this stage is often considered a time of reproductive quiescence, in fact in the uterus an important remodeling and repairing of the endometrium occurs, which is of upmost importance to the bitch fertility [13]. The length of this stage is the most variable in dogs, despite the reported average length of 18–20 weeks. The minimum length of anestrus is 7 weeks after the progesterone drop, but it can reach up to 10 months [6, 7]. It is important to remember, however, that the duration of the anestrus may be modulated by external environmental factors. An anestrous bitch can be stimulated to resume proestrus when in close proximity to a bitch in estrus [7]. This in fact contributes to the synchronization of estrous cycles often observed when bitches are housed together.

3. Nonsurgical contraceptive options

Lately, in most developed countries, a variety of possible contraceptive methods became available. Thus, allowing the owner of a female dog or the practitioner to adopt the plan that best suits a particular individual or situation, by weighting the owner's aims for treatment, the physiological condition of the bitch and the expected side effects of the selected method. However, in a significant number of countries, progestins may remain the option of choice, mainly due to economic constraints.

The target population or individual is an important parameter, along with the requested period of estrus suppression. The categories of dogs (owned dogs vs. community owned or ownerless, free-roaming dogs) [15] often dictate the selection, effectiveness, and feasibility of the contraceptive method, because they determine the regularity of the drug administration, the easiness of administration and the ability to survey the animal during treatment. Therefore, temporary contraception is most suitable for privately owned dogs, while for community owned or ownerless dogs, sterilization (surgical or chemical) remains the best decision.

Below the available therapeutic options for contraception of individual bitches will be discussed.
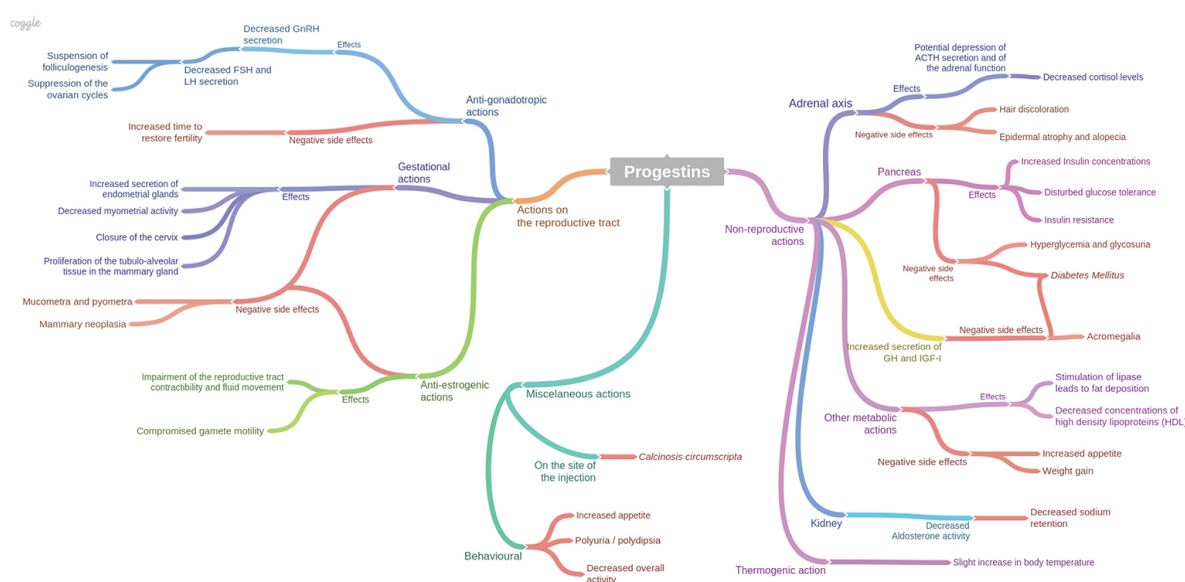
3.1. Progestins

Progestins (synthetic progesterone-like compounds, also known as progestogens) remained for long time the unique available medical contraceptive option in dogs. Intended for a short-term estrus suspension or postponement, chronic treatments longer than 2 years usually increase the negative effects that these drugs exert over the endocrine axis and the reproductive tract of the bitch.

Progestins are widely used, although these substances present major detrimental side effects in dogs, whose sensitivity to prolonged progesterone is high and predispose to uterine and mammary diseases [16]. This is a major drawback for the progestins use, particularly in chronic administration protocols or whenever the administration timing and doses are not followed adequately.

Progestins place the female under a prolonged artificial luteal stage. A constant supply of progestins causes the gonadotropin-releasing hormone (GnRH) down-regulation, which in turn depress the follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion, therefore suspending the follicular development in the ovaries. Also, progestins change the viscosity of the tubal and uterine secretions, and reduce the motility in the reproductive tract, compromising the transport of gametes and eggs and ruining the receptivity for a potential embryo [17]. Progestin actions are directly related to their side effects, as summarized in **Figure 2**.

The importance of the reactions to progestins administration increases the risk for a disease. This risk vary with: (1) the drug, its dose, the via of administration, and the frequency/length of the treatment; (2) the stage of the estrous cycle at the onset of treatment; and (3) some individual variations in sensitivity to the progestins that may be related to the age of the female (females older than 5 years are poor candidates for progestin treatment), existing pathologies or predispositions. Therefore, before starting any progestin treatment, the female should be subjected a thorough clinical examination. A careful and detailed anamnesis will allow to ascertain whether the female is postpubertal and in anestrus, whether the female is intended to breed within a 2-years period or eventually to understand if the owner will discontinue the treatment after a period of 18–24 months of progestin administration [4, 18] and willing to allow a full-term pregnancy to minimize the deleterious effects of progestins.

Figure 2. Summary of the main actions of progestins and the corresponding detrimental side effects in dogs.

The physical and reproductive examination will allow excluding pregnancy and obesity or any clinical evidence of hepatic, uterine, mammary, or metabolic disease, which might be exacerbated by the progestin treatment [17]. A female that is already in the proestrus stage is also a poor candidate for a progestin treatment, despite that these drugs might be (exceptionally) administered in the first day of heat [18]. The onset of treatment at the beginning of the follicular stage will increase the risks of pyometra [17] or mammary diseases.

There are several available progestins in the veterinary market, resulting from the research for less harmful products for dogs. However, the progestogen formulations approved for dogs may vary with the country. According to the chemical composition, progestins present different antigonadotrophic, gestagenic, and antiestrogenic properties that also define different risk potential. Older drugs (for instance, medroxyprogesterone acetate or megestrol acetate) usually possess stronger gestagenic actions and therefore more powerful negative side effects on the uterus and mammary glands than recent generation products, like proligestone.

In general, the particularities of the canine estrous cycle demand a different schedule for administration of oral progestins aiming the suspension of heat or the suppression of the estrous cycle. Thereby, in this species, the administration of progestins is more frequent as an injectable formula. However, it is important to know the length of the interestrous interval of a particular bitch and to adjust the subcutaneous administration of sequential progestins to avoid the breakdown effect (i.e., failure to control the cycle and by consequence the bitch enters in heat during the interval between administrations). Moreover, it should also be important to adjust the dose to the actual body weight, particularly in females of large and giant breeds.

Progestins available in the market for dogs include:

- **Medroxyprogesterone acetate** (MPA) — one of the first progestins used in dogs, it possesses high-antigonadotrophic action and a high-gestagenic action [17, 19]. The veterinary formulation may present different names according to the country (i.e., Supprestral® or Perlutex®) and

often is marketed for both oral and intramuscular administration. However, in several countries, the human medicine injectable formulation is often used due to its reduced cost. However, the putative MPA negative side effects are high, particularly when the correct doses are not followed (2 mg/kg every 3–4 months or 3–5 mg/kg at 5–6 months interval, for a maximal of four repetitive administrations). Individual variations can be observed in the response to estrus suppression in some females. Consequently, its use should be avoided in valuable females [19]. Close monitoring of treated females is crucial for an early detection of MPA side effects.

- **Megestrol acetate** (MA)—a short-acting progestin that shows less negative side effects than MPA and therefore it is most commonly used for temporary estrus suppression [17, 19]. In dogs, MA is often used in oral presentations (such as Ovarid®/Ovaban® or Pilucalm®, although the name of the product may vary with the country), in a daily administration at the doses of 0.5 mg/kg, for 32 to a maximum of 40 days, starting 14–30 days before the expected heat. It may be repeated at 6 months of interval, for a total of two administration cycles.

- **Delmadinone** (DMA) and **Chlormadinone acetate** (CMA) —the two progestins with a limited spread in the global veterinary market, and as consequence, information on its application in dogs is scant. DMA and CMA are usually used as antitestosterone in male dogs for the treatment of behavioral or prostate problems. The available DMA (Tardak®) doses for dogs are 1–2 mg/kg, to be injected subcutaneously, every 6 months. All treatments should start in anestrus [20]. The dose for the CMA injectable formulation in dogs is 3 mg/kg, subcutaneously, to be administered 1 month before the expected heat and repeated in a 6 months of interval [21]. When treatments start in anestrus, the product is said to be safer than MPA or MA, although it presents a similar increase in body weight.

- **Proligestone** (PRG)—a new generation progestin, possesses higher antigonadotrophic action but feebler gestational and antiestrogenic effects in comparison to MPA and MA [4, 19]. Therefore, it presents a lower incidence of mammary or uterine disease, compared to the other progestins. PRG (Delvosteron®/Covinan®, Intervet) is recommended at a dose of 10–33 mg/kg, starting 2 weeks before the expected season. The second administration should be repeated after 3 months, and afterwards at a 5-month interval. PRG is considered a safer drug than older progestins and reported to have minimal side effects [4, 19].

3.2. Androgens

Natural or synthetic androgens, like progestins, induce a down-regulation of the hypothalamus-pituitary-gonadal function. Thus, they can be used for heat suppression. Androgens were often used in racing Greyhounds to avoid estrus in training or racing females [22]. The anabolic side effects and the virilisation (clitoral hypertrophy and anal gland inspissation) associated with androgen administration [2, 20] were tolerated in Greyhounds, but may raise ethical concerns in the practice. Additional side effects described for androgen contraceptive treatments include vaginitis and urinary incontinence [18]. However, a major concern on the use of androgens for contraception was related to the induction of a rather prolonged anestrus (ranging between 1 and 2 years) [20]. Thereby their use would compromise the use of such

females for breeding after the interruption of treatment and dismissal from the racetrack [22]. Anyway, these drawbacks compromised the use of androgens in current clinical practice [7].

Few studies exist on the use of androgens as estrus suppressor in dogs. The oral administration of androgens is described for methyl testosterone (25 mg/dog, once a week [2]), orandrone (0.5 mg/kg, daily [20]), methyl testosterone associated with ethinylestradiol (7 mg/kg, daily, for 5–10 days.[20]), and mibolerone, a synthetic weak androgen (Cheque Drops, at a dose of 30–180 mcg/day, starting 30 days before the onset of heat; it should not be administered for more than 2 years [7]). Injectable androgen therapeutic options include the intramuscular administration of testosterone cypionate (1 mg/kg, every 2 weeks [22]), testosterone phenylpropionate (110 mg/dog, weekly or alternatively at 0.5–1 mg/kg, every 7–10 days [2] and [20], respectively) or a composition of four different testosterone esters (Durateston®, at a dose of 2.5–5 mg/kg every 6 months [20]).

3.3. GnRH agonists

The GnRH agonists are intended to suppress the pulsatility of GnRH and indirectly that of LH and FSH [23]; consequently, these compounds depress the follicular activity in the ovaries and reduce to baseline the secretion of sexual steroids. Shortly, they reset the bitch into a prepubertal stage or in anestrus. By suppressing the secretion of progesterone, these substances will minimize the risk for uterine or mammary diseases found in the progestins contraception. Furthermore, they are beneficial in controlling unwelcome sexual behavior associated with the female season and animal aggressiveness. However, these products are usually expensive, which limits their wider utilization and reduces their competitiveness compared to progestins.

The available commercial products include azagly-nafarelin implant (Gonazon®), deslorelin acetate implants (Suprelorin® or Ovuplant®), and leuprolide acetate implant (Lupron Depot®), although the application of buserelin (50 μg, single administration) may also accomplish the GnRH downregulation. However, the length of the induced anestrus is less precise and the individual variation in the response is higher.

GnRH agonists are presented today as a subcutaneous implant, allowing a prolonged controlled release of the drug into the system. Implants are injected subcutaneously at the interscapular or the postumbilical area [24]. This sustained exposition to the GnRH agonist would override the endogenous secretion of this hormone. The agonist acts at the level of the GnRH receptors [23], inducing the receptor downregulation, internalization and signal uncoupling [4], resulting in the termination of the signaling cascade triggered GnRH in cells. However, GnRH agonists act in a dual phase mechanism. Before acting as described before, the first effect of implants is to stimulate the pituitary axis ("flare-up" effect), triggering an initial release of FSH and LH [25], thus shortly originating a new season in treated bitches. The "flare-up" effect is usually observed within 1 month after the insertion of the implant [26]. This is, to date, the most significant drawback identified for the use of GnRH agonists in dog contraception: to first induce estrus before preventing it [27].

The flare-up effect is more frequent when treatment starts in late anestrus [28, 29], compared to any other stage of the canine cycle. Whether or not it may be decreased when the female is implanted in diestrus or given exogenous progestogen [30–32] is still controversial [33, 34].

Additional adverse side effects reported following the insertion of GnRH agonist implants include persistent estrus associated with the formation of ovarian cysts due to anovulation [35], galactorrhoea, metropathies, vomiting, cystitis, and allergic reactions [36]. These effects occur with variable incidence suggesting the existence of individual idiosyncratic factors. These may also comprise preexisting problems that remained clinically undiagnosed. Consequently, before injection of the implant, the female should be subjected to a thorough clinical and reproductive examination to exclude any ovarian and uterine pathology [24].

GnRH agonists can be used as short or long-term contraceptives in domestic carnivores [37, 38] and may be applied in prepubertal females to postpone the reproductive activity without apparent side effects to delay puberty [39, 40]. The effect of the implants may be fully reverted and fertility regained after the 12-month period of the implant action [23, 41]. However, in some cases, the implant effect can last up to 27 months [23, 32]. An anticipated removal of the implant would also permit the withdrawn of the effects over the hypothalamic-pituitary axis, and regain cyclicity earlier. Recently, it has stretched that Superlorin® presented no detrimental effects on the bitch fertility whether a short-term or the long-term treatment was implemented [24].

Figure 3 provides a summary analysis to GnRH agonists as contraceptives in dogs.
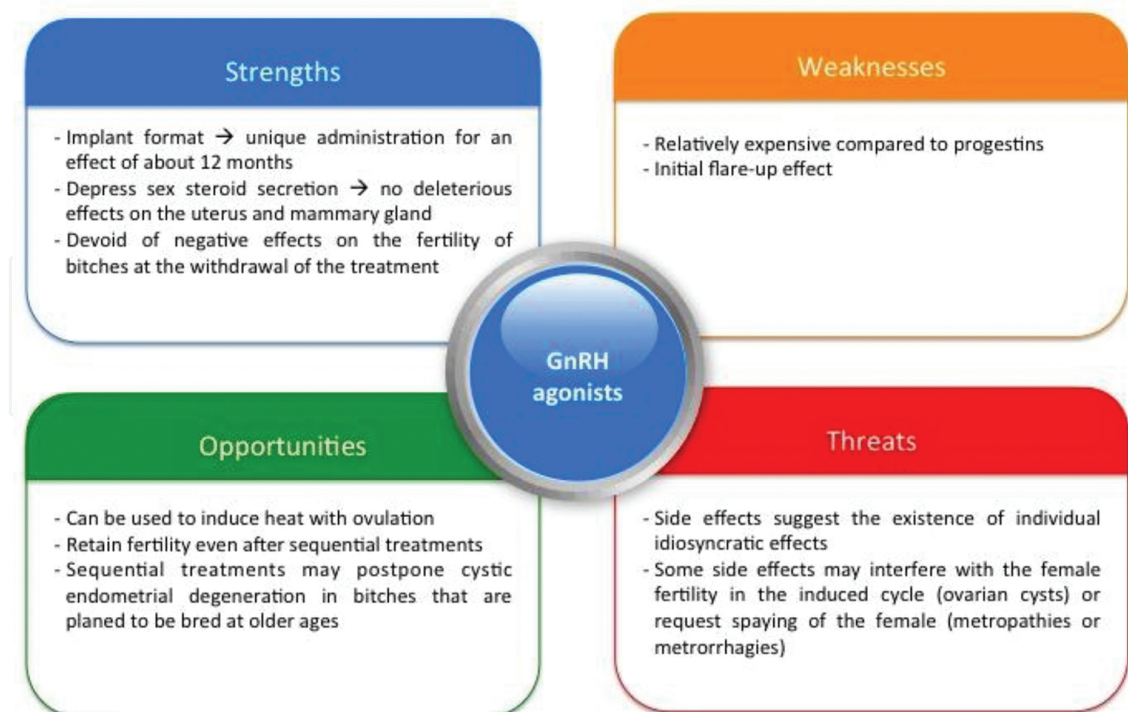
Figure 3. SWOT analysis to the use of GnRH agonists to control the bitch reproduction.

3.4. GnRH antagonists

The GnRH antagonists limit its action by a competitive block of the hormone receptors achieving the annulation of the effects of circulating GnRH. Consequently, the function of the hypothalamus-pituitary-gonadal axis is impaired. Long-term effects of GnRH antagonists also include the down-regulation of the GnRH receptors [4, 42]. Either way, follicular waves are suppressed and ovulation is compromised [19]. Several generations of peptides with GnRH antagonist activity have been tested in dogs, but their use is still limited all over the world, mainly because they present a rather low efficiency as contraceptives. Also, the first generation compounds showed several important side effects, derived from the need for higher doses of these peptides to reach the desired effect. Peptide GnRH antagonists act only for short-term estrus suppression [19, 43], which make them a poor agent when longer periods of contraception are foreseen. Therefore, its use is mostly restricted to the short-term contraception in show or work dogs [19].
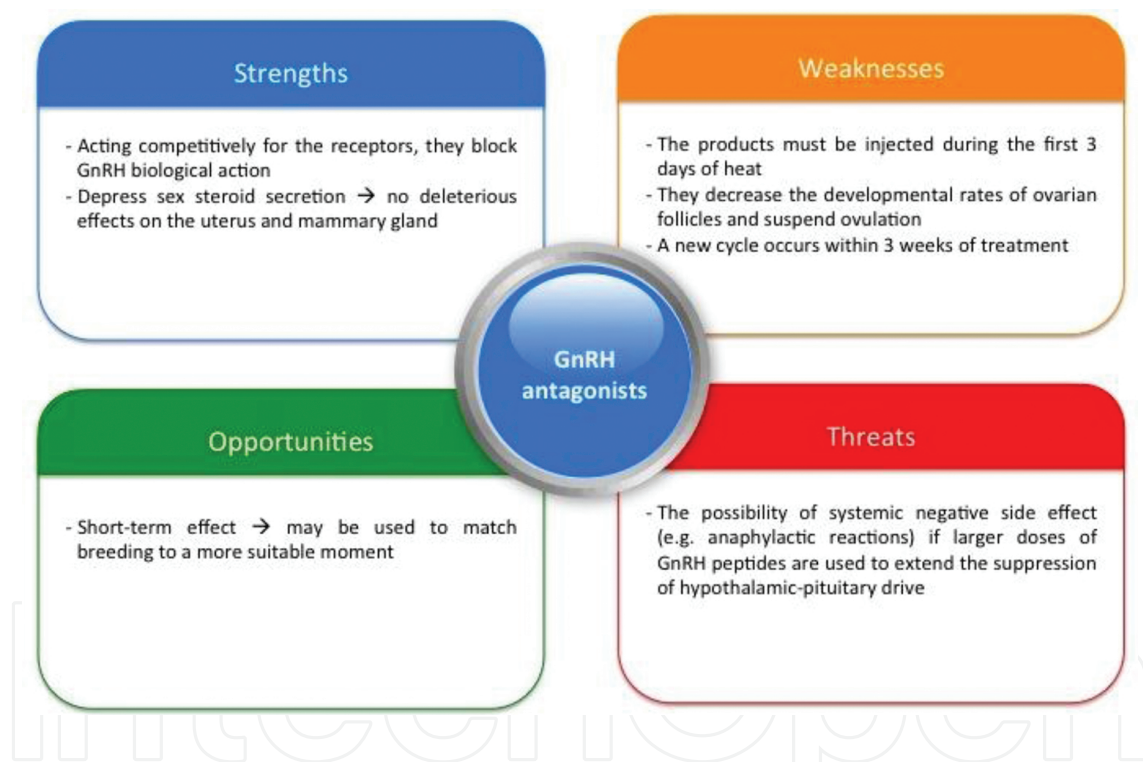

Strengths
- Acting competitively for the receptors, they block GnRH biological action
- Depress sex steroid secretion → no deleterious effects on the uterus and mammary gland

Weaknesses
- The products must be injected during the first 3 days of heat
- They decrease the developmental rates of ovarian follicles and suspend ovulation
- A new cycle occurs within 3 weeks of treatment

GnRH antagonists

Opportunities
- Short-term effect → may be used to match breeding to a more suitable moment

Threats
- The possibility of systemic negative side effect (e.g. anaphylactic reactions) if larger doses of GnRH peptides are used to extend the suppression of hypothalamic-pituitary drive

Figure 4. SWOT analysis to the use of GnRH antagonists as a contraceptive in dogs.

In dogs, the third generation GnRH antagonist, Acylin®, is the most used antagonist. It should be administered within the first 3 days of proestrus, subcutaneously, at a dose of 100 μg/kg. Suspension of the follicular stage is obtained, and ovulation inhibited; however, the bitch is expected to enter a new cycle within 3 weeks of treatment [4].

Companies are now exploiting some nonpeptide molecules as GnRH antagonists, alike those tested for humans, aiming to obtain the long-term release formulations that may be applied for the long-term contraception. However, to our best knowledge, no information is yet available on these molecules.

Figure 4 provides a summary analysis to the use of GnRH antagonists as contraceptives in dogs.

3.5. Immunocontraception

Immunocontraception is yearned for long estrus control, either for owned and free-roaming dogs. Classical targets in immunocontraception include the GnRH and LH along with their corresponding receptors, as well as the sperm or *Zona pellucida* (ZP) proteins [4, 44]. Vaccines are usually conjugated with various antigens to enhance the immune response against the target compound(s). Contraception would be maintained through regular boosting [45]. Either approach shows unsatisfactory results till present [4]. Particularly, the resumption of estrous cycles or fertility after withdrawal of the treatment is still a concern.

The use of vaccines targeting GnRH will induce suppression of the estrous cycle, while vaccines against LH will interfere with ovulation because the preovulatory LH-surge is suppressed, and progesterone secretion is also compromised. Depending on the vaccine used, the cycle may be suspended for periods ranging from 5 months to 5 years with a single administration. On the other hand, vaccines targeting sperm or *Zona pellucida* proteins will not disturb the normal estrous cycle of the female dog, but will inhibit egg-perm binding in the female genital tract and fertilization [15]. *Zona pellucida* vaccines do not succeed to induce infertility in dogs [4, 15].

GonaCon™ is a vaccine against GnRH. It was developed to control the reproduction in the wildlife population, in which infertility was achieved for a period of 1–4 years with a single vaccination [46]. However, its use in dogs is still controversial, as it seems that dogs present intense reactions at the site of injection, with formation of long-lasting abscesses and granulomas, due to a greater sensitivity to the adjuvant used in the vaccine. Also, there is no available data on the duration of estrus suppression [15]. Recently, in Mexico, a new formulation of GonaCon (with the adjuvant AdjuVac™) was tested in shelter dogs during a campaign for rabies and control of canine reproduction [47]. According to the data reported, the proportion of animals presenting abscesses at day 60 was lower than the expected from previous studies using different vaccine adjuvants, but it was still not devoid of other local side effects (like muscular atrophy) [47].

Another study, using an unidentified commercial vaccine against GnRH, administered twice at a 4-week interval, however, reported that none of the four animals used showed adverse reactions to vaccination, remaining clinically healthy for the length of the study (20 weeks) [48]. That study also showed that the reduction in LH and testosterone as well as in the size of the gonads started by week 4 and it was maximal by week 12. However, at week 20 the parameters were similar to those recorded at week 4, suggesting that the vaccine effects were reverting. However, the length of the study [48] does not confirm this hypothesis or establish the schedule for revaccination.

Figure 5 summarizes the analysis to the application of antiGnRH vaccines as contraceptives in dogs.

Strengths
- Different forms of action and outcomes would allow different applications
- Vaccines directed against GnRH are currently in test for dogs sterilization and contraception

Weaknesses
- The need for vaccination boosting is required for long-term contraception
- No available data on the length of infertility obtained, nor on the boosting interval
- No information on fertility regaining after suspension of treatment

Immune contraception

Opportunities
- Ideally, sterility obtained with one vaccination, devoid of side effects would be most suitable for control of spray dog populations

Threats
- Side effects at the place of injection with the first generation products include formation of long-lasting abscesses and granuloma

Figure 5. SWOT analysis to the use of antiGnRH vaccines as a contraceptive in dogs.

Immunocontraception holds great promise for canine contraception; still, several drawbacks need to be overcome before being widely introduced into the veterinary practice. The need for regular revaccination may not be an issue in owned dogs but important questions needing answers respect the maintenance of fertility and the time to fertility restoration at the withdrawal of the treatment.

4. Final comments

In this chapter, we have discussed that different methods are available for contraception in domestic dogs. Each one has its own advantages and disadvantages, which should be taken into consideration when discussing with the owner the best therapeutic option available for a particular bitch. When selecting the contraceptive treatment(s) to discuss with the owner, it is important to establish the purpose for the treatment (short- or long-term treatments vs. sterilization), the schedule of drug administration and the costs of the therapeutics, as well as the expected length of treatment and the objectives for the female fertility at the end of the treatment. It is also important to ascertain the dog category (ownerless or community vs. owned dog), the compliance of the owner with the schedule and its expectations toward the meaning of "chemical spaying." And, most of all, it is important to be confident that the selected treatment is adequate to the age of female and neither compromise an existing, undiagnosed, pregnancy, nor trigger or aggravate an existing disease.

Nowadays, safer and healthier alternatives to progestins are already available for medical contraception in dogs that are intended to be breed later in their lives. Major drawbacks for the use of progestins include their deleterious effects on the uterus and mammary gland and the possibility of fertility loss after chronic treatments. Bitches over the age of 5 years are poor candidates for progestin treatments. Good alternatives already exist, and should be recommended whenever the costs of the drug do not impose constraints. Most products can be applied independently of the age of the female and are devoid of side effects on the uterus or the mammary gland.

The identification of new safer methods for nonsurgical contraception in dogs, manufactured at a desirable scale to be provided at affordable rates and needing fewer applications (particularly for permanent and the long-term contraception) is still a challenge to the industry. Active research and increased knowledge in this field promises to change the paradigm of canine contraception in the future.

Acknowledgements

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